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TOXICOLOGICAL PROFILE FOR PHENOL

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Agency for Toxic Substances and Disease Registry

December 1998

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The use of company or product name(s) is for identification only and does not imply endorsement by the Agency for Toxic Substances and Disease Registry.

UPDATE STATEMENT

A Toxicological Profile for phenol was released in September 1997. This edition supersedes any previously released draft or final profile.

Toxicological profiles are revised and republished as necessary, but no less than once every three years. For information regarding the update status of previously released profiles, contact ATSDR at:

Agency for Toxic Substances and Disease Registry
Division of Toxicology/Toxicology Information Branch
1600 Clifton Road NE, E-29
Atlanta, Georgia 30333

FOREWORD

This toxicological profile is prepared in accordance with guidelines* developed by the Agency for Toxic Substances and Disease Registry (ATSDR) and the Environmental Protection Agency (EPA). The original guidelines were published in the *Federal Register* on April 17, 1987. Each profile will be revised and republished as necessary.

The ATSDR toxicological profile succinctly characterizes the toxicologic and adverse health effects information for the hazardous substance described therein. Each peer-reviewed profile identifies and reviews the key literature that describes a hazardous substance's toxicologic properties. Other pertinent literature is also presented, but is described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

The focus of the profiles is on health and toxicologic information; therefore, each toxicological profile begins with a public health statement that describes, in nontechnical language, a substance's relevant toxicological properties. Following the public health statement is information concerning levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Data needs that are of significance to protection of public health are identified by ATSDR and EPA.

Each profile includes the following:

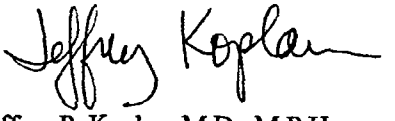
(A) The examination, summary, and interpretation of available toxicologic information and epidemiologic evaluations on a hazardous substance to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects;

(B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure that present a significant risk to human health of acute, subacute, and chronic health effects; and

(C) Where appropriate, identification of toxicologic testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

The principal audiences for the toxicological profiles are health professionals at the Federal, State, and local levels; interested private sector organizations and groups; and members of the public.

This profile reflects ATSDR's assessment of all relevant toxicologic testing and information that has been peer-reviewed. Staff of the Centers for Disease Control and Prevention and other Federal scientists have also reviewed the profile. In addition, this profile has been peer-reviewed by a nongovernmental panel and was made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.



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*Legislative Background

The toxicological profiles are developed in response to the Superfund Amendments and Reauthorization Act (SARA) of 1986 (Public Law 99-499) which amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law directed ATSDR to prepare toxicological profiles for hazardous substances most commonly found at facilities on the CERCLA National Priorities List and that pose the most significant potential threat to human health, as determined by ATSDR and the EPA. The availability of the revised priority list of 275 hazardous substances was announced in the *Federal Register* on November 17, 1997 (62 FR 61332). For prior versions of the list of substances, see *Federal Register* notices dated April 29, 1996 (61 FR 18744); April 17, 1987 (52 FR 12866); October 20, 1988 (53 FR 41280); October 26, 1989 (54 FR 43619); October 17,1990 (55 FR 42067); October 17, 1991 (56 FR 52166); October 28, 1992 (57 FR 48801); and February 28, 1994 (59 FR 9486). Section 104(i)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list.

QUICK REFERENCE FOR HEALTH CARE PROVIDERS

Toxicological Profiles are a unique compilation of toxicological information on a given hazardous substance. Each profile reflects a comprehensive and extensive evaluation, summary, and interpretation of available toxicologic and epidemiologic information on a substance. Health care providers treating patients potentially exposed to hazardous substances will find the following information helpful for fast answers to often-asked questions.

Primary Chapters/Sections of Interest

Chapter 1: Public Health Statement: The Public Health Statement can be a useful tool for educating patients about possible exposure to a hazardous substance. It explains a substance's relevant toxicologic properties in a nontechnical, question-and-answer format, and it includes a review of the general health effects observed following exposure.

Chapter 2: Health Effects: Specific health effects of a given hazardous compound are reported by *route of exposure*, by *type of health effect* (death, systemic, immunologic, reproductive), and by *length of exposure* (acute, intermediate, and chronic). In addition, both human and animal studies are reported in this section.

NOTE: Not all health effects reported in this section are necessarily observed in the clinical setting. Please refer to the Public Health Statement to identify general health effects observed following exposure.

Pediatrics: Four new sections have been added to each Toxicological Profile to address child health issues:

Section 1.6 How Can (Chemical X) Affect Children?
Section 1.7 How Can Families Reduce the Risk of Exposure to (Chemical X)?
Section 2.6 Children's Susceptibility
Section 5.6 Exposures of Children

Other Sections of Interest:

Section 2.7 Biomarkers of Exposure and Effect
Section 2.10 Methods for Reducing Toxic Effects

ATSDR Information Center

Phone: 1-800-447-1544 (to be replaced by 1-888-42-ATSDR in 1999)
or 404-639-6357 ***Fax:*** 404-639-6359
E-mail: atsdric@cdc.gov ***Internet:*** http://atsdr1.atsdr.cdc.gov:8080

The following additional material can be ordered through the ATSDR Information Center:

Case Studies in Environmental Medicine: Taking an Exposure History—The importance of taking an exposure history and how to conduct one are described, and an example of a thorough exposure history is provided. Other case studies of interest include *Reproductive and Developmental Hazards; Skin Lesions and Environmental Exposures; Cholinesterase-Inhibiting Pesticide Toxicity;* and numerous chemical-specific case studies.

Managing Hazardous Materials Incidents is a three-volume set of recommendations for on-scene (prehospital) and hospital medical management of patients exposed during a hazardous materials incident. Volumes I and II are planning guides to assist first responders and hospital emergency department personnel in planning for incidents that involve hazardous materials. Volume III—*Medical Management Guidelines for Acute Chemical Exposures*—is a guide for health care professionals treating patients exposed to hazardous materials.

Fact Sheets (ToxFAQs) provide answers to frequently asked questions about toxic substances.

Other Agencies and Organizations

The National Center for Environmental Health (NCEH) focuses on preventing or controlling disease, injury, and disability related to the interactions between people and their environment outside the workplace. *Contact:* NCEH, Mailstop F-29, 4770 Buford Highway, NE, Atlanta, GA 30341-3724 • Phone: 770-488-7000 • FAX: 770-488-7015.

The National Institute for Occupational Safety and Health (NIOSH) conducts research on occupational diseases and injuries, responds to requests for assistance by investigating problems of health and safety in the workplace, recommends standards to the Occupational Safety and Health Administration (OSHA) and the Mine Safety and Health Administration (MSHA), and trains professionals in occupational safety and health. *Contact:* NIOSH, 200 Independence Avenue, SW, Washington, DC 20201 • Phone: 800-356-4674 or NIOSH Technical Information Branch, Robert A. Taft Laboratory, Mailstop C-19, 4676 Columbia Parkway, Cincinnati, OH 45226-1998 • Phone: 800-35-NIOSH.

The National Institute of Environmental Health Sciences (NIEHS) is the principal federal agency for biomedical research on the effects of chemical, physical, and biologic environmental agents on human health and well-being. *Contact:* NIEHS, PO Box 12233, 104 T.W. Alexander Drive, Research Triangle Park, NC 27709 • Phone: 919-541-3212.

Referrals

The Association of Occupational and Environmental Clinics (AOEC) has developed a network of clinics in the United States to provide expertise in occupational and environmental issues. *Contact:* AOEC, 1010 Vermont Avenue, NW, #513, Washington, DC 20005 • Phone: 202-347-4976 • FAX: 202-347-4950 • e-mail: aoec@dgs.dgsys.com • AOEC Clinic Director: http://occ-env-med.mc.duke.edu/oem/aoec.htm.

The American College of Occupational and Environmental Medicine (ACOEM) is an association of physicians and other health care providers specializing in the field of occupational and environmental medicine. *Contact:* ACOEM, 55 West Seegers Road, Arlington Heights, IL 60005 • Phone: 847-228-6850 • FAX: 847-228-1856.

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THE PROFILE HAS UNDERGONE THE FOLLOWING ATSDR INTERNAL REVIEWS:

1. Health Effects Review. The Health Effects Review Committee examines the health effects chapter of each profile for consistency and accuracy in interpreting health effects and classifying end points.

2. Minimal Risk Level Review. The Minimal Risk Level Workgroup considers issues relevant to substance-specific minimal risk levels (MRLs), reviews the health effects database of each profile, and makes recommendations for derivation of MRLs.

3. Data Needs Review. The Research Implementation Branch reviews data needs sections to assure consistency across profiles and adherence to instructions in the Guidance.

PEER REVIEW

A peer review panel was assembled for phenol. The panel consisted of the following members:

1. Dr. Dietrich Hoffmann, Associate Director, Division of Environmental Carcinogenesis, American Health Foundation, Valhalla, NY.

2. Mr. Bruce Jacobs, Principal Consultant, Jacobs Environmental, Inc., Abingdon, MD.

3. Dr. Loren Koller, Dean and Professor, College of Veterinary Medicine, Oregon State University, Corvallis, OR.

These experts collectively have knowledge of phenol's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in Section 104(I)(13) of the Comprehensive Environmental Response, Compensation, and Liability Act, as amended.

Scientists from the Agency for Toxic Substances and Disease Registry (ATSDR) have reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply its approval of the profile's final content. The responsibility for the content of this profile lies with the ATSDR.

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1. PUBLIC HEALTH STATEMENT

This public health statement tells you about phenol and the effects of exposure.

The Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. These sites make up the National Priorities List (NPL) and are the sites targeted for long-term federal cleanup. Phenol has been found in at least 481 of the 1,467 current or former NPL sites. However, it's unknown how many NPL sites have been evaluated for this substance. As more sites are evaluated, the sites with phenol may increase. This is important because exposure to this substance may harm you and because these sites may be sources of exposure.

When a substance is released from a large area, such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment. This release does not always lead to exposure. You are exposed to a substance only when you come in contact with it. You may be exposed by breathing, eating, or drinking the substance or by skin contact.

If you are exposed to phenol, many factors determine whether you'll be harmed. These factors include the dose (how much), the duration (how long), and how you come in contact with it. You must also consider the other chemicals you're exposed to and your age, sex, diet, family traits, lifestyle, and state of health.

1.1 WHAT IS PHENOL?

Phenol is a colorless-to-white solid when pure; however, the commercial product, which contains some water, is a liquid. Phenol has a distinct odor that is sickeningly sweet and tarry. Most people begin to smell phenol in air at about 40 parts of phenol per billion parts of air (ppb), and begin to smell phenol in water at about 1-8 parts of phenol per million parts of water (ppm; 1 ppm is 1,000 times more than 1 ppb). These levels are lower than the levels at which adverse health effects have been observed in animals that breathed air containing phenol, or that drank

water containing phenol. Phenol evaporates more slowly than water, and a moderate amount can form a solution with water. Phenol can catch on fire.

Phenol is both a man-made chemical and produced naturally. It is found in nature in some foods and in human and animal wastes and decomposing organic material The largest single use of phenol is as an intermediate in the production of phenolic resins. However, it is also used in the production of caprolactam (which is used in the manufacture of nylon 6 and other synthetic fibers) and bisphenol A (which is used in the manufacture of epoxy and other resins). Phenol is also used as a slimicide (a chemical toxic to bacteria and fungi characteristic of aqueous slimes), as a disinfectant, and in medicinal preparations such as over-the-counter treatments for sore throats. Phenol ranks in the top 50 in production volumes for chemicals produced in the United States. Chapters 3 and 4 contain more information.

1.2 WHAT HAPPENS TO PHENOL WHEN IT ENTERS THE ENVIRONMENT?

Following small, single releases, phenol is rapidly removed from the air; generally, half is removed in less than 1 day. It is also relatively short-lived in the soil (generally, complete removal in 2-5 days). However, it can remain in water week or more. Phenol can remain in the air, soil, and water for much longer periods of time if a large amount of it is released at one time, or if it is constantly released to the environment. Levels of phenol above those found naturally in the environment are usually found in surface waters and surrounding air contaminated by phenol released from industrial activity and from the commercial use of products containing phenol. Phenol has been detected, however, in the materials released from landfills and hazardous waste sites, and it has been found in the groundwater near these sites. The levels of phenol found in indoor environments as a part of environmental tobacco smoke (ETS) are usually below 100 ppb, although much higher levels have been reported. One ppb or less of phenol has been found in relatively unpolluted surface water and groundwater, and low levels are also found in indoor environments and are principally derived from ETS. Only low levels of phenol are found in the organisms that live in water which also contains low levels of phenol. Chapters 4 and 5 contain more information.

1. PUBLIC HEALTH STATEMENT

1.3 HOW MIGHT I BE EXPOSED TO PHENOL?

Since phenol is used in many manufacturing processes and in many products, as well as being naturally produced, exposure may take place where you work or at home. Phenol is present in a number of consumer products which are swallowed, rubbed on, or added to various parts of the body. These include ointments, ear and nose drops, cold sore lotions, mouthwashes, gargles, toothache drops, analgesic rubs, throat lozenges, and antiseptic lotions. Phenol has been found in drinking water, tobacco smoke, air, and certain foods, including smoked summer sausage, fried chicken, mountain cheese, and some species of fish. It is also found in urine of children and adults.

The magnitude, frequency, and likelihood of exposure, and the relative contribution of each exposure route and source to total phenol exposure cannot be estimated using information currently available. Nonetheless, for persons not exposed to phenol in the workplace, possible routes of exposure include: breathing industrially contaminated air; inhaling cigarette, cigar, or pipe smoke, or ETS polluted air; drinking water from contaminated surface water or groundwater supplies; swallowing products containing phenol; changing diapers; and coming into contact with contaminated water and products containing phenol through bathing or skin application. Populations residing near phenol spills, waste disposal sites, or landfill sites may be at risk for higher exposure to phenol than other populations. If phenol is present at a waste site near homes that have wells as a source of water, it is possible that the well water could be contaminated. If phenol is spilled at a waste site, it is possible for a person, such as a child playing in dirt containing phenol, to have skin contact or to swallow soil or water contaminated with phenol. Skin contact with phenol or swallowing products containing phenol may lead to increased exposure. This type of exposure is expected to occur infrequently and generally occurs over a short time period.

At the workplace, exposure to phenol can occur from breathing contaminated air. However, skin contact with phenol during its manufacture and use is considered the major route of exposure in the workplace. It has been estimated that about 584,000 people in the United States are exposed

to phenol at work. Total exposure at the workplace is potentially higher than in non-workplace settings. Chapter 5 contains more information on sources of exposure.

1.4 HOW CAN PHENOL ENTER AND LEAVE MY BODY?

Phenol can enter the body when a person drinks contaminated water or other liquids such as tea and coffee, eats contaminated food, or swallows products containing phenol. Phenol spilled on the skin easily penetrates the skin and enters the body. Phenol also enters the body through the lungs when a person breathes in air or inhales smoke from tobacco which contains phenol.

The amount of phenol that enters the body from skin contact with water containing phenol depends on the concentration of phenol in the water, the length of time of skin contact, and the amount of skin that makes contact with the contaminated water. Greater amounts of phenol will enter the body if large areas of skin come into contact with weaker solutions of phenol than if small areas of skin come into contact with the solutions of phenol. If a person is exposed to air containing phenol, phenol can enter the body through the skin and lungs. It has been determined that entry through the skin can account for as much as one-half of the phenol that enters the body when a person is exposed to phenol in air. Although it is possible for a person to be exposed to air contaminated with phenol at a waste site, such an exposure is not likely because spilled phenol will mostly remain in soil or water rather than evaporate into air. If a person swallows phenol, the intestines will change much of it to a less harmful substance. If phenol enters through the skin, it may reach organs and cause adverse effects before it is changed into a less harmful substance.

Studies in humans and animals indicate that most of the phenol that enters the body through skin contact, breathing contaminated air, eating food or drinking water, or using products containing phenol, leaves the body in the urine within 24 hours. Chapter 2 contains additional information about how phenol enters and leaves the body.

1. PUBLIC HEALTH STATEMENT

It is also clear that phenol is produced by the body and excreted independent of external exposure to the compound. The normal range of phenol in the urine of unexposed individuals is 0.5-80 milligrams of phenol per liter of urine (mg/L).

1.5 HOW CAN PHENOL AFFECT MY HEALTH?

To protect the public from the harmful effects of toxic chemicals and to find ways to treat people who have been harmed, scientists use many tests.

One way to see if a chemical will hurt people is to learn how the chemical is absorbed, used, and released by the body; for some chemicals, animal testing may be necessary. Animal testing may also be used to identify health effects such as cancer or birth defects. Without laboratory animals, scientists would lose a basic method to get information needed to make wise decisions to protect public health. Scientists have the responsibility to treat research animals with care and compassion. Laws today protect the welfare of research animals, and scientists must comply with strict animal care guidelines.

A number of effects from breathing phenol in air have been reported in humans. Short-term effects reported include respiratory irritation, headaches, and burning eyes. Chronic effects of high exposures included weakness, muscle pain, anorexia, weight loss, and fatigue; effects of chronic low-level exposures included increases in respiratory cancer, heart disease, and effects on the immune system. Virtually all of the workplace exposures associated with these effects involved exposures to other chemicals, thus it is difficult to determine whether these are solely due to phenol, or are the result of mixed, multiple, or other chemical exposures.

In animals, exposure to high concentrations of phenol in air for a few minutes irritates the lungs, and repeated exposure for several days produces muscle tremors and loss of coordination. Exposure to high concentrations of phenol for several weeks results in paralysis and severe injury to the heart, kidneys, liver, and lungs, followed by death in some cases. When exposures involve

1. PUBLIC HEALTH STATEMENT

the skin surface, the size of the total surface area of exposed skin can influence the severity of the toxic effects.

The seriousness of the effect of a harmful substance can be expected to increase as both the level and duration of exposure increase. Repeated exposure to low levels of phenol in drinking water has been associated with diarrhea and mouth sores in humans Ingestion of very high concentrations of phenol has resulted in death. In animals, drinking water with extremely high concentrations of phenol has caused muscle tremors and loss of coordination.

Effects reported in humans following dermal exposure to phenol include liver damage, diarrhea, dark urine, and red blood cell destruction. Skin exposure to a relatively small amount of concentrated phenol has resulted in the death of humans. Small amounts of phenol applied to the skin of animals for brief periods can produce blisters and burns on the exposed surface, and spilling dilute phenol solutions on large portions of the body (greater than 25% of the body surface) can result in death.

It is not known if phenol causes cancer in humans. However, cancer has been shown to occur in mice when phenol was applied to the skin several times each week during the whole lifetime of the animal. When it is applied in combination with certain cancer-causing chemicals, a higher rate of cancer occurs than when the carcinogens are applied alone. Phenol did not cause cancer in mice or rats when they drank water containing phenol for 2 years. The International Agency for Research on Cancer (IARC) considers phenol not classifiable as to its carcinogenicity in humans.

Phenol can have beneficial effects when used for medical reasons. It is an antiseptic (kills germs) when applied to the skin in small amounts and may have antiseptic properties when gargled as a mouthwash. It is an anesthetic (relieves pain) and is a component of certain sore-throat lozenges and throat sprays or gargles. Small amounts of phenol in water have been injected into nerve tissue to lessen pain associated with certain nerve disorders. Phenol destroys the outer layers of skin if allowed to remain in contact with skin, and small amounts of concentrated solutions of

phenol are sometimes applied to the skin to remove warts and to treat other skin blemishes and disorders.

Chapter 2 contains a more thorough discussion of the health effects of phenol.

1.6 HOW CAN PHENOL AFFECT CHILDREN?

This section discusses potential health effects from exposures during the period from conception to maturity at 18 years of age in humans Potential effects on children resulting from exposures of the parents are also considered.

The exposure of children to phenol is likely to occur by most of the same routes experienced by adults, the major exception being that children are unlikely to be exposed due to their parents' occupations. There is clear evidence, however, that at least with certain products, children are at greater risk of accidental ingestion than adults. In the case of one product, a disinfectant containing 26% phenol, children under the age of 5 represented 60 of 80 (75%) of the poisoning cases associated with this product reported to a major poison control center between 1987-1991.

In humans, the effects of exposure to phenol on reproduction and the developing fetus are unknown. Several studies have not shown phenol to be active in developmental toxicity. However, in others, pregnant animals that drank water containing high concentrations of phenol gave birth to offspring with low birth weights and minor birth defects. The implications of these findings for humans is unclear, although it seems likely that any adverse developmental effects would require much higher doses than would normally be encountered at hazardous waste sites.

It is unknown whether infants or children are more susceptible than adults to the adverse effects of phenol; as stated above, developmental studies are inconclusive. Most of the information available on the toxic effects of phenol in infants and children comes from the use of phenol in medical treatments. Phenol was once used as an antiseptic in wound dressing products and there are several reports of deaths in children and infants following overzealous application of such

products to burns or open wounds. All of these cases occurred decades ago, however, and there is little indication that such products, which contained relatively high levels of phenol, are still in use.

Other phenol-containing products are used as "chemical peels" to remove skin lesions, and in the treatment of chronic pain or spasticity. These uses have occasionally been associated with adverse outcomes, like cardiac arrhythmias, that have been seen in both adults and children. These effects do not appear to occur more frequently in children than adults; however, the information on such effects in children is very limited.

1.7 HOW CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO PHENOL?

If your doctor finds that you have been exposed to significant amounts of phenol, ask if children may also be exposed. When necessary your doctor may need to ask your State Department of Public Health to investigate.

Since ETS contains phenol, reducing the amount of smoking indoors will reduce phenol exposures. Household products and over-the-counter medications containing phenol should be stored out of reach of young children to prevent accidental poisonings and skin burns. Always store household chemicals in their original labeled containers. Never store household chemicals in containers that children would find attractive to eat or drink from, such as old soda bottles. Keep your Poison Control Center's number next to the phone.

1.8 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO PHENOL?

Urine can be tested for the presence of phenol. This test can be used to determine if the urine has a higher than normal concentration of phenol, thus suggesting recent exposure to phenol or to substances that are converted to phenol in the body (e.g., benzene). There is no test available that will tell if a person has been exposed only to phenol since many substances are converted to phenol in the body. Because most of the phenol that enters the body is excreted in the urine

within 24 hours, this test can only detect exposures that have occurred within 1 or 2 days prior to the test. The test results cannot be used to predict what health effects might result from exposure to phenol. Measurement of phenol in urine requires special laboratory equipment and techniques that are not routinely available in most hospitals or clinics. Chapters 2 and 6 contain more information on tests for exposure to phenol.

1.9 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

The federal government develops regulations and recommendations to protect public health. Regulations can be enforced by law. Federal agencies that develop regulations for toxic substances include the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), and the Food and Drug Administration (FDA). Recommendations provide valuable guidelines to protect public health but cannot be enforced by law. Federal organizations that develop recommendations for toxic substances include the Agency for Toxic Substances and Disease Registry (ATSDR) and the National Institute for Occupational Safety and Health (NIOSH).

Regulations and recommendations can be expressed in not-to-exceed levels in air, water, soil, or food that are usually based on levels that affect animals, then they are adjusted to help protect people. Sometimes these not-to-exceed levels differ among federal organizations because of different exposure times (an 8-hour workday or a 24-hour day), the use of different animal studies, or other factors.

Recommendations and regulations are also periodically updated as more information becomes available. For the most current information, check with the federal agency or organization that provides it. Some regulations and recommendations for phenol include the following:

OSHA has set a limit of 5 ppm in air to protect workers during 8-hour workshifts of a 40-hour workweek. NIOSH recommends that the concentration in workroom air be limited to 5 ppm over

a 10-hour work shift, and that the workroom air concentration should not exceed 16 ppm during a 15-minute period. Note that these workplace air limits assume no skin contact with phenol.

Phenol is listed on the Food and Drug Administration's EAFUS (Everything Added to Foods in the United States) List (FDA 1998a), and is approved as a component of food packaging materials (FDA 1998b, 1998c, 1998d).

The EPA lifetime health advisory for phenol in water is 4 mg/L. EPA has determined that the level of phenol in ambient water (lakes, streams) should be limited to 3.5 mg/L in order to protect human health from the potential toxic effects of exposure to phenol through ingestion of water and contaminated aquatic organisms.

1.10 WHERE CAN I GET MORE INFORMATION?

If you have any more questions or concerns, please contact your community or state health or environmental quality department or:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road NE, Mailstop E-29
Atlanta, GA 30333

* Information line and technical assistance

Phone: 1-800-447-1544
Fax: (404) 639-6359

ATSDR can also tell you the location of occupational and environmental health clinics. These clinics specialize in recognizing, evaluating, and treating illnesses resulting from exposure to hazardous substances.

1. PUBLIC HEALTH STATEMENT

*To order toxicological profies. contact:

National Technical Information Service
5285 Port Royal Road
Springfield, VA 22161
Phone: (800) 553-6847 or (703) 487-4650

2. HEALTH EFFECTS

2.1 INTRODUCTION

The primary purpose of this chapter is to provide public health officials, physicians, toxicologists, and other interested individuals and groups with an overall perspective of the toxicology of phenol. It contains descriptions and evaluations of toxicological studies and epidemiological investigations and provides conclusions, where possible, on the relevance of toxicity and toxicokinetic data to public health.

It should be noted that phenol is the simplest form, or parent compound, of the class of chemicals commonly referred to as phenols or phenolics, many of which are natural substances widely distributed throughout the environment. There is some confusion in the literature as to the use of the term 'phenol'; in some cases it has been used to refer to a particular phenolic compound that is more highly substituted than the parent compound (Doan et al. 4979), whereas in other cases it has been used to refer to the class of phenolic compounds (Beveridge 1997). This chapter, however, addresses only those health effects which can be directlyattributable to the parent compound, monohydroxybenzene, or phenol. As Deichmann and Keplinger (1981) note: "It cannot be overemphasized that the structure-activity relationships of phenol and phenol derivatives vary widely, and that to accept the properties of individual phenolic compounds as being those of phenol is a misconception and leads to error and confusion."

A glossary and list of acronyms, abbreviations, and symbols can be found at the end of this profile.

2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

To help public health professionals and others address the needs of persons living or working near hazardous waste sites, the information in this section is organized first by route of exposure-inhalation, oral, and dermal; and then by health effect-death, systemic, immunological, neurological, reproductive, developmental, genotoxic, and carcinogenic effects. These data are discussed in terms of three exposure periods-acute (14 days or less), intermediate (15-364 days), and chronic (365 days or more).

Levels of significant exposure for each route and duration are presented in tables and illustrated in figures. The points in the figures showing no-observed-adverse-effect levels (NOAELs) or lowest-observed-adverse effect levels (LOAELs) reflect the actual doses (levels of exposure) used in the studies. LOAELS have been

classified into "less serious" or "serious" effects. "Serious" effects are those that evoke failure in a biological system and can lead to morbidity or mortality (e.g., acute respiratory distress or death). "Less serious" effects are those that are not expected to cause significant dysfunction or death, or those whose significance to the organism is not entirely clear. ATSDR acknowledges that a considerable amount of judgment may be required in establishing whether an end point should be classified as a NOAEL, "less serious" LOAEL, or "serious" LOAEL, and that in some cases, there will be insufficient data to decide whether the effect is indicative of significant dysfunction. However, the Agency has established guidelines and policies that are used to classify these end points. ATSDR believes that there is sufficient merit in this approach to warrant an attempt at distinguishing between "less serious" and "serious" effects. The distinction between "less serious" effects and "serious" effects is considered to be important because it helps the users of the profiles to identify levels of exposure at which major health effects start to appear. LOAELs or NOAELs should also help in determining whether or not the effects vary with dose and/or duration, and place into perspective the possible significance of these effects to human health.

The significance of the exposure levels shown in the Levels of Significant Exposure (LSE) tables and figures may differ depending on the user's perspective. Public health officials and others concerned with appropriate actions to take at hazardous waste sites may want information on levels of exposure associated with more subtle effects in humans or animals (LOAEL) or exposure levels below which no adverse effects (NOAELs) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels or MRLs) may be of interest to health professionals and citizens alike.

Levels of exposure associated with carcinogenic effects (Cancer Effect Levels, CELs) of phenol are indicated in Table 2-3.

A User's Guide has been provided at the end of this profile (see Appendix B). This guide should aid in the interpretation of the tables and figures for Levels of Significant Exposure and the MRLs.

2.2.1 Inhalation Exposure

2.2.1.1 Death

A cohort mortality study of workers in five formaldebyde-resin manufacturing facilities was conducted to evaluate whether excess mortality could be attributed to occupational exposure to phenol (Dosemeci et al.

1991). Workers (exposed and non-exposed) had a mortality rate, from all causes, similar to that of the general U.S. population Compared to either the general population or unexposed workers, exposed workers had small excesses in mortality due to Hodgkin's disease and esophageal and renal cancers. However, they also had small reductions in mortality due to: cancer of the stomach, testes, pancreas, buccal cavity/pharynx and brain; lymphosarcoma; liver cirrhosis; emphysema; diseases of the cardiovascular, circulatory, and digestive systems; motor vehicle accidents and all accidents. The ambiguity of these data, as well as the fact that dose-related trends occurred only for those diseases showing reductions in mortality, makes it difficult to assess the impact on mortality of long-term occupational exposure to phenol. However, the authors do hypothesize a protective effect for phenol based on its metabolism to chemicals that could play a role in mitigating oxidative damage.

Deichmann et al. (1944) exposed guinea pigs, rabbits, and rats to phenol vapor at levels ranging from 26 to 52 ppm for 28-88 days. After 28 days of exposure, 5 of 12 guinea pigs died, but no deaths occurred in rabbits or rats Since only a range was given for the exposure level, the exact level of phenol in air that resulted in death of guinea pigs was not established and may be as low as 26 ppm or as high as 52 ppm. Interpretation of this study is further complicated by an apparent lack of controls. However, since the effects observed in guinea pigs and rabbits (described in subsecluent sections in Chapter 2) were so severe, it is difficult to ascribe the mortality to any source other than the phenol exposure. The lower limit of the exposure range, 26 ppm, is recorded as a LOAEL in Table 2-1 and plotted in Figure 2-1. No deaths were reported in rhesus monkeys, rats, or mice exposed to 5 ppm phenol continuously for 90 days (Sandage 1961).

2.2.1.2 Systemic Effects

The highest NOAEL values and all LOAEL values from each reliable study for systemic effects in each species and duration category are recorded in Table 2-1 and plotted in Figure 2-1.

Respiratory Effects. Slight increases in mortality associated with respiratory cancers were seen in two epidemiological studies of workers exposed to phenol (Dosemeci et al. 1991; Kauppinen et al. 1986). However, after adjusting for smoking-related behavior, these increases became non-significant in the Kauppinen et al. (1986) study, and neither study showed a dose-related trend; thus, the relevance of these findings to respiratory disease *per se* is somewhat uncertain. Indeed in the latter study, there were slight, yet nonsignificant reductions in mortality associated with emphysema among exposed workers, leading the

TABLE 2-1. Levels of Significant Exposure to Phenol - Inhalation

Key to figure[a]	Species (strain)	Exposure/ duration/ frequency	System	NOAEL (ppm)	LOAEL Less serious (ppm)	LOAEL Serious (ppm)	Reference
ACUTE EXPOSURE							
Systemic							
1	Mouse (Swiss OF1)	5 min	Resp			166 M (50% decrease in respiration rate)	De Ceaurriz et al. 1981
Immunological/Lymphoreticular							
2	Mouse (CD-1)	5 d 3 hr/d		5 F			Aranyi et al. 1986
Neurological							
3	Rat Harlan-Wistar	1hr		234 F			Flickinger 1976
4	Rat Harlan-Wistar	8hr			234 F		Flickinger 1976
INTERMEDIATE EXPOSURE							
Death							
5	Gn Pig (NS)	4 wk 5 d/wk 7 hr/d				26 (5/12 deaths)	Deichmann et al. 1944

TABLE 2-1. Levels of Significant Exposure to Phenol - Inhalation (continued)

Key to figure[a]	Species (strain)	Exposure/ duration/ frequency	System	NOAEL (ppm)	LOAEL Less serious (ppm)	LOAEL Serious (ppm)	Reference
	Systemic						
6	Monkey (Rhesus)	90 d continuous	Resp	5 M			Sandage 1961
			Hemato	5 M			
			Hepatic	5 M			
			Renal	5 M			
			Bd Wt	5 M			
7	Rat (White)	15 d continuous	Hemato	26			Dalin and Kristoffersson 1974
			Hepatic		26	(serum activities of ALT, AST, LDH, and GLDH increased 2-6-fold; increased serum magnesium)	
			Bd Wt	26			
8	Rat (Sprague-Dawley)	90 d continuous	Resp	5 M			Sandage 1961
			Hemato	5 M			
			Hepatic	5 M			
			Renal	5 M			
			Bd Wt	5 M			
9	Mouse (NS)	90 d continuous	Resp	5 M			Sandage 1961
			Hemato	5 M			
			Hepatic	5 M			
			Renal	5 M			
			Bd Wt	5 M			

TABLE 2-1. Levels of Significant Exposure to Phenol - Inhalation (continued)

Key to figure[a]	Species (strain)	Exposure/ duration/ frequency	System	NOAEL (ppm)	LOAEL Less serious (ppm)	LOAEL Serious (ppm)		Reference
10	Gn Pig (NS)	6 wk 5 d/wk 7 hr/d	Resp			26	(acute lobular pneumonia with occasional abscesses and vascular damage)	Deichmann et al. 1944
			Cardio			26	(necrosis of the myocardium, extensive reactive inflammation)	
			Hepatic			26	(fatty changes, centrolobular degeneration and necrosis)	
			Renal			26	(edema of the convoluted tubules, slightly advanced focal cortical lesions, glomerular degeneration)	
11	Rabbit (NS)	12 wk 5 d/wk 7 hr/d	Resp			26	(confluent lobular pneumonia, chronic purulent bronchitis, hyperplastic peribronchial tissue, degenerative changes in pulmonary vessels)	Deichmann et al. 1944
			Cardio			26	(myocardial degeneration, necrosis of muscle bundles, interstitial fibrosis, lymphocytic infiltration)	
			Hepatic			26	(centrolobular degeneration and necrosis)	
			Renal			26	(edema of the convoluted tubules, focal cortical lesions, glomerular degeneration)	
	Neurological							
12	Monkey (Rhesus)	90 d continuous		5 M				Sandage 1961

TABLE 2-1. Levels of Significant Exposure to Phenol - Inhalation (continued)

Key to figure[a]	Species (strain)	Exposure/ duration/ frequency	System	NOAEL (ppm)	LOAEL				Reference
					Less serious (ppm)		Serious (ppm)		
13	Rat (White)	15 d continuous			26	(mild motor disorders during the first 4 days of exposure, 4.4° decrease in sliding angle)			Dalin and Kristoffersson 1974
14	Rat (Sprague-Dawley)	90 d continuous		5 M					Sandage 1961
15	Mouse (NS)	90 d continuous		5 M					Sandage 1961
16	Gn Pig (NS)	6 wk 5 d/wk 7 hr/d					26	(hindlimb paralysis)	Deichmann et al. 1944

[a]The number corresponds to entries in Figure 2-1.

ALT = alanine aminotransferase; AST = aspartate aminotransferase; Bd Wt = body weight; Cardio = cardiovascular; d = day(s); F = female; GLDH = glutamate dehydrogenase; Gn Pig = guinea pig; Hemato = hematological; hr = hour(s); LDH = lactate dehydrogenase; LOAEL = lowest-observed-adverse-effect level; M = male; min = minute(s); NOAEL = no-observed-adverse-effect level; NS = not specified; Resp = respiratory; wk = week(s)

Figure 2-1. Levels of Significant Exposure to Phenol - Inhalation

Acute (≤14 days)

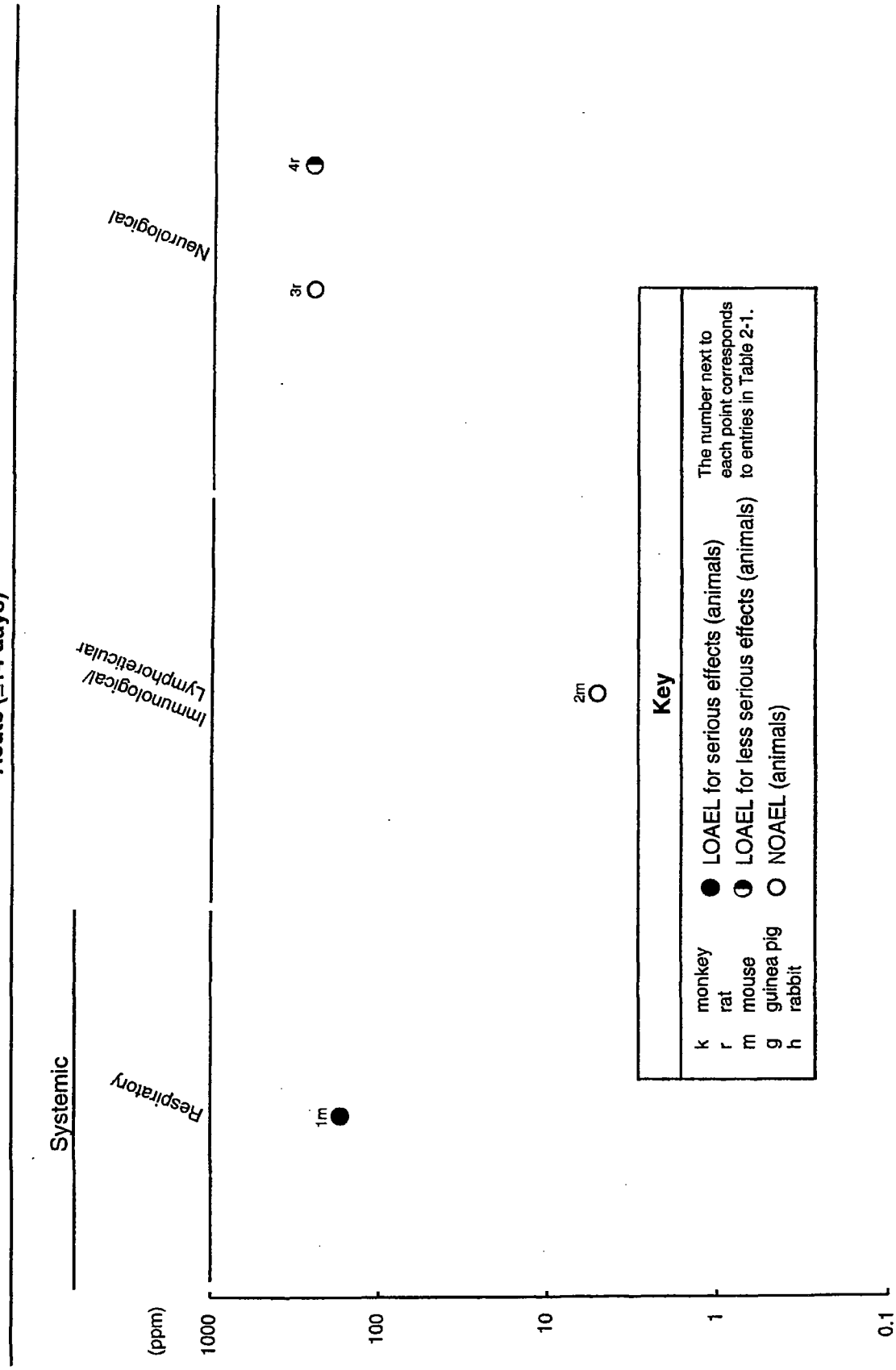
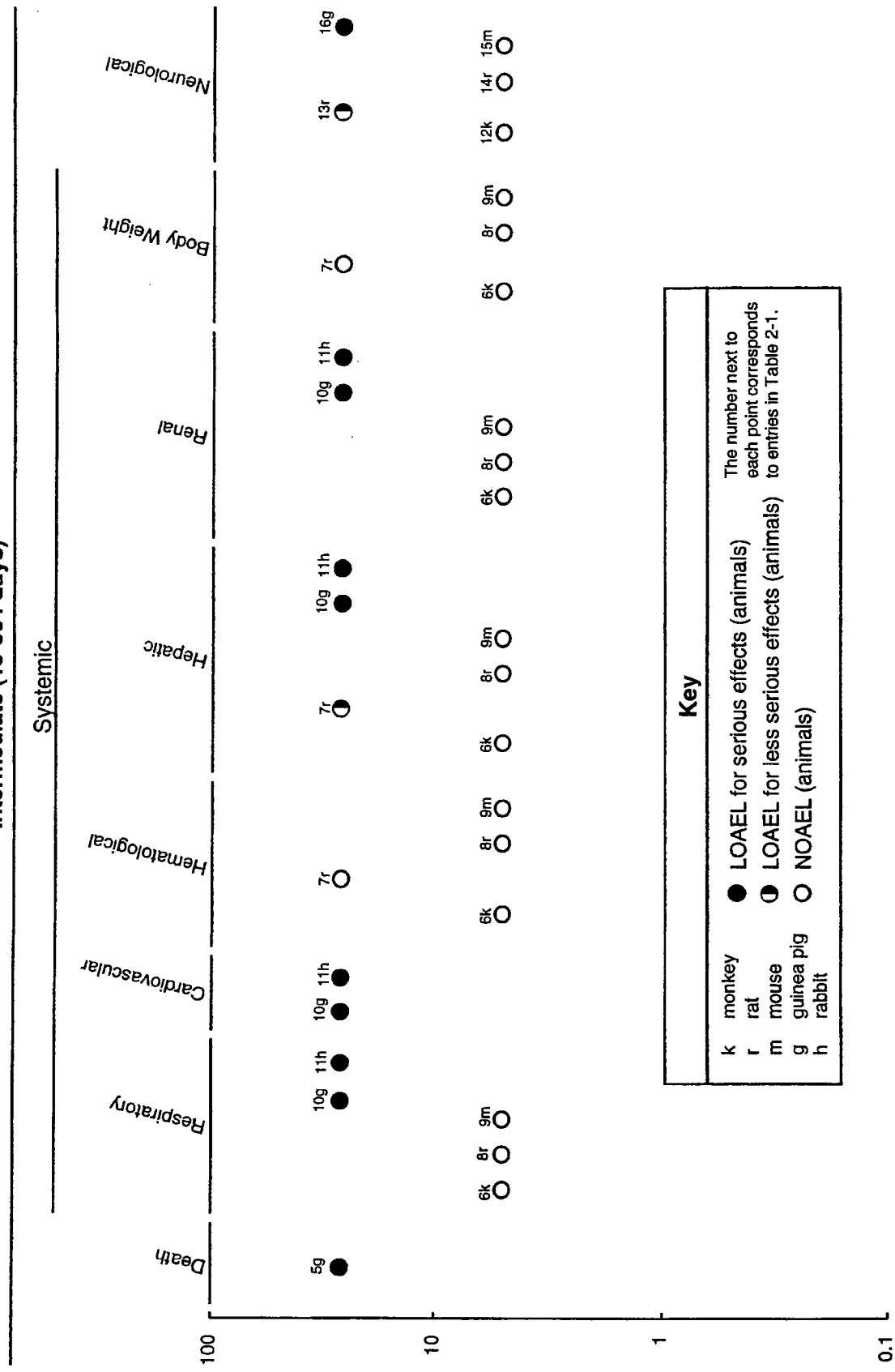


Figure 2-1. Levels of Significant Exposure to Phenol - Inhalation *(continued)*

Intermediate (15-364 days)



authors to suggest that exposure to phenol could have a protective effect for diseases involving free radical damage. (For more detail see above and Section 2.2.1.8.)

A case-control study of office workers was conducted by Baj et al. (1994) to evaluate the risks of chronic exposures to "inhaled formaldehyde, phenol, and isomers of organic chlorohydrocarbons from Ksylamit™. . " which is a widely used liquid wood preservative. It should be noted that in the report, Ksylamit™ is indicated to consist of " . . a mixture of chlorinated benzenes, pentachlorophenol, alphachloronaphthalene, chloroparaffin and kerosene . . ", and that the authors provide no discussion of how phenol and formaldehyde are produced through the use of such a mixture. Twenty-two workers (18 women and 4 men) exposed for at least 6 months were the cases, and 29 non-exposed, non-smoking volunteers matched for age, sex, and place of residence were the controls. The authors indicate that all exposed workers developed chronic complaints, among them cough and sore throat, but that no remarkable increase in morbidity was found during the 6 months of exposure to Ksylamit™ nor during the 3-year follow-up study (details of which were not provided). The authors attribute these symptoms to the irritant effect of the inhaled KsylamitrM probably (based on the references provided) due to the formaldehyde vapor they assert emanates from the wood-preserving liquid.

In laboratory animals, phenol is a respiratory irritant. De Ceaurriz et al. (1981) reported a dose-response function for reflex apnea, an index of respiratory irritation, in mice exposed to phenol vapor. From the log dose-response function for decreased breathing rate, the RD_{50} (RD designates respiratory depression), or level of phenol in air that resulted in a 50% decrease in breathing rate during a 5-minute head-only exposure, was established as 166 ppm. Based on the RD_{50} the study authors estimated that a concentration of 17 ppm ($0.1xRD_{50}$) would be a LOAEL for respiratory irritation in humans, and a concentration of 2 ppm ($0.01xRD_{50}$) would be a NOAEL.

In a study in which female Harlan Wistar rats were exposed for 1 hour to a phenol aerosol at a concentration of 234 ppm, then held for 2 weeks post-exposure, Flickinger (1976) observed signs of nasal irritation during exposure. However, all animals were normal by the post-exposure day 1, and no abnormal lesions were observed upon gross autopsy. No histopathology was performed; thus, this study is not presented as a LOAEL for rats.

Inflammation, cellular infiltration, pneumonia, bronchitis, endothelial hyperplasia, and capillary thrombosis occurred in guinea pigs exposed by inhalation to 26-52 ppm phenol for 41 days (Deichmann et al. 1944).

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Rabbits exhibited qualitatively similar but less severe effects after 88 days of similar exposure. Since only a range was given for the exposure level (26-52 ppm), the exact level of phenol in air that resulted in respiratory effects was not established and may be as low as 26 ppm or as high as 52 ppm. Interpretation of this study is further complicated by an apparent lack of controls. However, the lung pathology was so severe, particularly in the guinea pigs, that it is difficult to ascribe the effects to any source other than the phenol exposure. The lower limit of the exposure range, 26 ppm, can be considered a LOAEL for respiratory effects in guinea pigs and rabbits. Rats were also exposed to 26-52 ppm in a manner similar to rabbits and guinea pigs (Deichmann et al. 1944). The study authors indicate that there was no gross or microscopic evidence of injury, but the organs examined from the rats were not stated. Therefore, this study is not presented as a NOAEL for rats.

No significant histological abnormalities of the lungs were detected in rhesus monkeys, rats, or mice exposed to 5 ppm phenol continuously for 90 days (Sandage 1961).

Cardiovascular Effects. In a cohort mortality study of workers in a large rubber and tire manufacturing plant, Wilcosky and Tyroler (1983) found a significant increase in mortality from ischemic heart disease in phenol exposed workers. Of the 25 solvents used in the plant, phenol exposure showed the strongest association with mortality from heart disease, greater even than that observed for exposure to carbon disulfide, the only known occupational cause of atherosclerosis.

In a cohort-mortality study of workers from five phenol-formaldehyde resin plants, Dosemeci et al. (1991) found a slight reduction in mortality due to heart disease. These authors hypothesized a protective effect of phenol exposures; however, these results clearly conflict with those of Wilcosky and Tyroler (1983). As a consequence, without more definitive studies, it is difficult to assess the cardiovascular risk to humans, if any, posed by occupational exposure to phenol.

Myocardial injury was reported in guinea pigs exposed to 26-52 ppm for 41 days, and rabbits exhibited qualitatively similar but less severe effects after 88 days of similar exposure (Deichmann et al. 1944). The injury was characterized by myocardial inflammation, degeneration, and necrosis, interstitial fibrosis, and lymphocyte infiltration. Since only a range was given for the exposure level (26-52 ppm), the exact level of phenol in air that resulted in myocardial injury was not established and may be as low as 26 ppm or as high as 52 ppm. Interpretation of this study is further complicated by an apparent lack of controls. However, the heart pathology was so severe that it is difficult to ascribe the effects to any source other than the phenol

exposure. The lower limit of the exposure range, 26 ppm, can be considered a LOAEL for myocardial injury in guinea pigs and rabbits.

Gastrointestinal Effects. Historical information in a case report (Merliss 1972) indicates that 'carbol marasmus' was a common occupational disorder of physicians and their assistants during the mid-19th Century when carbolic acid sprays (1:40 phenol in water) were commonly used for antisepsis in operating rooms. Among the characteristics of this disorder were anorexia leading to progressive weight loss and excess production of saliva. Similar gastrointestinal effects were observed in one of the author's patients who was involved in the daily distillation of phenol over a 13.5 year period. Exposed both via inhalation of the vapors and dermally from frequent spills, the patient's symptoms included both loss of appetite and weight loss.

A cohort mortality study of workers in five phenol-formaldebyde resin manufacturing plants found that exposed workers showed a slight reduction in death rate due to cancers of the digestive system as compared to both non-exposed workers and the general population (Dosemeci et al. 1991). In a study of rats exposed continuously for 15 days to 26 ppm phenol vapor, Dalin and Kristoffersson (1974) noted the absence of impacts on the digestive system and attributed this to the relatively low exposure levels (as compared to studies using oral dosing).

Hematological Effects. A case-control study of office workers was conducted by Baj et al. (1994) to evaluate the risks of chronic exposures to "inhaled formaldehyde, phenol and isomers of organic chlorohydrocarbons from Ksylamitr™" which is a widely used liiquid wood preservative. It should be noted that in the report, Ksylamit™ is indicated to consist of "a mixture of chlorinated benzenes, pentachlorophenol, alpha-chloronaphthalene, chloroparaffin and kerosene," and that the authors provide no discussion of how phenol and formaldehyde are produced through the use of such a mixture. Twenty-two workers (18 women and 4 men) exposed for at least 6 months were the cases, and 29 non-exposed, non-smoking volunteers matched for age, sex, and place of residence were the controls. Using blood and urine samples drawn after 6 months of exposure, cases and controls were compared on a variety of biochemical, hematological, and immunological parameters. The exposed group showed no differences in any of the blood chemistry parameters examined, serum bilirubin, alanine, and aspartate aminotransferase activity, but had about a 30% increase in eosinophils, a 25% increase in monocytes, and a 70% decrease in erythrocytes. Measurement of the office air at the end of the 6-month period revealed a level of phenol of 0.34 ppm. Although the authors contend that their observations support the concern that chronic exposure to phenol could adversely

affect the hematopoietic system, it is important to consider not only that other volatile chemicals, chlorinated organics, were present in the wood-preserving liquid, but also that the chemical composition provided for Ksylamit™ opens up the possibility that the effects being evaluated result from exposure to pentachlorophenol rather than to phenol. This is particularly true since it was not possible to determine from the information presented if the analytical methods used would differentiate between phenol and pentachlorophenol.

Hematocrit and hemoglobin concentrations were not affected in rats exposed to 26 ppm phenol in air continuously for 15 days (Dalin and Kristoffersson 1974). Detailed hematological evaluations including red and white blood cell, reticulocyte, and platelet counts; white cell differential; hemoglobin and sulfhemoglobin, red cell fragility tests, as well as corpuscular volume, corpuscular hemoglobin, and corpuscular hemoglobin concentrations, did not reveal any effects in rhesus monkeys, rats, or mice exposed continuously to 5 ppm phenol in air for 90 days (Sandage 1961).

Musculoskeletal Effects. A case of muscle pain and weakness was described in an individual after intermittent chronic inhalation and dermal exposure to vapors and solutions of phenol, cresol, and xylenol (Merliss 1972). The symptoms lessened when the subject was removed from exposure. Although the exposure concentrations were not reported, the study author stated that the patient often detected heavy odors, and that phenol was often spilled on his clothes resulting in skin irritation. Since phenol is absorbed readily from the skin, dermal absorption of phenol may have contributed to the systemic effects that were observed. The above symptoms may represent neurological effects rather than injury to the muscle tissue.

In a study in which female Harlan Wistar rats were exposed for 8 hours to a phenol aerosol at a concentration of 234 ppm, Flickinger (1976) observed a slight loss of coordination with spasm of the muscle groups at 4 hours. By 8 hours, frank tremors were observed leading to a severe loss of coordination; however, all animals were normal by post-exposure day 1, and no abnormal lesions were observed upon gross autopsy.

Hepatic Effects. Enlarged liver and elevated serum levels of hepatic enzymes indicative of liver injury (lactate dehydrogenase, 2 times above normal; aspartate aminotransferase, 21 times above normal; alanine aminotransferase, 100 times above normal) were observed in an individual following chronic daily exposure to vapors and spills of phenol (Merliss 1972). The symptoms lessened when the individual was removed from the site of exposure. Although the exposure concentrations were not reported, the study author stated that the patient often detected heavy odors and that phenol was often spilled on his clothes resulting in skin

irritation. Since phenol is absorbed readily from the skin, dermal absorption may have contributed to the systemic effects that were observed.

No effects on activities of liver enzymes (alanine aminotransferase, aspartate aminotransferase, γ glutamyltranspeptidase, alkaline phosphatase) in the serum or changes in serum bilirubin or ceruloplasmin were noted in 22 workers exposed for 6 months to vapors from a wood-treatment liquid containing phenol, formaldehyde, and organic chlorohydrocarbons (Baj et al. 1994). Although the study authors considered a significant increase in serum iron to reflect an adverse effect on the liver that they attributed to phenol exposure, it is important to consider not only that other volatile chemicals, chlorinated organics, were present in the wood-preserving liquid, but also that the chemical composition provided for Ksylamit™ opens up the possibility that the effects being evaluated result from exposure to pentachlorophenol rather than phenol. Dosemeci et al. (1991) saw a dose-related decrease in mortality from liver cirrhosis in a cohort of workers occupationally exposed to phenol during their employment at five phenol-formaldehyde resin plants. These findings are complicated by the fact that workers were also exposed to other chemicals; however, the authors hypothesize that exposure to phenol could have a protective effect for diseases involving free radical damage. For more detail, see above and Section 2.2.1.8.

Centrilobular degeneration and necrosis of the liver were reported in guinea pigs exposed by inhalation to 26-52 ppm phenol for 41 days, and rabbits exhibited qualitatively similar but less severe effects after 88 days of similar exposure (Deichmann et al. 1944). Since only a range was given for the exposure level (26-52 ppm), the exact level of phenol in air that resulted in hepatic injury was not established and may be as low as 26 ppm or as high as 52 ppm. Interpretation of this study is further complicated by an apparent lack of controls. However, the liver pathology was so severe, particularly in the guinea pigs, that it is difficult to ascribe the effects to any source other than the phenol exposure.

Elevated activities of liver enzymes (lactate dehydrogenase, aspartate aminotransferase, alanine aminotransferase, glutamate dehydrogenase) were found in the serum of rats exposed continuously to 26 ppm phenol vapor for 15 days (Dalin and Kristoffersson 1974). Increased concentration of these enzymes in serum is often associated with liver injury but is not conclusive evidence for the type or severity of injury. Therefore, 26 ppm can be considered a less serious LOAEL in rats. Serum levels of magnesium were also increased in these rats, an effect the study authors suggested may also be a sign of liver injury. No significant histological abnormalities were detected in the livers of rhesus monkeys, rats, or mice exposed continuously to 5 ppm phenol in air for 90 days (Sandage 1961).

2. HEALTH EFFECTS

Renal Effects. In a case of chronic phenol poisoning, dark urine and glucose in the urine were noted in a man following intermittent exposure to vapors and solutions of phenol (Merliss 1972). The urine tested negative for protein and urobilinogen. The urine cleared 2-3 months after removal from exposure. Although the exposure concentrations were not reported, the study author stated that heavy odors were often detectable, and that phenol was often spilled on the patient's clothes resulting in skin irritation. Since phenol is absorbed readily from the skin, dermal absorption may have contributed to the systemic effects that were observed.

Renal proximal tubule and glomerular injury was reported in guinea pigs exposed by inhalation to 26-52 ppm phenol for 41 days, and rabbits exhibited qualitatively similar but less severe effects after 88 days of similar exposure (Deichmann et al. 1944). Since only a range was given for the exposure level (26-52 ppm), the exact level of phenol in air that resulted in renal injury was not established and may be as low as 26 ppm or as high as 52 ppm. Interpretation of this study is further complicated by an apparent lack of controls. However, the kidney pathology was so severe, particularly in the guinea pigs, that it is difficult to ascribe the effects to any source other than the phenol exposure. The lower limit of the exposure range, 26 ppm, can be considered a LOAEL for renal injury in guinea pigs and rabbits. Rats were also exposed to 26-52 ppm in a manner similar to rabbits and guinea pigs (Deichmann et al. 1944). The study authors indicated that there was no gross or microscopic evidence of injury, but the organs examined from the rats were not stated. Therefore, this study is not presented as a NOAEL for rats. No significant histological abnormalities were detected in the kidneys of rhesus monkeys, rats, or mice exposed continuously to 5 ppm phenol in air for 90 days (Sandage 1961).

Dermal Effects. Historical information in a case report Merliss (1972) indicates that 'carbol marasmus' was a common occupational disorder of physicians and their assistants during the mid-19th Century. Among the characteristics of this disorder was an odd form of pigmentation which commonly occurred in the urine but also occasionally colored the sclera of the eyes, the skin over the nose, and the cheek bones. NIOSH (1984) conducted a survey in an Oregon hospital in response to concerns about respiratory problems and contact dermatitis in housekeeping staff members who were exposed frequently to germicidal solutions containing phenol and other solvents (formaldehyde, cellosolve, ethanolamine). According to the survey, the housekeeping staff reported significantly more symptoms of cough, itching, sinus problems, and dermatitis than other employees. Air concentrations of phenol in the work areas were below the limit of detection (<0.01 ppm). Urinary phenol levels in housekeeping staff were not significantly different from those of other employees. Thus, while it is likely that the employees came into contact with irritants, the cause of the reported symptoms could not be assigned to phenol or any other specific substance in the work environment.

2. HEALTH EFFECTS

No studies were located regarding dermal effects in animals following inhalation exposure to phenol.

Ocular Effects. A case-control study of office workers was conducted by Baj et al. (1994) to evaluate the risks of chronic exposures to "inhaled formaldehyde, phenol and isomers of organic chlorohydrocarbons from Ksylamit™ which is a widely used liquid wood preservative reported to consist of "a mixture of chlorinated benzenes, pentachlorophenol, alpha-chloronaphthalene, chloroparaffin, and kerosene." Twenty-two workers (18 women and 4 men) exposed for at least 6 months were the cases, and 29 non-exposed, non-smoking volunteers matched for age, sex, and place of residence were the controls. The authors indicate that all of the exposed workers developed chronic complaints, among them burning eyes, but that no remarkable increase in morbidity was found during the 6 months of exposure to Ksylamit™, nor during the 3-year follow-up study (details of which were not provided). The authors attribute these symptoms to the irritant effect of the inhaled Ksylarnit™ probably (based on the references provided) due to the formaldehyde vapor they assert emanates from the wood-preserving liquid.

In a study in which female Harlan Wistar rats were exposed for 1 hour to a phenol aerosol at a concentration of 234 ppm, then held for 2 weeks post-exposure, Flickinger (1976) observed signs of ocular irritation during exposure. However, all animals were normal by post-exposure day 1, and no abnormal lesions were observed upon gross autopsy.

Body Weight Effects. Historical information in a case report (Merliss 1972) indicates that 'carbol marasmus' was a common occupational disorder of physicians and their assistants during the mid-19th Century. Among the characteristics of this disorder were anorexia accompanied by progressive weight loss. The author reported that his patient, a 44-year-old man involved in the daily distillation of phenol, showed many of the symptoms of this condition, including lack of appetite and severe weight loss, probably due to his daily workplace exposures to phenol vapors. Although the exposure concentrations were not reported, the report indicated that the patient often detected heavy odors, and that phenol was often spilled on his clothes resulting in skin irritation. Since phenol is absorbed readily from the skin, dermal absorption may have contributed to the systemic effects that were observed.

Body weight effects were not observed in adult female Harlan Wistar rats exposed to an aerosol containing 234 ppm phenol for 8 hours (Flickinger 1976), nor in rats exposed continuously to 26 ppm phenol in air for 15 days (Dalin and Kristoffersson 1974), nor in rhesus monkeys, rats, or mice exposed continuously to 5 ppm phenol in air for 90 days (Sandage 1961).

2. HEALTH EFFECTS

Other Systemic Effects. Dalin and Kristoffersson (1974) reported elevated serum concentrations of potassium and magnesium in rats exposed to 26 ppm phenol vapor continuously for 15 days. While not necessarily adverse, this effect may be related to the muscle tremors and neurological effects observed following inhalation exposure to phenol (see Section 2.2.1.4).

2.2.1.3 Immunological and Lymphoreticular Effects

A case-control study of office workers was conducted by Baj et al. (1994) to evaluate the risks of chronic exposures to "inhaled formaldehyde, phenol and isomers of organic chlorohydrocarbons from Ksylamit™," which is a widely used liquid wood preservative. Twenty-two workers (18 women and 4 men) exposed for at least 6 months were the cases, and 29 non-exposed, non-smoking volunteers matched for age, sex, and place of residence were the controls. Using blood samples drawn after 6 months of exposure, cases and controls were compared on a variety of immunological parameters. The exposed group showed significantly decreased ($P<0.05$) levels of the CD3+, CD4+, and CD8+ subsets of T-lymphocytes, a significant decrease ($p<0.001$) in lymphocyte responsiveness to the mitogen PHA, a significant decrease ($p< 0.05$) in NK cell cytotoxicity, and a significant decrease ($p< 0.0001$) in the mixed lymphocyte response assay. Measurement of the office air at the end of the 6 month period revealed a level of phenol of 0.34 ppm. Although the authors contend that their observations support the concern that chronic exposure to phenol could adversely affect the immune system, it is important to consider not only that other volatile chemicals, chlorinated organics, were present in the wood-preserving liquid, but also that the chemical composition provided for Ksylamit™ opens up the possibility that the effects being evaluated resulted from exposure to pentachlorophenol rather than phenol. This is particularly true since it was not possible to determine from the information presented if the analytical methods used would differentiate between phenol and pentachlorophenol.

An increased susceptibility to *Streptococcus zooepidemicus* aerosol was not observed in mice exposed to 5 ppm phenol for 3 hours, or for 5 daily 3-hour periods (Aranyi et al. 1986). Neither did the phenol exposures affect pulmonary bactericidal activity towards *Klebsiella pneumonia.* Although tests for vulnerability to infectious agents do not represent a comprehensive evaluation of immunological competence, the 5-ppm level can be considered a NOAEL for this specific immunological effect, and is recorded in Table 2-1 and plotted in Figure 2-1.

2. HEALTH EFFECTS

2.2.1.4 Neurological Effects

Historical information in a case report (Merliss 1972) indicates that 'carbol marasmus' was a common occupational disorder of physicians and their assistants during the mid- 19th Century. Among the characteristics of this disorder were anorexia, headache, and vertigo. The author reported that his patient, the subject of the case report, showed many of the symptoms of this condition, although his chief complaints were weakness and muscle pain in his arms and legs, progressive weight loss, and excess production of saliva. The symptoms lessened when the subject was removed from the site of exposure. Although it is possible that these symptoms resulted from injury to the muscle, it is more likely that they represent a neurological effect. No information on exposure concentrations was presented; however, the report indicated that the patient often detected heavy odors and that phenol was often spilled on his clothes resulting in skin irritation. Since phenol is absorbed readily from the skin, dermal absorption may have contributed to the systemic effects that were observed.

A case-control study of office workers was conducted by Baj et al. (1994) to evaluate the risks of chronic exposures to "inhaled formaldehyde, phenol and isomers of organic chlorohydrocarbons from Ksylamit^{TM}" which is a widely used liquid wood preservative. Twenty-two workers (18 women and 4 men) exposed for at least 6 months were the cases, and 29 non-exposed, non-smoking volunteers matched for age, sex, and place of residence were the controls. The workers complained of a variety of chronic symptoms, among them headache and fatigue. Measurement of the office air at the end of the 6 month period revealed a level of phenol of 0.34 ppm. Although these symptoms could be a sign that chronic inhalation exposure to phenol could adversely affect the neurological system, it is important to consider not only that other volatile chemicals, chlorinated organics, were present in the wood-preserving liquid, but also that the chemical composition provided for Ksylamit^{TM} opens up the possibility that the effects being evaluated resulted from exposure to pentachlorophenol rather than phenol. This is particularly true since it was not possible to determine from the information presented if the analytical methods used would differentiate between phenol and pentachlorophenol.

Female Harlan Wistar rats exposed for 1 hour or 8 hours to 234 ppm phenol delivered in an aerosol demonstrated no neurological effects at 1 hour, a slight loss of coordination with spasm of the muscle groups at 4 hours, and frank tremors leading to a severe loss of coordination by 8 hours (Flickinger 1976). All animals were normal by post-exposure day 1, and no abnormal lesions were observed upon gross autopsy

performed at the end of a 14-day observation period. These exposure levels are recorded in Table 2-1 and are plotted in Figure 2-1 as a NOAEL, a less serious LOAEL, and a serious LOAEL.

Rats exposed continuously to 26 ppm showed numerous symptoms and signs of neurological impairment, including muscle tremors, twitching, and disturbances in walking rhythm and posture during the first 3-5 days of exposure, and impaired performance (4.4' decrease in sliding angle) on a tilting plane test after 15 days of exposure (Dalin and Kristoffersson 1974). These effects are indicative of neurological impairment Because the tremors did not last during the whole exposure period, the effects were not considered severe.

Hindlimb paralysis was reported in guinea pigs exposed to 26-52 ppm phenol for 41 days (Deichmann et al. 1944). Rabbits and rats exhibited no overt neurological effects after 88 and 74 days of similar exposure, respectively. Since only a range was given for the exposure level (26-52 ppm), the exact level of phenol in air that resulted in hindlimb paralysis was not established and may be as low as 26 ppm or as high as 52 ppm. Interpretation of this study is further complicated by an apparent lack of controls. However, the neurological effect was so severe in the guinea pigs that it is difficult to ascribe the effects to any source other than the phenol exposure. The lower limit of the exposure range, 26 ppm, is recorded in Table 2-1 and plotted in Figure 2-1 as a LOAEL for serious neurological effects in guinea pigs. Since the presence or absence of overt neurological effects such as paralysis is not a sensitive endpoint for detecting neurological effects, 26-52 ppm is not considered a reliable NOAEL for neurological effects in rats and rabbits.

There are several differences in the experimental designs of the Dalin and Kristoffersson (1974) and Deichmann et al. (1944) studies that may account for the different results regarding neurological effects in rats. Dalin and Kristoffersson (1974) reported subtle effects that may have been overlooked in the Deichmann et al. (1944) study. Furthermore, Dalin and Kristoffersson (1974) subjected the rats to a specific test for neurological impairment, the tilting plane test. Although exposure concentrations were the same in both studies, Dalin and Kristoffersson (1974) exposed rats continuously, while Deichmann et al. (1944) exposed rats intermittently. Because phenol is metabolized quite rapidly (see Section 2.6.3), rats exposed intermittently may not develop neurological effects.

Histopathological changes in the brain were not observed in rhesus monkeys, rats, or mice exposed continuously to 5 ppm phenol in air for 90 days (Sandage 1961)

2. HEALTH EFFECTS

The highest NOAEL values and all LOAEL values from each reliable study for neurological effects in each species for acute and intermediate-duration exposure are recorded in Table 2-1 and plotted in Figure 2-1.

No studies were located regarding the following health effects in humans or animals after inhalation exposure to phenol:

2.2.1.5 Reproductive Effects

2.2.1.6 Developmental Effects

2.2.1.7 Genotoxic Effects

Genotoxicity studies are discussed in Section 2.5.

2.2.1.8 Cancer

In a nested case-control study of cancers associated with chemical exposures in the wood industry, Kauppinen et al. (1986) found a significantly increased risk of respiratory system cancer associated with exposure to phenol and phenol in wood dust. As is often the case in occupational settings, these exposures were confounded by smoking and exposures to other materials like pesticides. The increased risk observed for exposure to phenol was almost 5-fold (odds ratio of 4.94), but showed no dose-related increase. This risk dropped to 4-fold with adjustments for smoking history, and to less than 3-fold (and non-significant) when workers exposed to both phenols and pesticides were excluded from the analysis"

Similar to the findings of Kauppinen et al. (1986), a large (14,861) cohort mortality study of workers in the phenol-formaldehyde resin manufacturing industry found nondose-related increases in the risk of several respiratory system cancers in workers exposed to phenol (Dosemeci et al. 1991). The authors develop a semiquantitative exposure assessment by assigning exposure levels (none, low, medium, and high) to each job category. The increased risks were small; for instrance, for cancer of the larynx or lung, standard mortality ratios (SMRs) of 1.1 were less than those found for non-exposed workers. For a number of other cancers, including those of the esophagus, rectum, bladder, kidney, and Hodgkin's disease, the SMRs found for phenol-exposed workers were greater than those for the non-exposed workers, but none were considered indicative of "important excesses" of these diseases by the authors.

2. HEALTH EFFECTS

No studies were located regarding cancer in animals following inhalation exposure to phenol.

2.2.2 Oral Exposure

2.2.2.1 Death

There have been numerous reports of suicide or suicide attempts involving ingestion of large amounts of phenol However, the lack of accurate documentation of dose levels in these cases makes it difficult to identify a minimal dose at which lethality occurs Deichmann and Klepinger (1981), in summarizing the literature, indicated that an oral dose as low as 1 g could be fatal in humans, but that occasionally patients had survived doses as high as 65 g. Assuming that these patients were male with an average weight of 70 kg, the lower limit on the dose for death would be 14 mg/kg and the upper limit would be approximately 930 mg/kg. In a review of the toxicology of phenol, Bruce et al. (1987) summarized human oral lethality data from numerous case reports and estimated 140 mg/kg to be the minimal dose at which death occurs. Stajduhar-Caric (1968) reported a case in which a woman ingested ≈10-20 g of phenol and died within hours. The lower limit of the ingested dose was converted to 172 mg/kg, assuming a 58 kg body weight, to derive a dose for death which is recorded in Table 2-2 and plotted in Figure 2-2.

The oral LD_{50} has been determined in rats treated by gavage with phenol in water; the LD_{50} was found to decrease with increasing concentration of phenol in the gavage fluid. The reported LD_{50} values were 340 mg/kg in rats gavaged with a solution of 200,000 ppm phenol and 530 mg/kg in rats gavaged with a solution of 20,000 ppm phenol (Deichmann and Witherup 1944). After rats were treated by gavage with 600 mg/kg in a 5% solution, 9 of 30 five-week-old rats, 18 of 20 ten-day-old rats, and 12 of 20 adult rats died indicating that the 10day-old rat is more sensitive to phenol than rats in the other age groups tested (Deichmann and Witherup 1944). In pregnant rats treated on gestation days 6-15, seven of 10 rats died at a dose of 125 mg/kg/day when treated with a volume of 1 mL/kg, while 1 of 6 rats died at a dose of 160 mg/kg/day when treated with a volume of 5 mL/kg (Jones-Price et al. 1983a). In a 1-day dosing regimen study, female rats were given 0, 12, 40, 120, or 224 mg/kg in order to determine a single-dose oral LD_{50} of 400 mg/kg (Berman et al. 1995). Mortality was observed only at the highest dose where 2 of 8 rats treated died. All female rats treated for 14 days with a dose of 120 mg/kg/day died (Berman et al. 1995; Moser et al. 1995). In a 14-day dosing regimen with the same doses (except the 224 mg/kg), all animals died at the dose of 120 mg/kg.

TABLE 2-2. Levels of Significant Exposure to Phenol - Oral

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL		Reference
					Less Serious (mg/kg/day)	Serious (mg/kg/day)	
	ACUTE EXPOSURE						
	Death						
1	Human	once				172 F (death)	Stajduhar-Caric 1968
2	Rat (Fischer- 344)	once (GW)				400 F (LD_{50})	Berman et al. 1995
3	Rat (Fischer- 344)	14 d 1x/d (GW)				120 F (8/8 died)	Berman et al. 1995
4	Rat (Wistar)	once (GW)				340 (LD_{50})	Deichmann and Witherup 1944
5	Rat (CD)	10 d Gd 6-15 1 x/d (GW)				125 F (7/10 maternal deaths, treated with a volume of 1 mL/kg)	Jones-Price et al. 1983a
6	Rat (CD)	10 d Gd 6-15 1 x/d (GW)				160 F (1/6 maternal deaths, treated with a volume of 5 mL/kg)	Jones-Price et al. 1983a
7	Mouse (CD-1)	10 d Gd 6-15 1 x/d (GW)				280 F (4/35 maternal deaths)	Jones-Price et al. 1983b
8	Mouse (NS)	once (GO)				300 M (5/10 deaths)	Von Oettingen and Sharpless 1946
9	Rabbit (White)	once (GW)				420 (5/10 deaths)	Deichmann and Witherup 1944

TABLE 2-2. Levels of Significant Exposure to Phenol - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL		Reference
					Less Serious (mg/kg/day)	Serious (mg/kg/day)	
	Systemic						
10	Rat (Fischer- 344)	once (GW)	Hepatic	224 F			Berman et al. 1995
			Renal	120 F	224 F (renal tubular necrosis, protein casts, papillary hemorrhage)		
			Endocr	120 F	224 F (unspecified changes in the adrenal gland)		
			Bd Wt	224 F			
11	Rat (Fischer- 344)	14 d 1x/d (GW)	Hepatic	40 F			Berman et al. 1995
			Renal	40 F			
			Endocr	40 F			
			Bd Wt	40 F			
12	Rat (CD)	10 d Gd 6-15 1 x/d (GW)	Hepatic	120 F			Jones-Price et al. 1983a
			Bd Wt	120 F			
13	Rat (Fischer- 344)	14 d Gd 6-19 (GW)	Resp			40 F (dyspnea, rales)	Narotsky and Kavlock 1995
			Bd Wt			40 F (20% decrease in maternal body weight gain)	
14	Mouse (Swiss CD-1)	once - Gd 13 (GW)	Hemato		265 F (30-60% reduction in the ratio of poly/normo chromatic erythrocytes in the bone marrow of pregnant dams)		Ciranni et al. 1988
15	Mouse (CD-1)	10 d Gd 6-15 1 x/d (GW)	Hepatic	280 F			Jones-Price et al. 1983b
			Bd Wt	140 F		280 F (67% decrease in absolute maternal body weight gain)	

TABLE 2-2. Levels of Significant Exposure to Phenol - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference
	Immunological/Lymphoreticular						
16	Rat (Fischer- 344)	once (GW)		120 F	224 F (necrosis or atrophy of the spleen or thymus)		Berman et al. 1995
17	Rat (Fischer- 344)	14 d 1x/d (GW)		40 F			Berman et al. 1995
	Neurological						
18	Rat (Sprague-Dawley)	once (G)				207 M (muscle twitching, convulsions, coma)	Liao and Oehme 1981
19	Rat (Fischer- 344)	once (GW)		40 F		120 F (mild-to-severe whole-body tremors, decreased motor activity)	Moser et al. 1995
20	Rat (Fischer- 344)	14 d 1x/d (GW)		12 F	40 F (increased rearing)		Moser et al. 1995
21	Mouse (CD-1)	10 d Gd 6-15 1 x/d (GW)		70 F	140 F (mild tremors on the first 3 days of dosing)	280 F (tremors, ataxia in pregnant dams)	Jones-Price et al. 1983b
	Reproductive						
22	Rat (CD)	10 d Gd 6-15 1 x/d (GW)		120 F			Jones-Price et al. 1983a
23	Mouse (CD-1)	10 d Gd 6-15 1 x/d (GW)		280			Jones-Price et al. 1983b

TABLE 2-2. Levels of Significant Exposure to Phenol - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)		LOAEL Serious (mg/kg/day)		Reference
	Developmental								
24	Rat (CD)	10 d Gd 6-15 1 x/d (GW)		60	120	(7% decrease in average fetal body weight)			Jones-Price et al. 1983a
25	Rat (Fischer- 344)	14 d Gd 6-19 (GW)		40			53.3	(significant decrease in the number of live-born pups, associated with severe respiratory effects in the dams)	Narotsky and Kavlock 1995
26	Mouse (CD-1)	10 d Gd 6-15 1 x/d (GW)		140			280	(18% decreased fetal body weight, cleft palate 8/214)	Jones-Price et al. 1983b
	INTERMEDIATE EXPOSURE								
	Systemic								
27	Human	< 6 mo (W)	Gastro	0.003	0.14	(nausea, diarrhea)			Baker et al. 1978
			Renal	0.003	0.14	(dark urine)			
			Dermal	0.003	0.14	(mouth sores, skin rash)			

TABLE 2-2. Levels of Significant Exposure to Phenol - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference
28	Rat (Fischer- 344)	13 wk ad libitum (W)	Resp	1694 F			NCI 1980
			Cardio	1694 F			
			Gastro	1694 F			
			Musc/skel	1694 F			
			Hepatic	1694 F			
			Renal	1694 F			
			Endocr	1694 F			
			Dermal	1694 F			
			Bd Wt	467 M	1556M (16% decrease in body weight gain associated with decreased water intake)	1694 F (26% decrease in body weight gain associated with decreased water intake)	
				508 F			
29	Mouse (CD-1)	28 d ad libitum (W)	Resp	33.6 M			Hsieh et al. 1992
			Cardio	33.6 M			
			Hemato		1.8 M (32% decrease in red blood cell count)		
			Hepatic	33.6 M			
			Renal	33.6 M			
			Bd Wt	33.6 M			
30	Mouse (B6C3F1)	13 wk ad libitum (W)	Resp	2642 F			NCI 1980
			Cardio	2642 F			
			Gastro	2642 F			
			Musc/skel	2642 F			
			Hepatic	2642 F			
			Renal	2642 F			
			Endocr	2642 F			
			Dermal	2642 F			
			Bd Wt	741 M		2468 M (80% decrease in body weight gain associated with decreased water intake)	

TABLE 2-2. Levels of Significant Exposure to Phenol - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference
	Immunological/Lymphoreticular						
31	Mouse (CD-1)	28 d ad libitum (W)		1.8 M	6.2 M (decreased antibody production response to sheep red blood cells)		Hsieh et al. 1992
	Neurological						
32	Mouse (CD-1)	28 d ad libitum (W)			1.8 M (decreased levels of dopamine in the corpus striatum)		Hsieh et al. 1992
	Reproductive						
33	Rat (Fischer- 344)	13 wk ad libitum (W)		1694 F 1556 M			NCI 1980
34	Mouse (B6C3F1)	13 wk ad libitum (W)		2642 F 2468 M			NCI 1980
	CHRONIC EXPOSURE						
	Systemic						
35	Rat (Fischer- 344)	103 wk ad libitum (W)	Resp	721 F			NCI 1980
			Cardio	721 F			
			Gastro	721 F			
			Musc/skel	721 F			
			Hepatic	721 F			
			Renal	721 F			
			Endocr	721 F			
			Dermal	721 F			
			Bd Wt	360 F	322 M (about 12% decrease associated with a 20% decrease in water intake) 721 F (about 17% decrease associated with a 10% decrease in water intake)		

TABLE 2-2. Levels of Significant Exposure to Phenol - Oral (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL			Reference
					Less Serious (mg/kg/day)	Seriou (mg/kg/day)		
36	Mouse (B6C3F1)	103 wk ad libitum (W)	Resp	1204 F				NCI 1980
			Cardio	1204 F				
			Gastro	1204 F				
			Musc/skel	1204 F				
			Hepatic	1204 F				
			Renal	1204 F				
			Endocr	1204 F				
			Dermal	1204 F				
			Bd Wt	1204 F				

[a]The number corresponds to entries in Figure 2-2. Differences in levels of health effects and cancer effects between males and females are not indicated in Figure 2-2. Where such differences exist, only the levels of effect for the most sensitive gender are presented.

Bd Wt = body weight; Cardio = cardiovascular; d = day(s); Endocr = endocrine; F = female; (G) = gavage; Gastro = gastrointestinal; Gd = gestation day(s); (GO)= gavage, oil; (GW)= gavage, water; Hemato = hematological; LD_{50} = lethal dose (50% kill); LOAEL = lowest-observed-adverse-effect level; M = male; min = minute(s); mo = month(s); Musc/skel = musculoskeletal; NOAEL = no-observed-adverse-effect level; NS = not specified; Resp = respiratory; (W) = drinking water; wk = week(s); x = time(s)

Figure 2-2. Levels of Significant Exposure to Phenol - Oral

Acute (≤14 days)

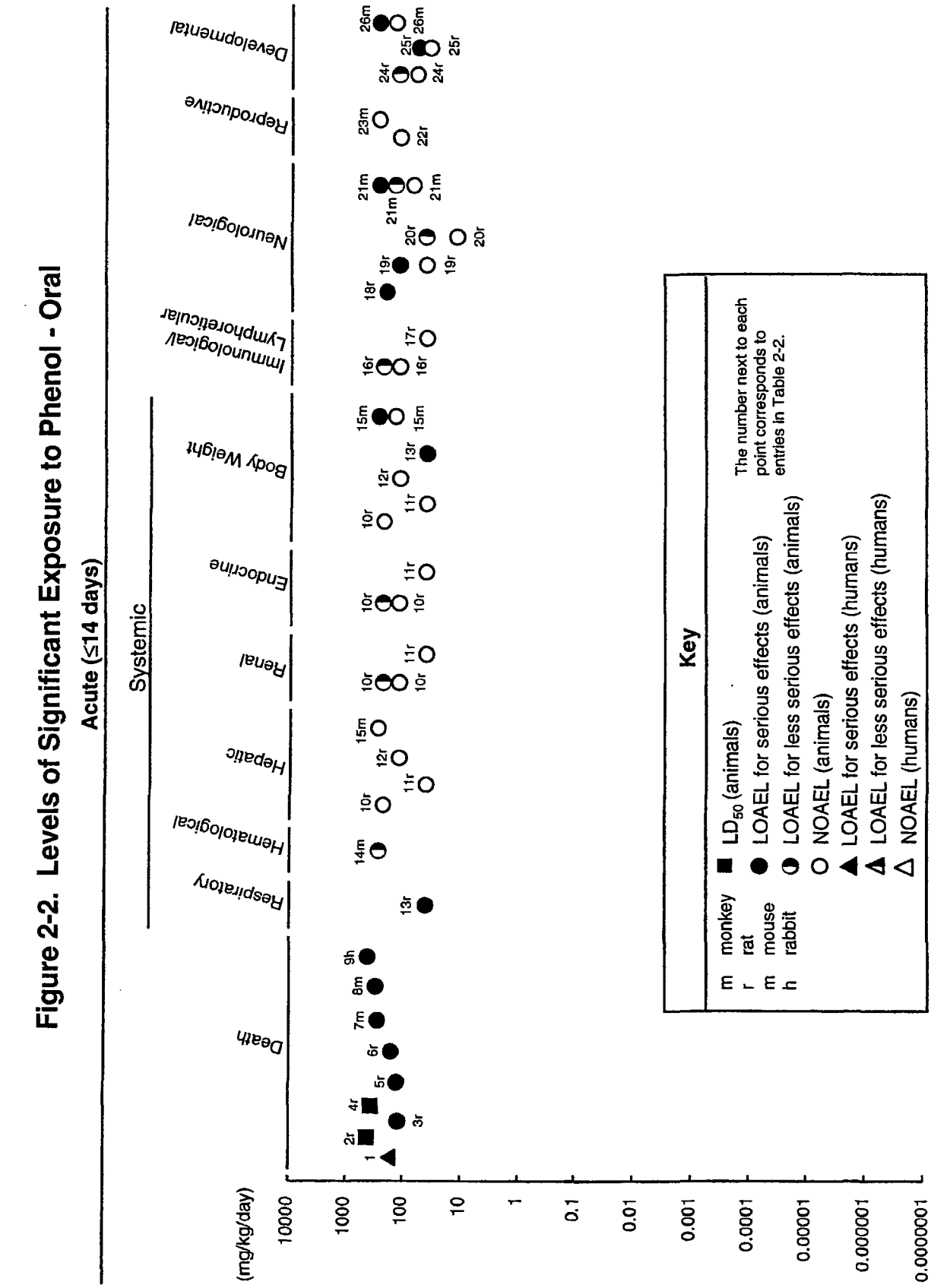


Figure 2-2. Levels of Significant Exposure to Phenol - Oral (*continued*)

Intermediate (15-364 days)

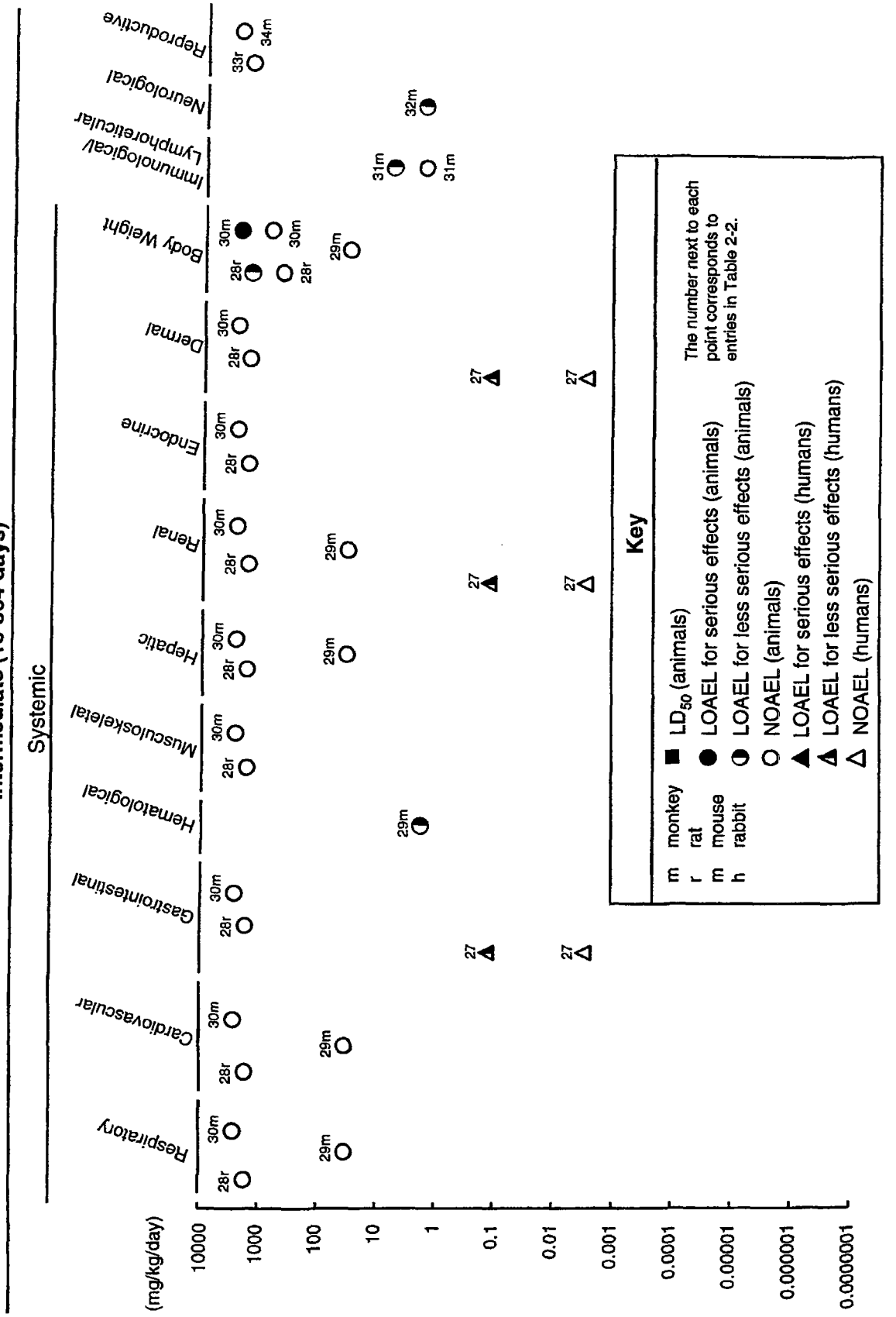
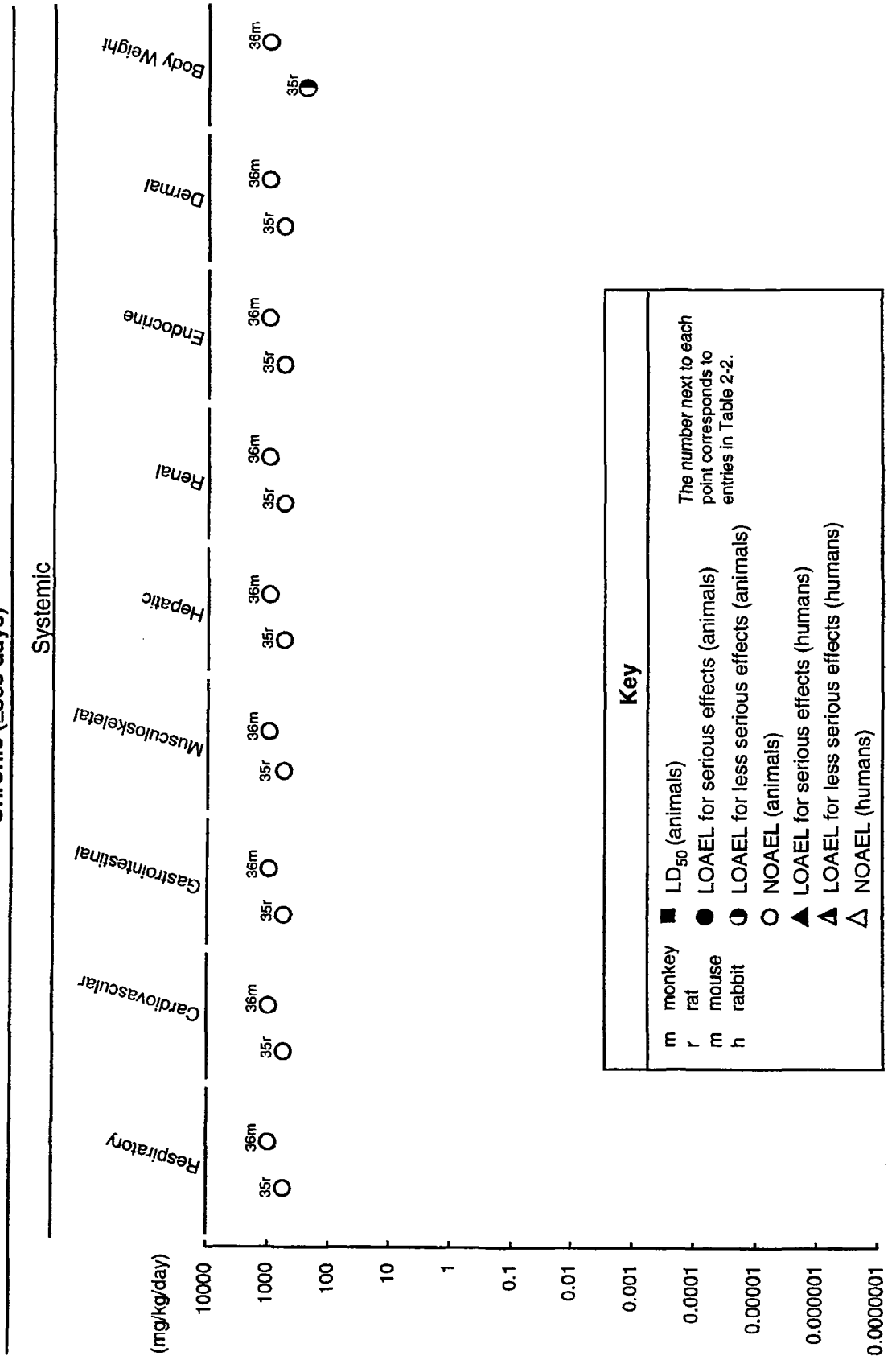


Figure 2-2. Levels of Significant Exposure to Phenol - Oral *(continued)*



2. HEALTH EFFECTS

The oral LD_{50} of phenol has been estimated as 300 mg/kg in mice (von Oettingen and Sharpless 1946). Five of lo rabbits treated with an oral dose of 420 mg/kg died (Deichmann and Witherup 1944). In pregnant mice treated on gestation days 6-15, four of 35 mice died at a dose of 280 mg/kg/day (Jones-Price et al. 1983b).

Flickinger (1976) gave male albino rats single doses of 0 200, 398, 795, and 1,580 mg/kg phenol by gavage and held the animals for 14 days post-dosing in order to determine an oral LD_{50}. No animals died following the 0,200, or 398 mg/kg doses; 4 of 5 animals died the first day following the 795 mg/kg dose, and 5 of 5 animals died within 2 hours following 1,580 mg/kg dose. From these data, the authors estimated an oral LD_{50}, of 650 mg/kg.

No effect on survival was observed in mice treated with phenol in the drinking water at doses up to 33.6 mg/kg/day for 28 days (Hsieh et al. 1992). Survival was not affected in rats and mice treated with phenol in drinking water for 13 or 103 weeks (NCI 1980). Both species were treated with drinking water concentrations up to 10,000 mg/L in the 13-week study (maximum doses in mg/kg/day: 1,694 for female rats, 1,556 for male rats; 2,643 for female mice, 2,468 for male mice), and up to 5,000 mg/L in the 103-week study (maximum doses in mg/kg/day: 721 for female rats, 645 for male rats; 1,204 for female mice, 1,180 for female mice).

The LD_{50} values and doses resulting in death from each reliable study in each species in the acute-duration category are recorded in Table 2-2 and plotted in Figure 2-2.

2.2.2.2 Systemic Effects

The highest NOAEL values and all LOAEL values from each reliable study for systemic effects in each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2.

Respiratory Effects. Stajduhar-Caric (1968) reported on a case in which a woman who ingested ~10-20 g of phenol, became comatose and died within a matter of hours. During the course of the poisoning and treatment, initially an increase in respiration was observed, then irregularities in breathing, and finally cessation of respiration. Upon autopsy, marked hyperemia of the tracheal and bronchial mucous membranes were observed as well as pulmonary edema. According to Deichmann and Keplinger (1981), the progression of impacts on the respiratory system summarized above are typical of oral poisonings in humans, although

often the intermediate stages are characterized by a decrease in respiration rate and magnitude. According to these authors, in acute intoxication, death usually results from respiratory failure.

Dyspnea and rales were observed in pregnant rats treated by gavage with phenol in water on gestation days 6-19 (Narotsky and Kavlock 1995). The respiratory effects were observed at both 40 and 53.3 mg/kg/day. Furthermore, developmental toxicity occurred on the litters of 1 of 5 low-dose and 3 of 16 high-dose dams that exhibited these effects, although not all dams with severe respiratory effects had abnormal outcomes.

Gross pathological examinations did not reveal any adverse changes in the lungs of mice treated with phenol in drinking water at doses of 1.8, 6.2, or 33.6 mg/kg/day for 28 days (Hsieh et al. 1992).

In a study reported by the National Cancer Institute (NCI 1980), rats exposed to 16-1,694 mg/kg/day (100-10,000 mg/L) and mice exposed to 25-2,642 mg/kg/day (100-10,000 mg/L) phenol in drinking water exhibited no indication of histopathological effects on the respiratory system after 13 weeks of exposure. No histological abnormalities of the respiratory tract were observed in rats or mice exposed to 2,500 or 5,000 ppm phenol in drinking water for 103 weeks (mg/kg/day doses: 322 or 645 for male rats; 360 or 721 for female rats; 590 or 1,180 for male mice; 602 or 1,204 for female mice) (NCI 1980).

Cardiovascular Effects. In a recent report on the clinical treatment of phenol poisoning, Langford et al. (1998) provide a summary of a case report in which a woman accidentally consumed an ounce of 89% phenol which had been mistakenly been given to her in preparation for an in-office procedure. Her immediate reaction upon consuming the phenol was to clutch her throat and collapse, and within 30 minutes she was comatose and had gone into respiratory arrest. Treatment was initiated with an endotracheal intubation. Ventilation with a bag and mask led to the detection of a lamp oil odor. Within an hour she developed ventricular tachycardia which responded to cardioversion; however, she subsequently developed (in the first 24 hours) supraventricular and ventricular dysrhythmias, metabolic acidosis, and experienced a grand mal seizure. After a 15-day hospital stay, she was completely recovered with no evidence of impaired motility or compromised gastrointestinal or cardiovascular systems.

Gross pathological examinations did not reveal any adverse changes in the hearts of mice treated with phenol in drinking water at doses of 1.8, 6.2, or 33.6 mg/kg/day for 28 days (Hsieh et al. 1992). In a study reported by the National Cancer Institute (NCI 1980), rats exposed to 16-1,694 mg/kg/day (100-10,000 ppm) and

mice exposed to 25-2,642 mg/kg/day (100-10,000 ppm) phenol in drinking water exhibited no indication of histopathological effects on the heart after 13 weeks of exposure. Histological abnormalities of the heart were not evident in rats after 103 weeks of exposure to 322 or 645 mg/kg/day for males or 360 or 721 mg/kg/day for females (2,500 or 5,000 ppm) or in mice after exposure to 590 or 1,180 mg/kg/day for males or 602 or 1,204 mg/kg/day for females (2,500 or 5,000 ppm). Cardiovascular function was not evaluated in these studies.

Gastrointestinal Effects. In a recent study on the clinical treatment of phenol poisoning, Langford et al. (1998) provide a summary of a case report in which a woman accidentally consumed an ounce of 89% phenol which had been mistakenly been given to her in preparation for an in-office procedure. Her immediate reaction upon consuming the phenol was to clutch her throat and collapse, and within 30 minutes she was comatose and had gone into respiratory arrest. Treatment was initiated with an endotracheal intubation, which revealed her mouth and hypopharynx to be white. Esophagitis and upper gastrointestinal bleeding occurred in the first week, and an examination of the esophagus on day 8 revealed hyperkeratosis, erythema, and a friable muchosa. After a 15-day hospital stay, she was completely recovered with no evidence of impaired motility or compromised gastrointestinal system.

In a retrospective study of 158 persons exposed to phenol in drinking water for several weeks following an accidental spill of phenol, significantly ($p<0.01$) increased gastrointestinal symptoms (mouth sores, nausea, diarrhea) were reported by 17 of the 39 most highly-exposed individuals (Baker et al. 1978). Exposure concentrations for the most highly-exposed group were >0. 1 mg/L, and the study authors estimated phenol intake during this period as 10-240 mg/person/day (0.14-3.4 mg/kg/day assuming a 70-kg body weight). Symptom rates were not increased among 61 persons exposed to concentrations of 0.1 mg/L (0.003 mg/kg/day assuming 2 L water per day and a 70-kg body weight) and less. Dermal exposure was not considered in these estimates of dose.

A case control study of 6,913 individuals living near a Korean river contaminated with 30 tons of 100% phenol found nausea, vomiting, diarrhea, and abdominal pain among 1,824 exposed subjects compared to 1,064 unexposed subjects (Kim et al. 1994). The level of phenol measured in the two reservoirs that served the community was 0.05 mg/L after the spill, while that in the chlorinated tap water was 0.0084 mg/L. It is uncertain whether the chlorination process may have converted a majority of the phenol to chlorophenol, thus possibly implicating this chemical as the cause of the effects.

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In a study reported by the National Cancer Institute (NCI 1980) rats exposed to 16-1,694 mg/kg/day and mice exposed to 25-2,642 mg/kg/day phenol in drinking water exhibited no indication of histopathological effects on the gastrointestinal system after 13 weeks of exposure. No histological abnormalities of the gastrointestinal tract were observed in rats or mice exposed to 2,500 or 5,000 mg/L phenol in drinking water for 103 weeks (mg/kg/day doses: 322 or 645 for male rats; 360 or 721 for female rats; 590 or 1,180 for male mice; 602 or 1,204 for female mice) (NCI 1980).

Hematological Effects. No studies were located regarding hematological effects in humans following oral exposure to phenol.

A 30-60% decrease in the ratio of polychromatic to normochromatic erythrocytes was observed in the bone marrow of pregnant mice treated by gavage with a single dose of 265 mg/kg phenol in water on gestation day 13 (Ciranni et al. 1988). Dose-related and significant decreases in red blood cell counts were observed in mice treated with phenol in the drinking water at doses of 1.8,6.2, or 33.6 mg/kg/day for 28 days (Hsieh et al. 1992). Red blood cell counts in cells x $10^6/mm^3$ were 7.17 in controls, 4.9 at the low dose, 4.64 at the middle dose, and 3.23 at the high dose. A significant decrease in hematocrit was only observed at the high dose (48% control, 44.1% high dose), and no changes were observed in total spleen cellularity, leucocyte numbers, or leucocyte differentials.

Musculoskeletal Effects. No studies were located regarding musculoskeletal effects in humans following oral exposure to phenol.

Rats exposed to 16-1,694 mg/kg/day (100-10,000 mg/L) and mice exposed to 25-2,642 mg/kg/day (100-10,000 mg/L) phenol in drinking water exhibited no histological abnormalities of the bone after 13 weeks of exposure (NCI 1980). No histological abnormalities of the bone were observed in rats or mice exposed to 2,500 or 5,000 mg/L phenol in drinking water for 103 weeks (mg/kg/day doses: 322 or 645 for male rats; 360 or 721 for female rats; 590 or 1,180 for male mice; 602 or 1,204 for female mice) (NCI 1980).

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Hepatic Effects. Serum markers of liver effects, bilirubin, glucose, cholesterol, and aspartate aminotransferase were not affected in 39 persons exposed to phenol in the drinking water at an estimated dose of 0.14-3.4 mg/kg/day for several weeks (Baker et al. 1978). Because these examinations were completed 7 months after the spill, this study does not provide conclusive evidence that there was no reversible liver damage.

Serum markers of liver effects (lactic dehydrogenase, alkaline phosphatase, alanine aminotransferase, bilirubin) and histopathological changes in the liver were observed in rats given single gavage doses of 224 mg/kg or 14 daily gavage doses of 40 mg/kg phenol in water (Berman et al. 1995). Changes in liver weight were not observed in pregnant rats treated by gavage with 120 mg/kg/day phenol in water on gestation days 6-15 (Jones-Price et al. 1983a), or in pregnant mice treated by gavage with 280 mg/kg/day phenol in water on gestation days 6-15 (Jones-Price et al. 1983b).

Gross pathological examinations did not reveal any lesions in mice treated with phenol in the drinking water at a dose of 33.6 mg/kg/day for 28 days (Hsieh et al. 1992).

In a study sponsored by the National Cancer Institute (NCI 1980), rats exposed to 16-1,694 mg/kg/day (100-10,000 ppm) and mice exposed to 25-2,642 mg/kg/day (100-10,000 ppm) phenol in drinking water exhibited no histological abnormalities of the liver after 13 weeks of exposure. No histological abnormalities of the liver were observed in rats or mice exposed to 2,500 or 5,000 ppm phenol in drinking water for 103 weeks (NCI 1980). Estimated mg/kg/day doses were 322 or 645 for male rats, 360 or 721 for female rats, 590 or 1,180 for male mice, and 602 or 1,204 for female mice.

Renal Effects. Although not adverse, dark urine (as a result of oxidation products of phenol or a result of hemoglobin or its breakdown products in the urine) is a common symptom observed in humans exposed to phenol. In persons exposed to about 0.14-3.4 mg/kg/day phenol in drinking water for several weeks after an accidental spill, dark urine was reported by 17.9% of the most highly-exposed individuals, while only 3.4% of the controls reported the effect (Baker et al. 1978). This difference was not statistically significant. A 3.3-fold increase in the prevalence of dark urine was reported by persons exposed to unspecified doses of phenol after an accidental spill in Korea (Kim et al. 1994). It is not known if the chlorination process, which may have converted a majority of the phenol to chlorophenol, contributed to this effect.

2.HEALTH EFFECTS

Renal tubular necrosis, protein casts, and papillary hemorrhage were not observed in rats treated with a single gavage dose of 120 mg/kg phenol in water, but were seen in 60% of animals examined at the next highest dose of 224 mg/kg (Berman et al. 1995). No histopathological changes in the kidney were observed after 14 daily doses of 12 mg/kg/day, but were observed in 3 of 8 animals given 14 daily doses of 40 mg/kg/day (Berman et al. 1995).

Gross pathological examinations did not reveal any adverse changes in the kidneys of mice treated with phenol in drinking water at doses of 1.8, 6.2, or 33.6 mg/kg/day for 28 days (Hsieh et al. 1992).

Rats exposed to 16-1,694 mg/kg/day (0.1-10 mg/L) and mice exposed to 25-2,642 mg/kg/day (100-10 mg/L) phenol in drinking water exhibited no indication of histopathological effects on the kidney after 13 weeks of exposure (NCI 1980). Compound-related histological changes in the kidneys were not observed in rats or mice exposed to 2,500 or 5,000 ppm phenol in drinking water for 103 weeks (NCI 1980). Estimated mg/kg/day doses were 322 or 645 for male rats, 360 or 721 for female rats, 590 or 1,180 for male mice, and 602 or 1,204 for female mice. A higher incidence of inflammation of the kidney was reported in male rats exposed to 624 mg/kg/day (96%) than in controls (74%); however, because of the high incidence of inflammation in the controls, it is impossible to ascertain whether this was related to the exposure to phenol (NCI 1980). A high age-related incidence of inflammation is expected in male rats of the Fischer-344 strain used in this study. Kidney function, including glomerular filtration rate and glomerular sieving, however, was not evaluated in this study. Furthermore, histological examination was limited to standard light microscopic examinations which would not have detected functionally significant glomerular abnormalities like disruption of the glomerular basement membrane or immune complex deposition.

Endocrine Effects. No studies were located regarding endocrine effects in humans following oral exposure to phenol.

Unspecified microscopic changes were observed in the adrenal glands of rats given a single gavage dose of 224 mg/kg phenol in water (Berman et al. 1995). No adrenal gland effects were observed in rats given a single gavage dose of 12,40, or 120 mg/kg or 14 daily gavage doses of 4, 12, or 40 mg/kg (Berman et al. 1995).

Rats exposed to 16-1,694 mg/kg/day (100-10,000 mgL) and mice exposed to 25-2,642 mg/kg/day (100-10,000 mg/L) phenol in drinking water exhibited no histopathological changes in the pancreas,

pituitary, adrenal glands, thyroid, or parathyroid after 13 weeks of exposure (NCI 1980). Exposure-related histopathological changes in the pancreas, pituitary, adrenal glands, thyroid, or parathyroid were also not observed in rats and mice exposed to 2,500 or 5,000 ppm phenol in drinking water for 103 weeks (NCI 1980). Estimated mg/kg/day doses were 322 or 645 for male rats, 360 or 721 for female rats, 590 or 1,180 for male mice, and 602 or 1,204 for female mice.

Dermal Effects. Skin rash and mouth sores were reported in persons living near a site with contaminated well water resulting from an overturned tanker car carrying 37,900 L of 100% phenol (Baker et al. 1978). The level of phenol in the drinking water of this cohort was >0.1 mg/L, and while substantial oral exposure probably occurred, dermal exposure cannot be ruled out. Increases in the prevalence of skin rashes and sore throats were reported by persons drinking water from a river contaminated by an accidental spill of phenol (Rim et al. 1994). Because the water was chlorinated before use, the effect may also have been a result of exposure to chlorophenol.

Rats exposed to 16-1,694 mg/kg/day (100-10,000 mg/L) and mice exposed to 25-2,642 mg/kg/day (100-10,000 mg/L) phenol in drinking water exhibited no histopathological changes in the skin after 13 weeks of exposure (NCI 1980). Exposure-related histopathological changes in the skin were also not observed in rats and mice exposed to 2,500 or 5,000 mg/L phenol in drinking water for 103 weeks (NCI 1980). Estimated mg/kg/day doses were 322 or 645 for male rats, 360 or 721 for female rats, 590 or 1,180 for male mice, and 602 or 1,204 for female mice.

Ocular Effects. No studies were located regarding ocular effects in humans or animals following oral exposure to phenol.

Body Weight Effects. No effects on body weight were observed in rats treated with a single gavage dose of 224 mg/kg phenol in water or 14 daily gavage doses of 40 mg/kg (Berman et al. 1995; Moser et al. 1995). Maternal body weight gain was approximately 20% lower in rats treated by gavage with 40 or 53.3 mg/kg/day phenol in water on gestation days 6-19 (Narotsky and Kavlock 1995). Maternal body weight gain was 67% lower than controls in mice treated by gavage with 280 mg/kg/day phenol in water on gestation days 6-15, with no effects on body weight gain observed at 140 mg/kg/day (Jones-Price et al. 1983b). Body weight gain was not affected in pregnant rats treated by gavage with 120 mg/kg/day phenol in water on gestation days 6-15 (Jones-Price et al. 1983a).

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Body weight was not affected in mice treated with phenoP in drinking water at a dose of 33.6 mg/kg/day for 28 days (Hsieh et al. 1992). During 13-week studies in rats and mice treated with phenol in drinking water, decreased body weight gain was associated with decreased water intake (NCI 1980). In rats provided with the highest concentration (10,000 ppm), body weight gain was decreased by 26% in females at 1,694 mg/kg/day, and by 16% in males at 1,556 mg/kg/day. An effect on body weight gain was not observed in rats at 3,000 ppm (467 mg/kg/day for males, 508 mg/kg/day for females). In mice provided with the highest concentration (10,000 ppm), body weight gain was decreased by 33% in females at 2,642 mg/kg/day, and by 80% in males at 2,468 mg/kg/day. An effect on body weight gain was not observed in mice at 3,000 ppm (741 mg/kg/day for males, 793 mg/kg/day for females).

Decreased mean body weight associated with decreased water intake was also observed in rats in a 103-week study (NCI 1980). At the high concentration (5,000 ppm), body weight was 19% lower than controls in males (645 mg/kg/day) and 17% lower than controls in females (721 mg/kg/day). At the low concentration (2,500 ppm), body weight was 12% lower than controls in males (322 mg/kg/day) and within 10% of controls in females (360 mg/kg/day). Body weight was not affected in mice treated with phenol in drinking water for 103 weeks at doses up to 1,180 for males and up to 1,204 mg/kg/day for females (NCI 1980).

2.2.2.3 Immunological and Lymphoreticular Effects

No studies were located regarding immunological or lymphoreticular effects in humans following oral exposure to phenol.

Necrosis or atrophy of the spleen or thymus was observed in 4 of 6 rats given a single gavage dose of 224 mg/kg of phenol in water, and 1 of 7 given 120 mg/kg/day (Berman et al. 1995). Based on this effect, which was not further described, the study authors considered 224 mg/kg to be a LOAEL for immunological effects. One of 8 animals given 12 mg/kg/day, and 2 of 8 given 40 mg/kg/day for 14 days showed these same effects.

Hsieh et al. (1992) conducted a 28 day study of the immunotoxicologic impact of phenol in which CD-1 mice were provided drinking water at nominal concentrations of 0, 5, 20, or 100 mg/L (measured concentrations of 4.7, 19.5, and 95.2 mg/L; equivalent doses of 0, 1.8, 6.2, or 33.6 mg/kg/day). When challenged with sheep red blood cells, a significant decrease was observed in the splenic concentration of anti-erythrocyte antibody-forming cells and in the anti-erythrocite antibody titer at the two highest doses, while a significant decrease in

the absolute number of anti-erythrocyte antibody-forming cells present in the spleen was observed only at the top dose.

Rats exposed to 16-1,694 mg/kg/day (100-10,000 ppm) and mice exposed to 25-2,642 mg/kg/day (100-10,000 ppm) phenol in drinking water exhibited no histopathological changes in the bone marrow, spleen, or lymph nodes after 13 weeks of exposure (NCI 1980). Exposure-related histopathological changes in the bone marrow, spleen, or lymph nodes were also not observed in rats or mice exposed to 2,500 or 5,000 ppm phenol in drinking water for 103 weeks (NCI 1980). Estimated mg/kg/day doses were 322 or 645 for male rats, 360 or 721 for female rats, 590 or 1,180 for male mice, and 602 or 1,204 for female mice.

The highest NOAEL values and all LOAEL values from each reliable study for immunological and lymphoreticular effects in each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2.

2.2.2.4 Neurological Effects

Headaches were reported six times more frequently by persons using drinking water contaminated with phenol than by controls (Rim et al. 1994). The water was used after chlorination; therefore, chlorophenol may have contributed to the observed effects.

Acute oral phenol poisoning in rabbits and rats was characterized by muscular tremors in the head region, which eventually spread to other regions of the body, with the lower extremities being the last affected. loss of coordination and convulsions preceded death at doses of 300-940 mg/kg (Deichmann and Witherup 1944). Liao and Oehme (1981) described tremors of the muscles around the eyes, followed by convulsions and coma, in rats after a sublethal oral dose of 207 mg/kg phenol. Mild-to-severe whole-body tremors and decreased motor activity were reported in rats given a single gavage dose of 120 mg/kg phenol in water (Moser et al. 1995). A dose of 40 mg/kg resulted in no neurological effects following a single dose, while increased rearing was reported following 14 daily doses (Moser et al. 1995). Pregnant mice treated by gavage with phenol in water on gestation days 6-15 exhibited tremors and ataxia at 280 mg/kg/day, mild tremors on the first 3 days of dosing at 140 mg/kg/day, and no adverse neurological effects at 70 mg/kg/day (Jones-Price et al. 1983b).

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Mice exposed for 28 days to phenol in drinking water exhibited a significant reduction in dopamine level in the corpus striatum at the 1.8 mg/kg/day dose, and significantly decreased levels of norepinephrine, serotonin, and Shydroxyindoleacetic acid in the hypothalamus at the 6.2 mg/kg/day dose (Hsieh et al. 1992). Levels of neurotransmitters in other brain regions were also significantly altered at higher doses of phenol.

Rats exposed to 16-1,694 mg/kg/day and mice exposed to 25-2,642 mg/kg/day phenol in drinking water exhibited no abnormal histology of the brain after 13 weeks of exposure (NCI 1980). Histopathological changes in the brain were not evident after 103 weeks of exposure to 322 or 645 mg/kg/day in male rats, 360 or 721 mg/kg/day in female rats, 590 or 1,180 mg/kg/day in male mice, and 602 or 1,204 mg/kg/day in female mice (NCI 1980). However, this study did not include tests for neurological impairment or histopathological examinations of tissues in the nervous system other than the brain.

The highest NOAEL values and all LOAEL values from each reliable study for neurological effects in each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2.

2.2.2.5 Reproductive Effects

No studies were located regarding reproductive effects in humans following oral exposure to phenol.

No effects on the number of offspring produced were observed in rats treated by gavage with 120 mg/kg/day phenol (Jones-Price et al. 1983a) or in mice treated by gavage with 280 mg/kg/day phenol (Jones-Price et al. 1983b) on gestation days 6-15. No evidence of impaired reproduction was found in rats exposed to phenol in drinking water at <5,000 ppm (estimated 571 mg/kg/day) for 3 generations or at <1,000 ppm (estimated 114 mg/kg/day) for 5 generations (Heller and Pursell 1938). Data regarding breeding habits, controls, and the methods used to evaluate the rats for reproductive impairment were not reported in sufficient detail to establish reliable NOAELs or LOAELs for presentation in Table 2-2 and Figure 2-2.

Rats exposed to 16-1,694 mg/kg/day (100-10,000 ppm) and mice exposed to 25-2,642 mg/kg/day (100-10,000 ppm) of phenol in drinking water exhibited no histopathological changes in the prostate, testes, uterus, or ovaries after 13 weeks of exposure (NCI 1980). Exposure-related histopathological changes in the prostate, testes, uterus, or ovaries were also not observed in rats or mice exposed to 2,500 or 5,000 ppm phenol in drinking water for 103 weeks (NCI 1980). Estimated mg/kg/day doses were 322 or 645 for male rats, 360 or 721 for female rats, 590 or 1,180 for male mice, and 602 or 1,204 for female mice.

2. HEALTH EFFECTS

The highest NOAEL values from each reliable study for reproductive effects in each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2.

2.2.2.6 Developmental Effects

No studies were located regarding developmental effects in humans following oral exposure to phenol.

In a multi-generational study of the effect of various levels of phenol administered orally in water, Heller and Pursell (1938) saw no effect on growth, reproduction, and normal rearing of young over 5 generations of rats given concentrations of ~1,000 mg/L phenol in drinking water (estimated dose of 114 mg/kg/day) nor over 3 generations of rats given concentrations of ~5,000 ppm (estimated dose 571 mg/kg/day). CD rat dams given doses as high as 120 mg/kg showed no maternal toxicity at any dose. There was, however, a dose related decrease in the average live fetal body weight per litter increase in the proportion of gravid uteri with resorption sites at the low- (30 mg/kg/day) and mid-dose (60 mg/kg/day), but not at the high-dose group.

Phenol in water was administered to pregnant rats by gavage (5 mL/kg) at dose levels of 0,30,60, or 120 mg/kg/day on days 6-15 of gestation (Jones-Price et al. 1983a). A dose-related decrease in fetal body weight with increasing dose was observed, with 60 mg/kg/day established as the NOAEL and 120 mg/kg/day as the LOAEL. Teratogenic effects were not observed and no signs of maternal toxicity were observed at any dose level. In a preliminary range-finding study conducted by Jones-Price et al. (1983a), a decrease in maternal weight gain and an increased incidence of maternal mortality were observed at >160 mg/kg. Tremors, a typical symptom of phenol toxicity, were also observed.

In a study of the developmental toxicity of substituted phenols, Kavlock (1990) examined the effects of 0, 100, 333, 667 and 1,000 mg/kg phenol given by gavage on day 11 of gestation. Twenty-seven chemicals were tested in this study. In order for the data to be comparable, a single vehicle was used consisting of a 4:4:1:1 mixture of water, Tween 20, propylene glycol, and ethanol. Because of the massive quantities of data such a study generates, the author focused his analytic efforts on five key variables, four of which were sampled at two time points. The 5 variables were maternal weight change (at 24 and 72 hours post-dosing), litter size (postnatal day [PD] 1 and 6), perinatal loss, pup weight (in g on PD 1 and 6), and litter biomass (in g on PD 1 and 6).

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Within these five parameters, a significant impact of phenol dosing was seen only on maternal weight change, and only at the two highest doses. However, at these same doses, a syndrome of malformations involving the limbs and tail was seen. At a dose of 667 mg/kg, pups in 21.4% of the litters were affected. (At a dose of 1,000 mg/kg, pups in 27.3% of the litters were affected.) The effect on tails was one of shortening or crimping (i.e., 'kinky' tails). The hindlimb effect consisted of paralysis and/or palsy. In animals with palsy, the limb function would alternate between normal strides and a several second-long period of tetany. Because limb function matures postnatally, this effect was not evident in the newborn but required 7-10 days to become obvious. In the case of phenol, the syndrome did not interfere with postnatal growth and viability; thus, by the statistical criteria used in the report to categorize developmental potency, phenol was not considered an active developmental toxicant.

In a subsequent study, Narotsky and Kavlock (1995) found that a significant decrease in the number of livebom pups associated with severe respiratory effects in the dams was observed in pregnant rats treated by gavage with 53.3 mg/kg/day phenol in water on gestation days 6-19. In addition, in one high dose litter, two of four surviving pups had kinked tails; this finding was not analyzed for significance but was consistent with earlier observations (Kavlock 1990) and may reflect a teratogenic effect of phenol. Developmental effects were not significant at 40 mg/kg/day.

Phenol in water was administered to pregnant mice by gavage (10 mL/kg) at dose levels of 0,70, 140, or 280 mg/kg/day on days 6-15 of gestation (Jones-Price et al. 1983b). Decreased maternal weight gain, tremors, and increased maternal mortality were observed at 280 mg/kg/day. In the fetuses, growth retardation, decreased prenatal viability, abnormal structural development, and an increased incidence of cleft palate were observed at 280 mg/kg/day. Developmental effects were not observed at 140 mg/kg/day. In pregnant mice that received 265 mg/kg phenol by gavage on day 13 of gestation, Ciranni et al. (1988) found no evidence of fetal cellular toxicity, as measured by a reduction in the polychromatic erythrocyte/normochromatic erythrocyte

The highest NOAEL values and all LOAEL values from each reliable study for developmental effects in each species in the acute-duration category are recorded in Table 2-2 and plotted in Figure 2-2.

2. HEALTH EFFECTS

2.2.2.7 Genotoxic Effects

No studies were located regarding genotoxic effects in humans following oral exposure to phenol.

In pregnant female mice given 265 mg/kg phenol by gavage on day 13 of gestation, Ciranni et al. (1988) found no evidence of genotoxicity, as measured by an increase in micronuclei in maternal bone marrow or fetal liver.

An increase in DNA synthesis was observed in the kidneys of suckling mice treated by gavage with a dose of phenol 15-50% of the LD_{50} (Amlacher and Rudolph 1981). DNA synthesis in the liver of mice treated by gavage with a single dose of 300 or 600 mg/kg phenol was not affected (Miyagawa et al. 1995).

Spermatocytes were examined for chromosomal aberrations in mice from a multigeneration study (Bulsiewicz 1977). The mice were treated by gavage with phenol in water at concentrations of 0, 0.08, 0.8, or 8 mg/L (approximately 0.006, 0.06, or 0.6 mg/kg/day). Both male and female mice were treated for 30 days before mating. Female mice continued to receive phenol during gestation and lactation; this procedure was repeated for five generations. Three F_3 and F_5 mice treated with 0.8 mg/kg/day became moribund and refused to eat and were killed before the end of the study. No spermatocytes from these mice were available for examination. The lack of spermatogenesis in these mice is probably secondary to their poor health rather than a direct effect of phenol. Chromosomal aberrations were detected in 27% of the spermatogonia and 5% of the primary spermatocytes in the 0.006 mg/kg/day group, in 52% of the spermatogonia and 22% of the primary spermatocytes in the 0.06 mg/kg/day group, and in 81% of the spermatogonia and 24% of the primary spermatocytes in the 0.6 mg/kg/day group. No data on the control group were provided. The study focused on chromosomal aberrations; no information on the reproductive success, teratogenicity, or any other health effects in exposed mice was reported.

Other genotoxicity studies are discussed in Section 2.5.

2.2.2.8 Cancer

No studies were located regarding carcinogenicity in humans following oral exposure to phenol.

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The carcinogenicity of orally administered phenol was examined in rats and mice in a study reported by the National Cancer Institute (NCI 1980). Rats and mice received 0,2,500, or 5,000 ppm in drinking water for 103 weeks. Calculated intakes for rats were 322 and 645 mg/kg/day for males and 360 and 721 mg/kg/day for females. Calculated intakes for mice were 590 and 1,180 mg/kg/day for males and 602 and 1,204 mg/kg/day for females. Statistically significant increased incidences of pheochromocytomas of the adrenal gland and leukemia or lymphomas were observed in male rats exposed to 322 mg/kg/day (2,500 ppm), but not in male rats exposed to 645 mg/kg/day (5,000 ppm). No significant effects were seen in female rats or mice of either sex exposed to either exposure level. Since cancer occurred only in males of one of the two species tested and a positive dose-response relationship could not be established, these results are inconclusive regarding the carcinogenic potential of orally administered phenol.

2.2.3 Dermal Exposure

2.2.3.1 Death

Application of phenol to the skin can be lethal. Death occurred within 10 minutes after ≈25% of an individuals body surface was exposed to liquid phenol (Griffiths 1973). The cause of death was reported to be cardiac and respiratory depression. In another report, an individual died after being painted with a brush that had been soaked in a solution of phenol and thoroughly washed before use (Lewin and Cleary 1982). In neither case was the dose known with sufficient accuracy to establish a lethal dose.

A 10-year-old boy was hospitalized with serious burns; during the next 2.5 days his burns were treated by applying 7.5 L of an antiseptic solution containing 2% phenol; his urine became dark, respiration became labored, he fell into a coma, and died. *Post mortem* analysis of urine showed 200 mg/L of conjugated phenol (Cronin and Brauer 1949).

Lethality associated with dermal exposure to phenol is greatly influenced by the surface area exposed as well as the concentration of the applied solution. Mortality can vary depending on concentration; a dose of 100% phenol may be less toxic than the same dose of phenol given as a diluted solution. When a dose of 53.5 mg/kg was applied to the shorn backs of rats, 100% phenol resulted in the death of 1 of 5 rats, 33% resulted in the death of 3 of 5 rats, 50% resulted in the death of 4 of 5 rats, and 66% phenol resulted in the death of all 5 rats (Conning and Hayes 1970). Iu rats treated with 3,000 mg/kg phenol in a 6% solution over l/6 of the total body surface, all 22 treated animals died (Deichmann and Witherup 1944). Increased lethality

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with decreased concentration has also been observed in rabbits treated dermally with 2,000 mg/kg; 95% phenol resulted in the death of 53% of treated rabbits, while 10% phenol in water resulted in the death of 100% of treated rabbits (Deichmann and Witherup 1944). The cause of death was not stated in these studies.

In rats given a single treatment of 5% phenol in water to achieve a dose of 3,000 mg/kg, 10-day-old rats were more sensitive than 5-week-old rats or adult rats (Deichmann and Witherup 1944). Within 2-14 hours after dosing, 13 of twenty 10 day-old rats died; 5 of twenty 5-week-old rats died 2-3 hours after dosing, and 9 of 20 adult rats died 30-180 minutes after dosing.

The dermal LD_{50} of undiluted phenol in rats was reported to be 669.4 mg/kg (Conning and Hayes 1970). The LD_{50} of an unspecified concentration of phenol in rabbits was reported to be 1,400 mg/kg (Vernot et al. 1977). Flickinger (1976) determined a dermal LD_{50} by exposing male albino rabbits to 0, 252, 500, 1,000, or 2,000 mg/kg phenol which was placed "in contact" with "abraded and intact skin for a maximum period of 24 hours." No animals died in the 0, 252, or 500 mg/kg groups whereas 3 of 4 in the 1,000 mg/kg group and all in the 2,000 mg/kg group died the first day following dosing. From these data the authors estimated a "single dose skin penetration LD_{50} of 850 mg/kg.

Among pigs treated with a single dose of 500 mg/kg of undiluted phenol on 35-40% of the total body surface (about 1,136 cm^2; 0.44 $mg/cm^2/kg$), 2 of 3 died (Pullin et al. 1978). The study authors reported that a general state of lethargy, cyanosis, convulsions, and coma were observed 5-7 minutes before death.
No effects on survival were observed in mice treated dermally with an unspecified volume of 5% phenol (3 times/week) or 10% phenol (2 times/week) in acetone for 12 months (Wynder and Hoffmann 1961). Pretreatment with a single dose of 7,12-dimethylbenz[a]anthracene (DMBA) followed by phenol resulted in increased skin tumors and decreased survival.

All LOAEL and LD_{50} values from each reliable study are recorded in Table 2-3.

TABLE 2-3. Levels of Significant Exposure to Phenol - Dermal[a]

Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/cm2/kg)	LOAEL			Reference
				Less Serious (mg/cm2/kg)	Serious (mg/cm2/kg)		
ACUTE EXPOSURE							
Death							
Rat (Alderly Park)	24 hr				669.4 mg/kg	F (LD_{50})	Conning and Hayes 1970
Rat (Wistar)	once				3000 mg/kg	(13/20 deaths 10-day-old, 5/20 deaths 5-week-old, 9/20 deaths adult)	Deichmann and Witherup 1944
Rabbit (New Zealand)	NS				1400 mg/kg	F (LD_{50})	Vernot et al. 1977
Pig (Mixed breed)	24 hr				0.44	F (2/3 died)	Pullin et al. 1978
Systemic							
Human	1 hr	Cardio			75 mg/kg	M (cardiac arrhythmia)	Warner and Harper 1985

TABLE 2-3. Levels of Significant Exposure to Phenol - Dermal (continued)[a]

Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/cm2/kg)	LOAEL Less Serious (mg/cm2/kg)	LOAEL Serious (mg/cm2/kg)	Reference
Rat (Alderly Park)	24 hr	Renal			107.1 F mg/kg (severe hemoglobinuria, hematin casts in the tubules)	Conning and Hayes 1970
		Dermal			107.1 F mg/kg (severe edema, coagulative necrosis, erythema)	
Mouse (ICR)	once	Dermal	12 F	15 F (skin irritation indicated by thickening of treated ear)		Patrick et al. 1985
Rabbit (NS)	once	Cardio			23.8 M (cardiac arrhythmias, ventricular tachycardia)	Wexler et al. 1984
Pig (Mixed breed)	24 hr	Resp			0.44 F (dyspnea)	Pullin et al. 1978
		Dermal			0.44 F (necrosis of the skin)	
Neurological						
Rat (Alderly Park)	24 hr				107.1 F mg/kg (severe muscle tremors, marked twitching, generalized convulsions, loss of consciousness and prostration)	Conning and Hayes 1970

TABLE 2-3. Levels of Significant Exposure to Phenol - Dermal (continued)[a]

Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/cm2/kg)	LOAEL			Reference
				Less Serious (mg/cm2/kg)	Serious (mg/cm2/kg)		
Pig (Mixed breed)	24 hr				0.44 F	(twitching, tremors)	Pullin et al. 1978
INTERMEDIATE EXPOSURE							
Cancer							
Mouse (S albino)	24-32 wk 1 x/wk				20%	(CEL: skin tumor promotor)	Salaman and Glendenning 1957
CHRONIC EXPOSURE							
Death							
Mouse (Swiss)	15 mo 2-3 x/wk						Wynder and Hoffmann 1961
Cancer							
Mouse (Swiss)	15 mo 2-3 x/wk				5%	(CEL: skin tumor promotor)	Wynder and Hoffmann 1961

[a]Studies in which dose units could not be expressed as mg/cm^2/kg have their dose units listed following the dose levels.

Cardio = cardiovascular; CEL = cancer effect level; F = female; hr = hour(s); LD_{50} = lethal dose (50% kill); LOAEL = lowest-observed-adverse-effect level; M = male; mo = month(s); NOAEL = no-observed-adverse-effect level; NS = not specified; Resp = respiratory; wk = week(s); x = time(s)

2. HEALTH EFFECTS

2.2.3.2 Systemic Effects

The highest NOAEL values and all LOAEL values from each reliable study for systemic effects in each species and duration category are recorded in Table 2-3.

Respiratory Effects. No studies were located regarding respiratory effects in humans following dermal exposure to phenol.

Dyspnea was reported in pigs treated with a single dose of 500 mg/kg of undiluted phenol over 35-40% of the total body surface area (0.44 mg/cm^2/kg) (Pullin et al. 1978). This treatment resulted in the death of two of the three treated pigs.

Cardiovascular Effects. There have been several reports of cardiac arrhythmias associated with application of phenol solutions to the skin in connection with the surgical procedure of skin peeling (Gross 1984; Truppman and Ellenby 1979; Warner and Harper 1985). In this procedure, a mixture of phenol (≈50% w/v), hexachlorophene, and croton oil is applied to the skin while the patient is under anesthesia. In a series of 54 patients in which the whole face was peeled in 1 day, cardiac arrhythmias were reported in 39%, while in a series of patients in which half the face was treated on 1 day, and the second half was treated 24 hours later, cardiac arrhythmias were reported in 22% (Gross 1984). The study author also indicated that the arrhythmias were less severe in the patients treated over a longer period of time.

Cardiac arrhythmia and bradycardia were reported in a man that splashed an unspecified concentration of a phenol-water solution over his face, chest wall, hand, and both arms (Horch et al. 1994). The cardiac effects were noted during the first 6 hours after exposure. The serum levels of phenol in µg/L were 11,400 after 1 hour, 17,400 after 4 hours, and 6,000 after 8 hours.

Cardiac arrhythmia has also been noted in rabbits treated with 2 mL of a 50% phenol solution on a 15-cm2 area (23.8 mg/cm^2/kg) (Wexler et al. 1984). Reducing plasma concentrations of phenol by forced diuresis or a longer application time reduced the cardiac effects.

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Gastrointestinal Effects. During the first few days after a man splashed a phenol-water solution (concentration not stated) on his face, chest wall, hand, and both arms, he complained of nausea and vomited twice (Horch et al. 1994). A worker who was partially immersed for only a few seconds in a shallow vat containing a mixture of 40% phenol in dichloromethane, collapsed after showering and was taken to a hospital where he was found to have burns over 50% of his body. Initial observations were stable; however, after drinking fluids, he developed nausea and vomiting (Foxall et al. 1989).

No studies were located regarding gastrointestinal effects in animals following dermal exposure to phenol.

Hematological Effects. No studies were located regarding hematological effects in humans following dermal exposure to phenol.

Hemoglobinuria and hematin casts were reported in the renal tubules of rats treated dermally with 107.7 mg/kg phenol (Conning and Hayes 1970). These observations are indicative of red blood cell hemolysis; however, this was not confirmed with hematological examinations.

Musculoskeletal Effects. Muscle pain in the arms and legs was reported in a case of chronic phenol poisoning (Merliss 1972). The man worked in a laboratory for 13.5 years where he distilled phenol several times a day. During the process, heavy odors were detectable, phenol was often spilled on his clothes, and he noted skin irritation. The man recovered after 2-3 months away from the exposure.

No studies were located regarding musculoskeletal effects in animals following dermal exposure to phenol.

Hepatic Effects. Two days after a man was splashed with a phenol-water solution over his face, chest wall, hand, and both arms, serum bilirubin increased 2-fold (Horch et al. 1994). After 5 days, serum bilirubin returned to normal. An enlarged and tender liver and increased liver enzymes in the serum were reported in a case of chronic phenol poisoning (Merliss 1972). Lactate dehydrogenase was about 2-fold greater than normal, aspartate aminotransferase was about 21-fold greater than normal, and alanine aminotransferase was about 100-fold greater than normal. The man worked in a laboratory for 13.5 years where he distilled phenol several times a day. During the process, heavy odors were detectable, phenol was often spilled on his clothes, and he noted skin irritation.

No studies were located regarding hepatic effects in animals following dermal exposure to phenol.

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Renal Effects. A case of acute renal failure was reported by Foxall et al. (1989) in a worker who accidentally fell into a shallow vat containing a mixture of phenol (40%) in dichloromethane. The worker was partially immersed for only a few seconds and avoided ingesting any of the solution. He showered immediately, subsequently collapsed and was admitted to the hospital with surface burns over 50% of his body (involving the face, chest, genitals, and both legs). Following admission he became anuric and plasma creatinine levels rose. He was transferred to the regional renal unit where he was diagnosed with phenolinduced burns, acute tubular necrosis, and fluid overload. For the first 2 weeks, the patient demonstrated ammo aciduria, glycosuria, and lactic aciduria consistent with renal cortical necrosis This was followed by a period of polyuria revealing a biochemical pattern consistent with renal papillary damage. Treatment consisted of administration of a diuretic intravenously and hemodialysis daily for a week followed by an additional 18 days of hemodialysis at gradually increasing intervals. The patient was discharged 42 days after admission once renal clinical chemistry values had return to normal, although NMR spectroscopic analysis still revealed abnormalities consistent with renal papillary damage. One year after the incident the patient was still polyuric.

Dark urine was reported in a case of chronic phenol poisoning (Merliss 1972). The man worked in a laboratory for 13.5 years where he distilled phenol several times a day. During the process, heavy odors were detectable, phenol was often spilled on his clothes, and he noted skin irritation. The study authors indicated that the urine was so dark that it suggested hemoglobinuria. Glucose was present in the urine, although the urine was negative for homogentistic acid (a substance whose presence can cause urine to darken upon standing) and urobilinogen. The urine cleared 2-3 months after the subject was removed from phenol exposure.

Hemoglobinuria and hematin casts in the distal convoluted tubules and tubular lumens located in the medulla and papilla were reported in rats after a single dermal exposure to 107.1 mg/kg liquid phenol (Conning and Hayes 1970). These phenomena are probably related to red blood cell lysis and increased glomerular filtration of hemoglobin. Hemoglobinuria is characteristic of lethal or near-lethal exposures by the dermal route.

Dermal Effects. Application of phenol to the skin of humans results in dermal inflammation and necrosis (Horch et al. 1994; Merliss 1972; Truppman and Ellenby 1979). Data concerning minimal effective exposure levels in humans were not found. NIOSH (1984) conducted a survey in an Oregon hospital in response to concerns about respiratory problems and contact dermatitis in housekeeping staff members who

were exposed frequently to germicidal solutions containing phenol and other solvents (formaldehyde, cellosolve, ethanolamine). The housekeeping staff reported significantly more symptoms of cough, itching, sinus problems, and dermatitis than did other employees. Air concentrations of phenol in the work areas were below the limit of detection (<0.01 ppm). Urinary phenol levels in the housekeeping staff members were not significantly different from those of the other employees Thus, while it is likely that the employees came into contact with irritants, the cause of the reported symptoms could not be attributed to phenol or any other specific substance in the work environment. Therefore, this study is not recorded in Table 2-3.

Application of 0.1 mL of molten phenol/kg (≈100 mg/kg) (Brown et al. 1975) or 107.1 mg/kg (Conning and Hayes 1970) to the skin of rats for 24 hours (surface area not reported) produced severe edema, erythema, and necrosis. In pigs, application of 500 mg/kg molten phenol to 35-40% of the body surface (0.44 mg/cm^2/kg) resulted in skin discoloration after 20-30 minutes of exposure and severe necrosis after 8 hours of exposure. Two of 3 pigs died within 95 minutes after exposure (Pullin et al. 1978). Necrosis, hyperemia of superficial dermal vessels, and dense perivascular infiltration of lymphocytes and neutrophils were noted in the skin of pigs treated dermally with an unspecified amount of 89% phenol (Hunter et al. 1992). The dose-effect relationship and time course for skin irritation and inflammation have been studied in mice (Patrick et al. 1985). The endpoint examined was swelling (increased thickness) of the ear after dermal application to the ear pinna. Application of 12 mg/cm^2/kg of phenol to the ear resulted in swelling in 4 of 9 mice within 1 hour after application. Severity of skin irritation increased as the concentration of the applied phenol solution increased. Swelling persisted for 6 weeks after application of 18 mg/cm^2/kg. Swelling was observed in only 1 of 8 mice treated with 12 mg/cm^2/kg phenol. Application of an unspecified amount of a 1:6 or 1:9 phenol: water solution to the skin of guinea pigs for 1 minute resulted in erythema and increased skin vascular permeability indicated by dye permeability (Steele and Wilhelm 1966).

Skin crusts were reported on mice exposed repeatedly to 5 mg phenol as a 5% (w/v) solution for 32 weeks, whereas skin ulceration was observed in mice exposed to 5 mg phenol as a 20% (w/v) solution (Salaman and Glendenning 1957). The skin ulceration healed in 4 weeks after the end of the exposure. In a 52-week study, mice were exposed 2 times each week to 41.7 or 83.3 mg/kg of phenol in a 5 or 10% solution in benzene (Boutwell and Bosch 1959). Severe skin damage was reported after 36 weeks in the mice exposed to 83.3 mg/kg. Skin papillomas were reported in mice exposed at 4 1.7 mg/kg. Because phenol was applied in benzene which is also a skin irritant, this study is not presented in Table 2-3.

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Ocular Effects. No studies were located regarding ocular effects in humans following dermal exposure to phenol.

A modified Draize test was used to assess ocular damage resulting from application of 5% phenol to the center of the cornea in New Zealand rabbits (Murphy et al. 1982). The eyes of 1 group of rabbits were irrigated with water 30 seconds after exposure, while the eyes of another group were unirrigated. Conjunctivitis developed in all treated groups and lasted through the 7 days of observation. Corneal opacities became apparent in 4 of 9 rabbits 24 hours after phenol application in unirrigated eyes, but only 1 hour after application in 4 of 9 rabbits receiving irrigation. The opacities lasted through the 7-day observation period in the unirrigated eyes, but were cleared by day 7 in the irrigated eyes. Based on these observations, phenol was designated as a severe eye irritant in unirrigated eyes, and as a moderate eye irritant in irrigated eyes (Murphy et al. 1982).

Body Weight Effects. A man chronically exposed to phenol at a laboratory where he distilled it several times a day was 71.5 inches tall, weighed 135 pounds, and was described as emaciated (Merliss 1972). loss of appetite and a slow weight loss were symptoms that the subject reported during the 13.5 years he worked at the laboratory. During the distillation process, heavy odors were detectable, phenol was often spilled on his clothes, and he noted skin irritation.

No studies were located regarding body weight effects in animals following dermal exposure to phenol.

Other Systemic Effects. No studies were located regarding other systemic effects in humans following dermal exposure to phenol.

Direct application of phenol to the inner ear of rats has resulted in external otitis, inner ear damage, and decreased brain-stem auditory response (Schmidt et al. 1990), and inflammation of the tympanic membrane (Schmidt and Hellstrom 1993). These studies were conducted because phenol has been used as a topical anesthetic in infected ears.

2.2.3.3 Immunological and Lymphoreticular Effects

No studies were located regarding immunological or lymphoreticular effects in humans or animals following dermal exposure to phenol.

2.2.3.4 Neurological Effects

Fatal dermal exposure to an 80% phenol solution in a 24-year-old man being treated for skin rash was characterized by severe convulsions prior to death (Lewin and Cleary 1982).

Muscle tremors and convulsions are characteristic effects of acute dermal phenol toxicity in laboratory animals. Tremors that developed into convulsions and prostration were reported in rats exposed to 107.1 mg/kg liquid phenol; application surface areas were not reported (Conning and Hayes 1970). In pigs, application of 500 mg/kg over 35-40% of the body surface (0.44 $mg/cm^2/kg$) resulted in muscular tremors in the head region within 3-5 minutes of exposure (Pullin et al. 1978). This was followed by dilation of the pupils, loss of coordination, and excess salivation and nasal discharge within 5 minutes of exposure. It was followed by convulsions, coma, and death 5-7 minutes after exposure in two of three pigs. Direct application of a dose of 37.5 mg/kg phenol to the inner ear resulted in a reduced threshold for auditory brainstem response (Schmidt et al. 1990).

No studies were located regarding the following health effects in humans or animals after dermal exposure to phenol.

2.2.3.5 Reproductive Effects

2.2.3.6 Developmental Effects

2.2.3.7 Genotoxic Effects

Genotoxicity studies are discussed in Section 2.5.

2.2.3.8 Cancer

No studies were located regarding cancer in humans following dermal exposure to phenol.
In a study of the promoting effects of phenol, mice were exposed to 9,10-dimethyl-1,2-benzanthracene (DMBA) (300 μg) followed by weekly dermal exposure to 5 mg phenol in either a 5 or 20% phenol solution in acetone for 32 weeks (Salaman and Glendenning 1957). Exposure to DMBA followed by phenol (5 or

20%) resulted in a significantly greater incidence of tumors, including carcinomas, than exposure to 20% phenol alone; tumors, but no carcinomas, resulted from exposure to 20% phenol, and no tumors resulted from exposure to 5% phenol. Application of 5% phenol alone resulted in skin "crusting" at the site of application, whereas 20% phenol resulted in skin ulceration. The study authors concluded that phenol was an effective tumor promoter after a single application of DMBA. Although this study did not include a group of animals which had been exposed to DMBA alone, the authors indicated that previous work done in their laboratory provided the data from such animals and that it was thus the comparison between such historical information and the information from this study which led to their conclusion about the promotional effects of phenol.

A similar promoting activity was observed when au unspecified volume of 10% phenol in acetone was placed on the backs of mice 2 times/week for 12 months and when 5% phenol in acetone was placed on the backs of mice 3 times/week for 12 months (Wynder and Hoffmann 1961). CELs from these studies are presented in Table 2-3.

Additional studies indicate that phenol applied to the skin is a cancer promoter and possibly a complete carcinogen (i.e., promoter and initiator) in mice. Boutwell and Bosch (1959) examined the carcinogenic effects of phenol in several strains of mice. Mice were exposed to a single dermal application of DMBA (75 mg) followed by repeated dermal applications of a 5 or 10% phenol solution in benzene (41.7 or 83.3 mg/kg/treatment), twice each week for 52 weeks. Two other experimental groups of mice were exposed to DMBA alone or phenol alone. Severe skin damage, decreased body weight, and increased mortality were observed in phenol-treated animals. Sutter strain mice (inbred for 3 generations for susceptibility to the initiator DMBA) treated with DMBA followed by 10% phenol developed papillomas (95% in 13 weeks) and carcinomas (43% in 42 weeks) at a much higher incidence than mice treated with DMBA alone (14% with papillomas at 42 weeks; no carcinomas), or phenol alone (36% with papillomas at 52 weeks; no carcinomas). One fibrosarcoma was observed after 52 weeks of exposure to phenol alone. An elevated incidence of papilloma was also observed in CAF1, C3H, and Holtzmann mice exposed to DMBA followed by phenol, and in Holtzmann mice exposed to 10% phenol alone. The promoting effect of phenol was dose related; application of 5% phenol (41.7 mg/kg) following DMBA treatment resulted in fewer tumors than a similar protocol using DMBA followed by 10% phenol (83.3 mg/kg). Phenol elicits skin tumors in mice even without treatment with DMBA. Ten out of 30 albino mice treated twice weekly for 12 weeks with a 20% phenol solution in dioxane developed papilloma of the skin; also, 8 out of 30 mice treated with 10% phenol solution in benzene for 15 weeks developed papilloma, and 3 developed carcinoma of the skin (Boutwell and

Bosch 1959). Because the phenol was administered in benzene or dioxane, both of which are skin irritants and/or de-fatting agents, this study is not presented in Table 2-3.

The effect of phenol on benzo[a]pyrene (B [a]P) carcinogenicity has been examined (Van Duuren and Goldschmidt 1976; Van Duuren et al. 1971) 1973). Dermal application of 3 mg phenol in acetone simultaneously with 5 μg B [a]P resulted in significantly fewer tumors than application of B [a]P alone. Application surface areas were not reported and could not be estimated from the description of the application procedure. Mice treated dermally with B [a]P followed by dermal application of brewed tea on alternate days over a period of 55 days developed epithelial cell carcinoma or exhibited various stages of squamous cell tumors (Kaiser 1967). The brewed tea contained an unspecified level of phenol, the presumed cancer promoter in this experiment, as well as cresols and dimethylphenols.

2.3 TOXICOKINETICS

Phenol is readily absorbed and widely distributed following inhalation, oral, and dermal exposure. The distribution of phenol is thought to be dependent on blood flow. Conjugates with glucuronic acid and sulfate are the major metabolites of phenol, although small amounts of the hydroxylation products catechol and hydroquinone are also produced. Sulfotransferase and glucuronyltransferases are present in most tissues, although the major sites of phenol conjugation are the gastrointestinal tract, liver, lung, and kidney. Because of the large capacity of the intestines and liver to conjugate phenol, the fact that the first-pass effect occurs following oral exposure but not following dermal exposure may contribute to the greater potential for phenol to result in adverse effects following dermal exposure. Phenol and its conjugates are predominantly excreted in the urine.

2.3.1 Absorption

2.3.1.1 Inhalation Exposure

Phenol is absorbed readily after inhalation exposure. Eight subjects were exposed to phenol vapors (1.6-5.2 ppm) for 8 hours (Piotrowski 1971). Subjects were exposed through a face mask in order to eliminate the possibility of percutaneous absorption. The concentration of phenol in inhaled and exhaled air was determined, and urine was analyzed for total phenol (phenol and phenol conjugates). Steady-state

appeared to be achieved within 3 hours after initiating exposure; steady-state retention was 60-88%. Urinary recovery of phenol that had been retained in the lungs was 99±8% within 24 hours after initiating exposure.

Total urinary phenol was determined at about 7 hours into an 8-hour shift in Bakelite workers exposed to airborne phenol at 0.16-32 ppm (Ohtsuji and Ikeda 1972). Daily urinary excretion of total phenol was 99% of the estimated amount inhaled indicating that phenol is readily absorbed. However, lung retention was not measured, and the contribution of percutaneous absorption to urinary phenol could not be evaluated in this study.

Rats exposed by intratracheal instillation to [^{14}C]-labeled phenol also demonstrated rapid absorption kinetics, with most of the radioactivity being excreted within 72 hours (Hughes and Hall 1995).

2.3.1.2 Oral Exposure

Based on the rapid excretion of phenol and its metabolites in urine, it has been concluded that phenol is readily absorbed by the oral route in humans (Capel et al. 1972) and a variety of mammalian species including monkeys (Capel et al. 1972), rodents (Capel et al. 1972; Edwards et al. 1986; Hughes and Hall 1995; Kao et al. 1979; Kenyon et al. 1995), dogs (Capel et al. 1972), rabbits (Capel et al. 1972), cats (Capel et al. 1972; French et al. 1974), and pigs (Capel et al. 1972; Kao et al. 1979). In 3 men given a single oral dose of 0.01 mg/kg [^{14}C]-labeled phenol in food or drink, about 90% (range 85-98%) of the dose was excreted in the urine in 14 hours (Capel et al. 1972). In this same study, urinary recovery of orally administered [^{14}C]-labeled phenol was determined in 18 other mammalian species; mean 24-hour recoveries of ^{14}C ranged from 95% in the rat to 31% in the squirrel monkey. Rats exposed orally to radiolabeled phenol demonstrated rapid absorption and excretion, with most of the radioactivity being excreted within 72 hours (Hughes and Hall 1995). The gastrointestinal absorption of phenol has also been studied in rats with *in situ* preparations. The absorption kinetics of [^{14}C]-labeled phenol administered directly into the small intestines of rats were described as first-order, with a rate constant for intestinal absorption of 0.127±0.003 minute^{-1} and a half-life in the intestines of 5.5±0.5 minutes (Humphrey et al. 1980). Two hours after [^{14}C]-labeled phenol was injected into the small intestines of anesthetized rats, recoveries in the urine were 77.9+2% after a 12.5-mg/kg dose, and 76.9±5.8% after a 25-mg/kg dose (Kao et al. 1979).

2. HEALTH EFFECTS

2.3.1.3 Dermal Exposure

Phenol is absorbed quite readily through the skin, and the skin is considered the primary route of entry during occupational exposure (ACGIH 1991). Whole-body skin exposures in human subjects were completed with subjects lightly clothed and unclothed (Piotrowski 1971). The subjects were exposed to phenol vapor (35% humidity, 26°C) at concentrations of 1.3,2.6, or 6.5 ppm for 6 hours. Fresh air was supplied to the subjects through a face mask in order to prevent absorption of phenol through the lungs. The total amount of phenol excreted in urine during and after exposure (minus baseline excretion) was used as a measure of absorption. Absorption increased proportionately with exposure level. Percutaneous clearance (mg phenol absorbed through the skin per hour/mg phenol per m^3 of air) was estimated to be 0.35 m^3/hour. Thus, an amount of phenol equivalent to that contained in 0.35 m^3 of air was absorbed through the skin each hour.

The data reported by Piotrowski (1971) provide a basis for comparing the relative contributions of lung and percutaneous absorption during exposures to phenol vapor. Assuming a ventilation rate for the human of 0.8 m^3/hour (EPA 1986a) and a steady-state lung retention of inhaled phenol of 0.7 (Piotrowski 1971), clearance of airborne phenol through the lung is ≈0.6 m^3/hour. Thus, an amount of phenol equivalent to that contained in 0.6 m^3 of air was absorbed through the lungs each hour. It can be concluded that at any given exposure level within the range of 5-25 mg/m^3 (1.3-6.4 ppm), percutaneous absorption (0.35 m^3/hour) will be ≈½ that of absorption through the lungs (0.6 m^3/hour).

Percutaneous absorption of phenol applied in solution directly to the forearm (15.6 cm^2) of volunteers has been measured (Baranowska-Dutkiewicz 1981). Absorption rate from a 2-mL reservoir of an aqueous phenol solution (2.5, 5.0, or 10.0 g/L) was constant for 60 minutes (0.08 mg/cm^2/hour) and increased proportionately with applied concentration. Approximately 13% of the applied dose was absorbed in 30 minutes, of which 80% (range 58-98%) was recovered in the urine within 24 hours.

When human skin was treated *in vitro* with 0.0013-0.0027 mg/cm^2 [^{14}C]-labeled phenol and left unoccluded, 20% of the radioactivity was absorbed when analyzed 72 hours later, while 7% remained on the skin surface (Hotchkiss et al. 1992). Covering the skin with a teflon cap resulted in the absorption of 47%, with 3% recovered in the skin. When rat skin was subjected to the same exposure regime in this study, 72 hours later 24% of the radioactivity was absorbed with 22% recovered in the skin when the skin was unoccluded, and 36% was absorbed with 3-4% recovered in the skin when the skin was occluded.

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In rats in which a 0.03-mg/kg dose of [^{14}C]-labeled phenol was placed on the skin, only 1-5% of the dose remained in the body 72 hours later (Hughes and Hall 1995). The dermal absorption of phenol was studied in three pigs in which undiluted phenol was placed on the skin for 1 minute, and the peak plasma level was determined (Pullin et al. 1978). Plasma levels were not measurable in 1 pig treated with a dose of 90 mg/kg over a surface area of 91.6 cm^2. In pigs treated with a dose of 500 mg/kg, peak plasma levels of 0.9 and 30.5 ppm were reported in pigs treated over surface areas of 91.6 and 1,135.5 cm^2, respectively.

Permeability coefficients for phenol in isolated skin patches from nude mice have been determined (Behl et al. 1983). The permeability coefficient increased as the concentration of the applied aqueous phenol solution increased; doubling the concentration from 20 to 40 g/L resulted in a 12-fold increase in mean permeability coefficient (0.007-0.085 cm/hour). The value obtained for the permeability coefficient when 60 g/L was applied to the skin patch (0.169 cm/hour) was similar to that obtained for skin patches in which the stratum corneum had been removed. It was concluded that phenol concentrations exceeding 20 g/L may destroy a diffusion barrier normally provided by the intact stratum corneum, permitting increased percutaneous absorption.

Dermal absorption of phenol in the presence of various types of soil was measured *in vitro* using skin patches from pigs (Skowronski et al. 1994). Maximum phenol penetration occurred between 2 and 4 hours after treatment in all cases. Compared to samples with no soil present, the presence of sandy soil reduced the peak penetration by one-half, and the presence of clay soil reduced peak penetration by two-thirds.

2.3.2 Distribution

2.3.2.1 Inhalation Exposure

No studies were found regarding tissue distribution of phenol in humans after inhalation exposure.
Rats exposed by intratracheal instillation to radiolabeled phenol were sacrificed 72 hours later and analyzed for tissue distribution of the radioactivity (Hughes and Hall 1995). Of the radioactivity remaining in the body (1-5%), a majority was distributed in the lungs (0.13%), skin (0.13%), blood (0.07%), muscle (0.03%), fat (0.02%), and liver (0.02%).

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No information was found on the placental transfer and distribution of phenol; however, Ghantous and Danielsson (1986) examined this question for benzene, the principal metabolite of which is phenol. Mice at gestation day 11) 14, and 17, were exposed by inhalation to ^{14}C benzene and the distribution of benzene and its volatile and non-volatile metabolites examined using whole body autoradiaography and assessment of tissue concentrations of ^{14}C (day 17 only). The authors indicated that the exposure regimen (50 μCi of ^{14}C benzene in maize oil, volatilized by gentle heating) would theoretically produce 2,000 ppm in the inhalation chamber. Measurements of the difference between the amount added to the chamber and the amount inhaled by the animals indicated an uptake of 90% (i.e., 45 μCi). These authors did not specifically characterize the metabolites, but were able to show that the ^{14}C labeled volatile and non-volatile activity crossed the placental barrier. There was no evidence of preferential accumulation. Indeed, the concentration of volatile and nonvolatile radioactivity in fetal tissues was much lower than that observed in the corresponding maternal tissues. As a metric of the relative accumulation, the authors noted that compared to maternal brain tissue, fetal uptake of benzene was only 8%.

2.3.2.2 Oral Exposure

No studies were found regarding tissue distribution of phenol in humans after oral exposure.

Data are available for rabbits (Deichmann 1944) and rats (Hughes and Hall 1995; Liao and Oehme 1981). In these species, distribution is rapid, with peak tissue concentrations achieved in most tissues within 1 hour after dosing. The highest peak concentrations and fraction of administered dose are found in the liver; >90% of the administered dose is eliminated from tissues within 24 hours.

The levels of phenol in various tissues of 5 rabbits given a lethal (LD_{50}) oral dose of phenol (500 mg/kg) were determined (Deichmann 1944). The rabbits were killed within l-3 minutes after dosing when twitching, the first sign of systemic toxicity, appeared. The highest concentrations of total phenol (free plus conjugates) were found in the liver (20.9-30.4 mg/100 g tissue), lungs (5.1-17.1 mg/100 g), blood (6.1-12.6 mg/100 g), brain and spinal cord (3.1-10.4 mg/100 g), and kidneys (2.3-7.1 mg/100 g).

The kinetics of tissue distribution of [^{14}C]-labeled phenol in rats given 207 mg/kg of [^{14}C]-labeled phenol, a sublethal (≈0.5 x LD_{50}) oral dose, were studied (Liao and Oehme 1981). Although all rats survived for 16 hours, signs of systemic toxicity were observed including twitching of muscles around the eyes and ears, convulsions, and coma persisting for 15-30 minutes. Thirty minutes after dosing, 28.4% of administered ^{14}C

was recovered in tissues (liver, kidney, adrenal, thyroid, spleen, blood, lung, thymus, brain, testes, heart, muscle, and fat). Sixteen hours after dosing, 0.3% of the administered dose was recovered in tissues. Concentrations of ^{14}C were highest in all tissues 30 minutes after dosing, with the exception of the thyroid gland, in which peak concentrations were achieved after 2 hours. The highest concentration and fraction of administered dose were found in the liver; 42% (range 29-56%) of the administered dose was recovered in the liver 30 minutes after dosing. Approximately 67-85% of the ^{14}C in blood was present in the plasma fraction, of which 41-50% was bound to plasma proteins or other macromolecules. The elimination half-time for ^{14}C was <4 hours. Based on their results, the study authors suggested that blood flow determines the tissue uptake of the radiolabel from phenol.

Rats exposed orally to radiolabeled phenol were sacrificed 72 hours later and analyzed for tissue distribution of the radioactivity (Hughes and Hall 1995). Of the radioactivity remaining in the body, a majority was distributed in the muscle (0.08%), skin (0.07%), fat (0.02%), liver (0.02%), and blood (0.02%).

No evidence of exposure-related DNA adduct formation in femur bone marrow, Zymbal gland, liver, or spleen was seen in rats treated orally with 75 mg/kg/day phenol for 4 days (Reddy et al. 1990). In this study, concurrent *in vitro* exposures of these tissues did produce adducts, suggesting that efficient detoxification and excretion mechanisms may be operating *in vivo*.

2.3.2.3 Dermal Exposure

No studies were found regarding tissue distribution of phenol in humans after dermal exposure.
Rats exposed dermally to radiolabeled phenol were sacrificed 72 hours later and analyzed for tissue distribution of the radioactivity (Hughes and Hall 1995). Of the radioactivity remaining in the body (1-5%), a majority was distributed in the skin (0.021%), muscle (0.02%), fat (0.03%), liver (0.01%), and blood (0.02%).

2.3.2.4 Other Routes of Exposure

No studies were located regarding distribution of phenol in humans after exposure by other routes.

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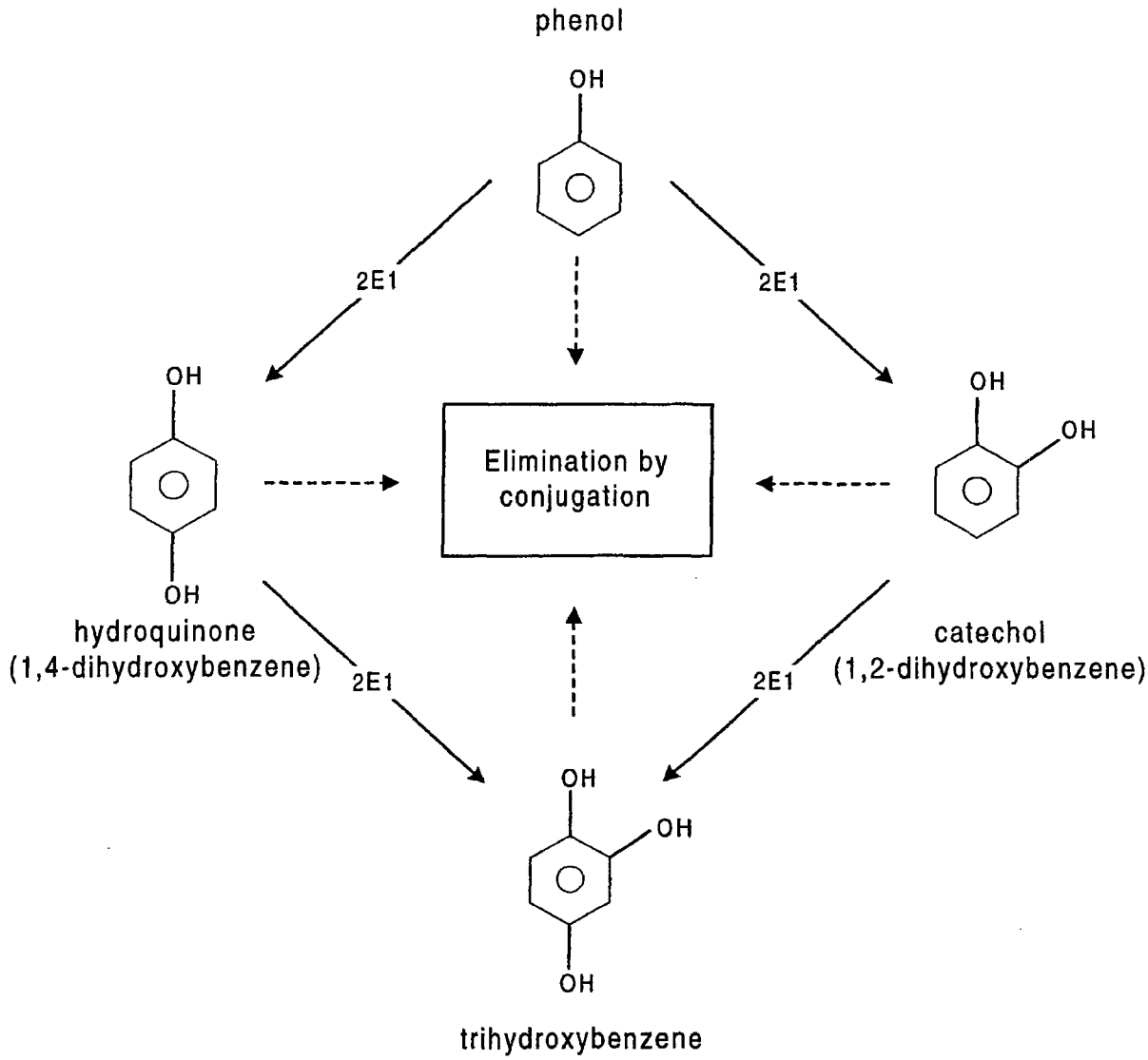
Microdialysis sampling has been used in rats infused with phenol (0.181 nmol/minute for 90 minutes) to study excretion into the bile (Scott and Lunte 1993). For all phenol metabolites, bile concentrations were higher than liver concentrations indicating that the metabolites are actively excreted in the bile.

The distribution of phenol in the liver has been studied in mice treated intravenously with 31.4 mg/kg phenol (Davies and Lunte 1996). Microdialysis probes used to monitor the distribution of phenol metabolites in three regions of the liver (anterior, median, posterior) indicated that phenol-glucuronide was the most prevalent metabolite in all three regions, but the level was significantly lower in the anterior region compared to the other regions. When phenol was delivered to the liver through microdialysis probes, no regional differences in the delivery of phenol or metabolite formation were observed, indicating that clearance of phenol from the liver is dominated by blood flow rather than metabolism.

2.3.3 Metabolism

Figure 2-3 shows the metabolic pathways that transform phenol prior to its excretion in the urine. Three different enzymes systems catalzye the reactions that transform phenol. Cytosolic phenol sulfotransferases catalyze the transfer of inorganic sulfur from the activated 3'-phosphoadenosine-5'-phosphosulfate donor molecule to the hydroxyl group on phenol. Microsomal membrane-located uridine diphosphate glucuronosyltransferases (UDP-glucuronosyltransferases) catalyze the transfer of an activated glucuronic acid molecule to the hydroxyl moiety of phenol to form an O-glucuronide conjugate. Cytochrome P4502E1, also microsomally located, catalyzes the hydroxylation of phenol to form hydroquinone (and to a much lesser extent catechol), which is then acted upon by the phase II enzymes (Benet et al. 1995; Campbell et al. 1987; Gut et al. 1996; McFadden et al. 1996). All three enzyme systems are found in multiple tissues and there is competition among them not only for phenol but for subsequent oxidative products, like hydroquinone. As a consequence, the relative amount of the products formed can vary based on species, dose and route of administration. *In vivo,* the gastrointestinal tract, liver, lung, and kidney appear to be the major sites of phenol sulfate and glucuronide conjugation of simple phenols (Cassidy and Houston 1984; Powell et al. 1974; Quebbemann and Anders 1973; Tremaine et al. 1984).

Figure 2-3. Scheme for Metabolism of Phenol*



—2E1→ Oxidative reaction catalyzed by cytochrome P450 2E1

- - - - - → Conjugation reactions (may be catalyzed by phenol sulfotransferase, UDP-glucuronosyl transferase, or glutathione-S-transferase)

*Adapted from Schlosser et al. 1998

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Four principal metabolites have been identified in mammals: two phenol and two hydroquinone conjugates (of sulfate and glucuronide) (Capel et al. 1972; Kenyon et al. 1995; Wheldrake et al. 1978). In humans, rats, and mice, given low doses of phenol orally, sulfate conjugates of phenol were found to predominate. However, in guinea pigs, pigs, and fruit bats, the glucuronide conjugates were dominant (Capel et al. 1972). In humans given an oral dose of 0.01 mg/kg, 77% of the urinary ^{14}C was identified as phenyl sulfate, 16% as phenyl glucuronide, with trace amounts (<1%) as the sulfate and glucuronide conjugates of hydroquinone (Capel et al. 1972).

In mice, phenyl sulfate was the predominant urinary metabolite for low doses (1-21 mg/kg) of phenol administered either by gavage and intravenously; however, as the dose increased, a decrease in phenol sulfation and a concomitant increase in glucuronidation of both phenol and hydroquinone was seen suggesting saturation of the sulfation pathway (Kenyon et al. 1995). The degree of saturation appeared to be slightly greater following gavage administration, and intravenous administration resulted in higher proportions of the products of oxidative metabolism, with male mice being more sensitive than female mice. These latter observations suggest that the oxidative pathway become more prominent when phenol is introduced directly into the circulation, bypassing an initial intestinal sulfate conjugation process, and also suggests, that the sulfate conjugation process saturates at a lower concentration in males than in females.

Similarly, in the rat, the ratio of phenyl sulfate/glucuronide conjugates in urine decreases from 2.6 to 0.7 when the intravenous dose level is increased from 1.2 to 25 mg/kg (Weitering et al. 1979). This phenomenon appears to be, at least in part, the result of a lower K_m for the sulfotransferase enzyme for phenol rather than for the glucuronyltransferase enzyme (Koster et al. 1981; Mulder and Scholtens 1977; Ramli and Wheldrake 1981). Treatment of rats with an intraperitoneal dose of phenol (23-188 mg/kg) has also been shown to result in dose-dependent decreases in hepatic 3'-phosphoadeonsine 5'-phosphosulfate (PAPS), the cosubstrate for the sulfate conjugation of phenol, as well as sulfate (Kim et al. 1995). The depletion of PAPS may also contribute to the saturation of sulfation at high doses of phenol.

All three enzyme systems have other substrates, which can competitively inhibit the metabolism of phenol thereby changing the balance among metabolites. Inhibition of phenol sulfotransferase with chlorinated phenols (e.g., pentachlorophenol) results in increased glucuronide conjugation of simple phenols (Mulder ant Scholtens 1977). Similarly, benzene is metabolized by CYP2E1, thus high exposures to benzene may competitively inhibit phenol metabolism resulting in decreasing hydroquinone production (and its corresponding sulfate and glucuronide conjugates) (Medinsky et al. 1995; Schlosser et al. 1993).

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Age- and sex-related changes in phenol sulfoconjugation were studied in hepatic cytosolic preparations from fetal, newborn, and adult rats (Iwasaki et al. 1993). Phenol sulfoconjugation activity was higher in adult males (1.94±0.1 nmol/mg/min) than females (1.07±0.03 nmol/mg/min), although there were no sex-related differences in the younger rats. Activity in fetal rats was very low (0.04±0.01 nmol/mg/min). Activity at 2 days after birth was ½ that in adult females and 1/4 that in adult males, and remained constant until 25 days after birth. At 2 years of age, activity was intermediate between young adult male and female activities, and there were no sex-related differences.

Several other minor metabolites of phenol have been identified *in vitro*. The formation of 1,4-dihydroxybenzene and 1,2-dihydroxybenzene in a 20: 1 molar ratio was observed in isolated rat liver microsomes incubated with phenol (Sawahata and Neal 1983). Further catalysis to-p-benzoquinone, 4,4'-biphenol, and biphenoquinone has been demonstrated in microsomes and in *in vitro* peroxidase preparations. The benzoquinone products react nonenzymatically with nucleophiles, including cysteine and reduced glutathione, to yield *S*-conjugates of 1,4-dihydroxybenzene and 4,4-biphenol (Eastmond et al. 1986; Lunte and Kissinger 1983; Subrahmanyam and O'Brien 1985).

2.3.4 Elimination and Excretion

Phenol, in its free and conjugated forms, is a normal constituent of human urine. Piotrowski (1971) reported 8.7±2.0 mg/day as the daily excretion rate of total phenol (free plus conjugates) in human subjects with no known exposure to phenol. Others have reported a range of values. In a study of workers employed in the distillation of high-temperature phenolic fractions of tar, the rate mean values of phenol in the urine of 13.8 mg/L in 26 male non-exposed workers and 67.8 mg/L in 89 exposed workers were reported (Bieniek 1994). The highest concentration was found 2 hours after the end of the work shift. Quint et al. (1998) evaluated the urinary phenol concentration before and after using phenol to chemically cauterize the lesion created by excision of chrondroblastoma in 11 patients. Preoperatively, the average urinary concentration of phenol was 5.1 mg/L. Ling and Hanninen (1991) studied the effect of phenol on serum and urinary concentrations in patients who switched from a conventional diet to an uncooked "vegan" diet. Patients were tested at week 0, were on the vegan diet for 4 weeks, and then on the regular diet for the second month. Urinary and serum levels of phenol were measured at weeks 0, 2, 4, and 9. A significant decrease in both urinary and serum concentrations of phenol was seen within 2 weeks of adopting the vegan diet. At 2 weeks, the serum concentration had dropped from about .75 mg/L to 0.5 mg/L (about 30%), and levels in urine had dropped from about 7 mg/L to about 3 mg/L (about 60%). These data indicate that phenol is a natural

product of metabolism that may vary significantly depending at least on diet, but probably also due to other factors.

Horch et al. (1994) make the statement "urine phenol concentrations should be monitored in exposed persons to determine if they are within normal range (0.5-81 mg/L)," but they provide no citation for the range given. It should be noted that as late as 1980, gas chromatographic analyses of urine used to determine phenol levels showed fairly large interlaboratory variation (Van Roosmaleu et al. 1981). Thus the range of values given above, if derived from multiple references including the older literature, may be artificially broad.

2.3.4.1 Inhalation Exposure

Phenol absorbed through the lungs is excreted rapidly in urine in its free and conjugated forms. Within 24 hours after human subjects inhaled phenol at concentrations of 6-20 mg/m^3 (1.5-5.1 ppm), 99±8% of the phenol retained in the lungs was excreted (Piotrowski 1971). The urinary excretion of phenol was studied in 106 men occupationally exposed to phenol, cresols, xylenols, and other phenolic derivatives, and 26 unexposed controls (Bieniek 1994). Urine samples were taken after 4 hours at work, and in 16 workers every 2 hours for 24 hours after an 8-hour shift. The mean level of phenol in urine of the exposed workers was 87.3 mg/L, compared to 11.7 mg/L in controls. The highest phenol concentrations were recorded between 8 and 10 hours after the beginning of the exposure. Exposure concentrations were not reported in this study.

Urinary excretion of total phenol (free and conjugates) is considered a biomarker of exposure for phenol. The biological exposure index (BEI) for phenol, for exposure to 5 ppm in air, is 250 mg/g creatinine when measured at the end of the shift (ACGIH 1991).

In rats exposed by intratracheal instillation to radiolabeled phenol, elimination was 95% complete after 72 hours, with the primary elimination route being through the urine (Hughes and Hall 1995). Fecal elimination was slower and accounted for less overall.

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2.3.4.2 Oral Exposure

Phenol absorbed from the gastrointestinal tract is excreted rapidly in urine as free phenol or conjugates (Capel et al. 1972; Deichmann 1944; Edwards et al. 1986; French et al. 1974; Kao et al. 1979; Kenyon et al. 1995; Lao and Oehme 1981). In 3 human subjects who received a single oral dose of 0.01 mg/kg [^{14}C]-labeled phenol, the mean 24-hour urinary recovery of ^{14}C was 90% (range 85-90%) of the administered dose (Capel et al. 1972). In this same study, urinary recovery of orally administered [^{14}C]-labeled phenol was determined in 18 other mammalian species; the mean 24-hour recoveries of ^{14}C ranged from 95% in the rat to 31% in the squirrel monkey.

Both urinary and fecal excretion of r4C was determined in rats administered an oral dose of 1.2 mg/kg of [^{14}C]-labeled phenol (Edwards et al. 1986). Rats excreted 80.3±11.2% in the urine and 1.8±1.6% in the feces in 24 hours. In rats exposed orally to radiolabeled phenol, elimination was 95% complete after 72 hours, with the primary elimination route being through the urine (Hughes and Hall 1995). Fecal elimination was slower and less overall.

2.3.4.3 Dermal Exposure

Phenol absorbed through the skin is rapidly excreted in urine as free phenol or conjugates. Following an industrial accident in which a phenol-water solution was splashed over a man's face, chest wall, hand, and both arms, phenol in the urine decreased from 566 mg/L after 4 hours to 0.75 mg/L 46 hours after the exposure (Horch et al. 1994). Subjects exposed to dermally applied reservoirs containing phenol solutions (2.5-10 mg/L) excreted 80% (range 58-98%) of the absorbed phenol in the urine within 24 hours (Baranowska-Dutkiewicz 1981). Another study in which human subjects were dermally exposed for 7 hours to phenol vapors, both clothed and unclothed, while breathing clean air to avoid inhalation exposure, found that almost 100% of the absorbed phenol was excreted in the urine within 1 day, with clothing providing no apparent protection (Piotrowski 1971).

In rats exposed dermally to radiolabeled phenol, elimination was 95% complete after 72 hours, with the primary elimination route being through the urine (Hughes and Hall 1995). Fecal elimination was slower and less overall.

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2.3.5 Physiologically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PD) Models

Physiologically based pharmacokinetic (PBPK) models use mathematical descriptions of the uptake and disposition of chemical substances to quantitatively describe the relationships among critical biological processes (Krishnan et al. 1994). PBPK models are also called biologically based tissue dosimetry models. PBPK models are increasingly used in risk assessments, primarily to predict the concentration of potentially toxic moieties of a chemical that will be delivered to any given target tissue following various combinations of route, dose level, and test species (Clewell and Andersen 1985). Physiologically based pharmacodynamic (PBPD) models use mathematical descriptions of the dose-response function to quantitatively describe the relationship between target tissue dose and toxic end points.

PBPK/PD models refine our understanding of complex quantitative dose behaviors by helping to delineate and characterize the relationships between: (1) the external/exposure concentration and target tissue dose of the toxic moiety, and (2) the target tissue dose and observed responses (Andersen et al. 1987; Andersen and Krishnan 1994). These models are biologically and mechanistically based and can be used to extrapolate the pharmacokinetic behavior of chemical substances from high to low dose, from route to route, between species, and between subpopulations within a species. The biological basis of PBPK models results in more meaningful extrapolations than those generated with the more conventional use of uncertainty factors.

The PBPK model for a chemical substance is developed in four interconnected steps: (1) model representation, (2) model parametrization, (3) model simulation, and (4) model validation (Krishnan and Andersen 1994). In the early 1990s, validated PBPK models were developed for a number of toxicologically important chemical substances, both volatile and nonvolatile (Krishnan and Andersen 1994; Leung 1993). PBPK models for a particular substance require estimates of the chemical substance-specific physicochemical parameters, and species-specific physiological and biological parameters. The numerical estimates of these model parameters are incorporated within a set of differential and algebraic equations that describe the pharmacokinetic processes. Solving these differential and algebraic equations provides the predictions of tissue dose. Computers then provide process simulations based on these solutions.
The structure and mathematical expressions used in PBPK models significantly simplify the true complexities of biological systems. If the uptake and disposition of the chemical substance(s) is adequately described, however, this simplification is desirable because data are often unavailable for many biological processes. A

simplified scheme reduces the magnitude of cumulative uncertainty. The adequacy of the model is, therefore, of great importance, and model validation is essential to the use of PBPK models in risk assessment.

PBPK models improve the pharmacokinetic extrapolations used in risk assessments that identify the maximal (i.e., the safe) levels for human exposure to chemical substances (Andersen and Krishnan 1994). PBPK models provide a scientifically-sound means to predict the target tissue dose of chemicals in humans who are exposed to environmental levels (for example, levels that might occur at hazardous waste sites) based on the results of studies where doses were higher or were administered in different species. Figure 2-4 shows a conceptualized representation of a PBPK model.

If PBPK models for phenol exist, the overall results and individual models are discussed in this section in terms of their use in risk assessment, tissue dosimetry, and dose, route, and species extrapolations.

PBPK models for phenol are discussed below.

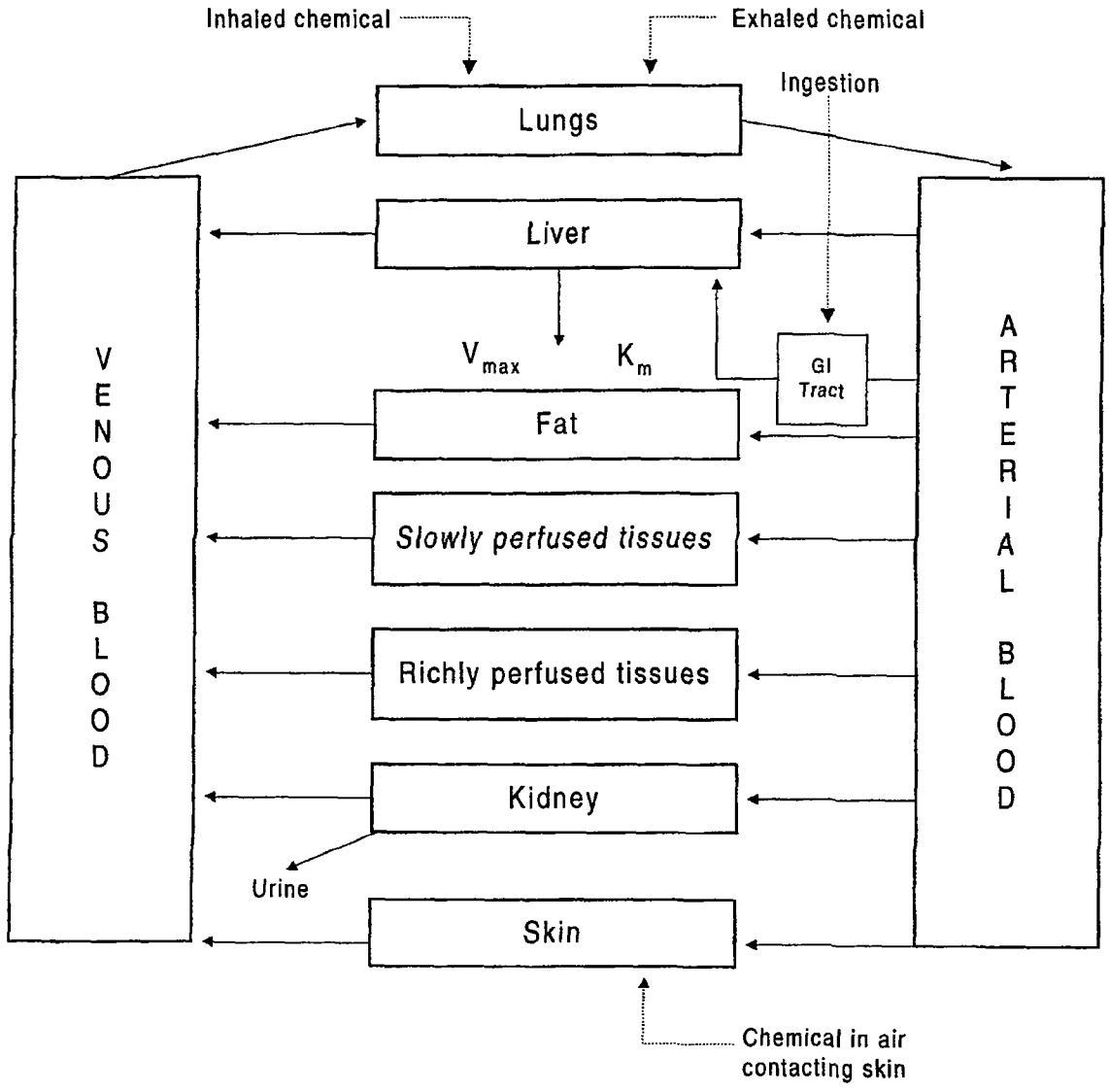
2.3.5.1 Summary of PBPK Models

Physiologically based pharmacokinetic models regarding phenol have typically been developed as part of the attempt to understand the toxicity of benzene, of which phenol is the primary metabolite. Human exposure to benzene is widespread, and much of the toxicity of benzene is due to the action of its metabolites. Thus, while no studies were located involving PBPK models specific to phenol exposure, several models relating to benzene exposure exist and are appropriate to this discussion.

2.3.5.2 Phenol PBPK Model Comparison

The complexities of benzene and phenol metabolism are not yet fully understood, and so appropriate PBPK models are still being developed. Several factors involving the metabolism and toxic effects of these chemicals should be considered. First is the apparent differential toxicity of the two chemicals, benzene being generally more toxic and carcinogenic, while phenol has no apparent carcinogenicity following inhalation and oral exposure. Second is the fact that phenol is a metabolite of benzene and also competes with benzene for the same oxidation enzymes, so that either chemical may inhibit the metabolism of the other chemical by saturating all available active enzyme sites. Finally, each chemical has several metabolic pathways that may be followed, some of which may produce metabolites more toxic than the parent compounds.

Figure 2-4. Conceptual Representation of a Physiologically Based Pharmacokinetic (PBPK) Model for a Hypothetical Chemical Substance



Note: This is a conceptual representation of a physiologically based pharmacokinetic (PBPK) model for a hypothetical chemical substance. The chemical substance is shown to be absorbed via the skin, by inhalation, or by ingestion, metabolized in the liver, and excreted in the urine or by exhalation.

Thus, modeling the kinetics of benzene and phenol metabolism involves considering an array of compounds which may themselves be responsible for any observed toxic effects.

The two models discussed below are derived from *in vitro* and *in* viva rodent studies. It is important to keep in mind that these models were developed specifically to describe benzene metabolism, and as such, they may not fully consider the metabolism of phenol. PBPK models specific to phenol have yet to be developed.

2.3.5.3 Discussion of Models

The Bois et al. (1991) Model

A PBPK model was developed by Bois et al. (1991) to explore the question of why benzene, but not phenol, is carcinogenic in rats and humans.

Risk assessment. The levels of phenol in blood and bone marrow and total hydroquinone (an oxidation metabolite of phenol) predicted by the model were substantially higher after phenol administration than after benzene administration" This result seems to refute the argument that phenol or hydroquinone plays a direct role in the carcinogenicity of benzene, and suggests that other metabolites must therefore be involved. The study authors suggest that catechol, a potentially genotoxic oxidation metabolite produced in much larger amounts following benzene as opposed to phenol administration, may contribute to benzene's carcinogenicity.

Description of the model. Beginning with a compartmentalized model of phenol distribution, which includes fat, well-perfused tissue, poorly-perfused tissue, bone marrow, liver, lung, and gut (which incorporated first-pass effects), the model addresses the notion that first-pass gut metabolism and the phenolto-hydroquinone pathway are responsible for the carcinogenic effects. Monte Carlo simulation of 64 parameters was performed. Because of the large number of parameters utilized in this model, standard fitting techniques could not be easily incorporated. Thus, the study authors used parameter ranges rather than individual values, which had the effect of reducing the statistical power of the results, allowing only general statements rather than precise predictions to be made about the expected tissue distributions of phenol. Metabolic transformations in both the liver and bone marrow were also included. Experimental conditions, similar to those used in a National Cancer Institute oral study of phenol (NCI 1980), were incorporated into the model.

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Calibration was done using data from a study involving intravenous, intra-arterial, intraduodenal, and hepatic portal exposure to benzene (Cassidy and Houston 1984).

Different compartments pertaining to separate metabolic systems were assessed by selective injection as follows: jugular vein to assess first-pass metabolism across lung, hepatic portal vein to assess hepatic firstpass metabolism, duodenum to assess intestinal mucosa metabolism, and carotid artery to assess immediate tissue distribution.

Validation of the model. Validation of this model using empirical data was not done, and this may cast doubt on some of its predictions. Of particular interest is the prediction that hydroquinone production is greater following phenol administration as compared to benzene administration. This is in opposition to the prediction of the Medinsky et al. (1995) model, described below.

Target tissues. The target tissues were blood and bone marrow. The expected levels of phenol in blood and bone marrow, and total hydroquinone were substantially higher after phenol administration than after benzene administration.

Species extrapolation. Extrapolation of this model from the rodent studies on which it is based to human exposure has not yet been done.

Interroute extrapolation. This model concerned itself primarily with the injection route of exposure, although the use of several injection sites was intended to simulate various distribution routes for orally ingested phenol. Extrapolation to other routes was not done.

The Medinsky et al. (1995) Model

The model by Medinsky et al. (1995) considered the dosimetry of benzene and its metabolites in bone marrow in order to help explain their hematotoxic and myelotoxic effects. It is well known that none of the metabolites alone produces the effects seen with benzene exposure. Although it is not yet a fully developed PBPK model, this study lays the groundwork for further model development.

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Risk assessment. Urinary metabolite profiles resulting from oral exposure indicated that excretion of hydroquinone glucuronide was greater after benzene exposure compared with phenol exposure, suggesting that hydroquinone, a genotoxic compound, is produced in greater amounts after benzene exposure, and thus may play a role in benzene's carcinogenicity. This contrasts with the prediction of the Bois et al. (1991) model described above. The study authors further suggest that this increased hydroquinone production after benzene administration may be due to the zonal distribution of metabolizing enzymes in the liver and the effects of first-pass intestinal conjugation of phenol

Description of the model. Benzene and its metabolites (phenol, catechol, and hydroquinone) were assumed to compete for the same reaction site on the enzyme cytochrome P-450 2El. In addition, phenol can undergo both oxidation and conjugation, althougb the enzymes for each of these reactions are localized in different compartments of the liver, and competition between them is thereby regulated. This model incorporates observations made in an earlier kinetic study that investigated benzene and phenol metabolism *in vitro* in mouse and rat liver microsomes (Schlosser et al. 1993). In that study, the following reaction sequences were postulated: benzene → phenol → catechol → trihydroxybenzene and phenol → hydroquinone → trihydroxybenzene.

The Medinsky et al. (1995) model also incorporates results from an *in vivo* study that quantified urinary metabolites in mice treated orally with phenol (Kenyon et al. 1995). Differences in the metabolism of phenol and benzene were incorporated as possible explanations for the differences between these two chemicals in terms of their carcinogenic potency.

Validation of the model. Validation of the model was performed using data from rat and mouse liver microsome preparations (Schlosser et al. 1993). The assumption that benzene and its metabolites compete for the same enzyme reaction site was supported in part by the observation of a lag time in the benzene-to-hydroquinone reaction as compared to the phenol-to-hydroquinone reaction. This lag could be explained by the fact that benzene is first hydrolyzed to phenol, which is then hydrolyzed to hydroquinone, and if all compounds are substrates for P-450 2E1, the kinetics of this pathway would be slowed compared to those of the direct phenol-to-hydroquinone pathway. The model also adequately predicted phenol depletion and concomitant hydroquinone formation resulting from phenol incubations.

2. HEALTH EFFECTS

Target tissues. The target tissue considered by this model was primarily the bone marrow.

Species extrapolation. Extrapolation of this model from the rodent studies on which it is based to human exposure has not yet been done.

Interroute extrapolation. This model concerned itself primarily with the oral route of exposure. Extrapolation to other routes was not done.

2.4 MECHANISMS OF ACTION

2.4.1 Pharmacokinetic Mechanisms

Absorption of phenol occurs fairly rapidly via the inhalation (Hughes and Hall 1995; Ohtsuji and Ikeda 1972; Piotrowski 1971), oral (Capel et al. 1972; Edwards et al. 1986; French et al. 1974; Hughes and Hall 1995; Kao et al. 1979; Kenyon et al. 1995), and dermal (Baranowska-Dutkiewicz 1981; Hughes and Hall 1995; Piotrowski 1971) routes. Because it is an irritant, tissue damage, inflammation, or other irritation effects may occur at the sites of absorption. Because of its high pK_a ionization will not occur within the acid environment of the gut. The action of gut microflora on phenol breakdown is not expected to be significant.

When it is absorbed through the lungs, gut, or skin, phenol enters the bloodstream where it can then be distributed throughout the body. The dilution of phenol in water enhances the dermal absorption of phenol, as indicated by the greater toxicity of a water-phenol solution compared to neat phenol (Conning and Hayes 1970).

Conjugation with glucuronic acid and conjugation with sulfate are the main routes of detoxification of phenol. Following oral exposure, much of the metabolism is expected to occur during a first-pass through the intestines and the hepatic system, where phenol may be further oxidized or conjugated to form glucuronides and sulfides. A lack of first-pass metabolism following skin absorption may contribute to the toxicity of phenol following dermal exposure (Skowronski et al. 1994). Phenol that is absorbed is rapidly excreted in the urine as free phenol or conjugates (Baranowska-Dutkiewicz 1981; Capel et al. 1972; Deichmann 1944; Edwards et al. 1986; French et al. 1974; Hughes and Hall 1995; Kao et al. 1979; Kenyon et al. 1995; Liao and Oehme 1981; Piotrowski 1971).

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2.4.2 Mechanisms of Toxicity

Phenol is a hydrolyzed metabolite of benzene and is itself further hydrolyzed or conjugated to produce other compounds. Therefore, the toxic effects of phenol exposure may be due to a combination of the parent compound and its metabolites. The major tissues in which metabolism appears to occur are the liver, gut, lung, and kidney (Cassidy and Houston 1984; Powell et al 1974; Quebbemann and Anders 1973; Tremaine et al. 1984). Since phenol, benzene, and their major metabolites all seem to compete for the same P450 and conjugating enzymes, metabolic reactions are presumed to be saturable.

It has been suggested that phenol exposure results in cardiac effects because it blocks the cardiac sodium channel subtype, with little effect on sodium channels in skeletal muscle (Zamponi et al. 1994). Phenol does not appear to be carcinogenic following oral exposure (NCI 1980), although the chemical combinations that result from benzene and phenol metabolism may contain compounds that do initiate or promote cancer. Metabolites such as hydroquinone and catechol have been demonstrated to be genotoxic and clastogenic.

2.4.3 Animal-to-Human Extrapolations

Although mammals all metabolize phenol to the same metabolites, the amounts of each metabolite vary between species. For example, in the old world monkeys and prosimians, sulfation is the major phenol conjugation pathway, while in the new world monkeys, glucuronidation predominates (Mehta et al. 1978). Cats and pigs have low activities of phenol glucuronyltransferase, and metabolize phenol to phenyl sulfate nearly exclusively (Capel et al. 1972; French et al. 1974; Miller et al. 1976). Because humans have a greater capacity to glucuronidate phenol, cats and pigs would not be good models for the metabolism of phenol by humans.

2.5 RELEVANCE TO PUBLIC HEALTH

Issues relevant to children are explicitly discussed in 2.6 Children's Susceptibility and 5.6 Exposures of Children.

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Overview

There is a long history of human exposure to phenol. Phenol was once used by surgeons in the operating room as an antiseptic. Effects in humans attributed to chronic phenol exposure include anorexia, progressive weight loss, diarrhea, headache, vertigo, salivation, and a dark coloration of the urine (Merliss 1972). Methemoglobinemia and hemolytic anemia, as well as liver damage, have also been reported following human exposure to phenol (ACGIH 1991). Direct skin contact with phenol results in irritation and necrosis. Unfortunately, the doses resulting in these effects are not well defined, and the reports describing these effects are anecdotal. The irritation effect on the skin has been used for medical purposes, as in the use of phenol for the surgical procedure of skin peeling. During this procedure, exposure to phenol has resulted in cardiac arrhythmias (Gross 1984; Truppman and Ellenby 1979; Warner and Harper 1985).

Human exposure to low levels of phenol is widespread because it is contained in many consumer products including mouthwashes, gargles, tooth drops, throat lozenges, and ointments (Douglas 1972; EPA 1980). Phenol is a normal product of protein metabolism, and it is also a metabolite of benzene. In persons not exposed to phenol or benzene, the total phenol concentration in the urine generally does not exceed 20 mg/L and is usually <10 mg/L (ACGIH 1991).

Phenol is absorbed from the lungs, gastrointestinal tract, and skin. A study that examined the absorption of phenol vapor through the skin indicates that it is readily absorbed (Piotrowski 1971), and dermal absorption is considered the primary route of entry for vapor, liquid, and solid phenol (ACGIH 1991). Conjugation of phenol with glucuronic acid and conjugation with sulfate are the main detoxification pathways. Conjugation occurs predominantly in the lungs, gastrointestinal tract, liver, and kidneys. The skin has relatively low potential to detoxify phenol. Therefore, absorption through the skin represents the greatest hazard from phenol because it readily passes through the skin, and because there is no first-pass metabolic effect as is observed following oral exposure.

Exposure of animals to high doses of phenol results in neurological effects including muscle tremor and loss of coordination (Conning and Hayes 1970; Dalin and Kristoffersson 1974; Jones-Price et al. 1983b; Liao and Oehme 1981; Moser et al. 1995; Pullin et al. 1978). Examples of additional effects reported in animals exposed to phenol include decreased red blood cell counts (Hseih et al. 1992), decreased body weight gain (NCI 1980), and skin necrosis and inflammation following direct application (Brown et al. 1975; Conning and Hayes 1970; Patrick et al. 1985). Exposure of pregnant animals to phenol (at doses that resulted in

maternal toxicity, including dyspnea and rales, and decreased maternal body weight gain) has resulted in a decrease in the number of live births and reduced fetal body weights (Jones-Price et al. 1983a; Nartosky and Kavlock 1995). It is not known if phenol causes reproductive or developmental effects in humans.

Decreased body weight gain associated with decreased water intake was the only adverse effect noted in rodents in a study of chronic exposure to phenol (NCI 1980). Phenol did not cause cancer in either rats or mice in this study. Phenol (20% in acetone) has been shown to act as a cancer promoter following skin application (Salaman and Glendenning 1957). *In vitro* studies have shown that phenol can cause chromosomal aberrations in mammalian cells (Bulsiewicz 1977; Ciranni et al. 1988), although other studies have shown negative results (Barale et al. 1990; Chen and Eastmond 1995a; Pashin et al. 1987). *In vitro* studies have shown both positive results (Crebelli et al. 1987; Demerec et al. 1951; Gocke et al. 1981; Morimoto and Wolff 1980; Paschin and Bahitova 1982) and negative results (Florin et al. 1980; Haworth et al. 1983; Nagel et al. 1982; Pool and Lin 1982) for genotoxic effects. It is not known if phenol can cause cancer in humans.

Minimal Risk Levels for Phenol

Inhalation MRLS

No MRLs were derived for inhalation exposure to phenol. Human inhalation studies of phenol alone were not identified. Inhaled phenol is a respiratory irritant in animals and decreased respiration rate in mice by 50% during a 5 minute exposure at 166 ppm (De Ceaurriz et al. 1981). Based on their studies in mice, De Ceaurriz et al. (1981) estimated that a level of 2 ppm would be a NOAEL for respiratory effects in humans. A study in rhesus monkeys, rats, and mice did not find significant effects following a 90-day continuous exposure at 5 ppm (Sandage 1961). Intermittent exposure of guinea pigs and rabbits to 26-52 ppm phenol resulted in severe respiratory, cardiovascular, hepatic, and renal toxicity (Deichmann et al. 1944). Similar effects were not observed in rats exposed in a similar manner.

Oral MRLs

An acute-duration oral MRL was not derived for phenol. The lowest LOAEL was a serious effect reported in a developmental study (Narotsky and Kavlock 1995). Dyspnea, rales, and a 20% decrease in maternal body weight gain were reported in pregnant rats treated by gavage with phenol in water at a dose of 40 mg/kg/day

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on gestation days 6-19. A significant decrease in the number of liveborn pups was observed at 53.3 mg/kg/day and was associated with severe respiratory effects. This study is limited in that the number of dams with respiratory effects was not stated.

An intermediate oral MRL was not derived for phenol. The lowest LOAEL reported for an intermediate exposure was for a less serious effect reported in an immunological study (Hsieh et al. 1992). A significant decrease in red blood cells was seen in CD-1 mice given phenol in drinking water for 4 weeks at a concentration of 4.7 mg/L (1.8 mg/kg/day). However, this was a single report; similar effects have not been reported in humans except for mixed exposures where the presence of phenol was reported but may have been chlorophenol (Baj et al. 1994).

Furthermore, phenol is a United States Pharmacopeia (USP) approved ingredient used in a number of over-the-counter treatments for sore throats, including gargles, sprays, and lozenges. Cepastat® cherry and extra strength throat lozenges, for example, contain 14.5 and 29 mg phenol/lozenge, respectively. If a patient were to take the maximum dose per day of 300 mg (the 'not to exceed' dosage recommended for a maximum of 7 days for adults and children 6 or older) (PDR 1998), this could result in doses as high as 8 mg/kg/day.

Death. Reported deaths associated with phenol are rare and largely confined to intentional oral exposure (suicides) and accidents involving exposure of a large fraction of the skin surface (>25%) to concentrated phenol solutions (Griffiths 1973; Lewin and Cleary 1982; Stajduhar-Caric 1968). The death of a woman was reported following subarachnoid injection of 3 mL of a 6% phenol solution in glycerin to achieve a cervical subarachnoid block (Holland and Yousef 1978). At autopsy, the effects noted included demyelination, degeneration of cervical nerve roots, fibrous thickening of leptomeninges, and cerebellar cortical infarct.

The minimal lethal oral dose in humans was estimated to be ≈140 mg/kg (Bruce et al. 1987), which is similar to the lethal oral dose for a variety of animal species (see Table 2-2). Regardless of the route of administration, the sequence of events leading to death appears to be similar in a variety of animal species: muscle weakness and tremors, loss of coordination, paralysis, convulsions, coma, and respiratory arrest. These symptoms implicate central or peripheral nervous system toxicity as a primary cause of death. Injury to other organ systems may also contribute to death. In one inhalation study, extensive injury to the lung, heart, liver, and kidney was reported in guinea pigs exposed to lethal concentrations of phenol in air (Deichmann et al. 1944). However, these findings have not been corroborated. In a dermal lethality study, hematuria and related kidney damage were noted in rats at necropsy, suggesting that hemolysis may have

contributed to the cause of death (Conning and Hayes 1970). Phenol diluted with water was more toxic than neat phenol, suggesting that water enhances the absorption of phenol.

An injection study indicates that phenol was more toxic to rabbits following intravenous injection compared to subcutaneous or intraperitoneal injection (Deichmann and Wither-up 1944). Following injection of a 5% aqueous phenol solution, the LD_{50} values were 180 mg/kg following intravenous injection and 620 mg/kg following subcutaneous or intraperitoneal injection Death is unlikely to occur at concentrations of phenol that occur in the environment or at hazardous waste sites

Systemic Effects

Respiratory Effects. Following inhalation exposure, phenol is a respiratory irritant at high concentrations (ACGIH 1991; De Ceaurriz et al. 1981). In a review by Babich and Davis (1981), it was observed that inhalation of phenol causes damage to lungs including hyperemia, infarcts, bronchopneumonia, purulent bronchitis, and hypoplasia of the peribronchial tissues. Acute lobular pneumonia, with occasional abscesses and vascular damage, was seen in guinea pigs exposed to high concentrations of phenol by inhalation (Deichmann et al. 1944). Widespread confluent lobular pneumonia, lesions of chronic purulent bronchitis, hyperplastic peribronchial tissue, and degenerative changes in pulmonary vessels were seen in rabbits similarly exposed in the same study. At lower concentrations, respiratory effects have not been reported following inhalation exposure of monkeys, rats, or mice (Sandage 1961). Dyspnea and rales have been reported in pregnant rats following gavage dosing with phenol (Narotsky and Kavlock 1995). An *in vitro* study using tracheal mucosa of the rabbit has shown that exposure to a concentration of 0.1% phenol in water resulted in ciliostasis after about 55 minutes, while a concentration of 5% resulted in ciliostasis after 2.5 minutes (Dalhamn and Lagerstadt 1966). This study suggests that inhalation exposure to phenol may decrease mucociliary clearance. Studies in which phenol was administered in drinking water did not report respiratory effects (Hsieh et al. 1992; NCI 1980). Following dermal exposure, dyspnea was reported in pigs after undiluted phenol was applied to 35-40% of the total body surface area (Pullin et al. 1978). Respiratory effects are unlikely to occur at concentrations of phenol that occur in the environment or near hazardous waste sites.

Cardiovascular Effects. Cardiac arrhythmias have been reported in individuals undergoing chemical face peels involving application of concentrated solutions of phenol (50%) in combination with hexachlorophene and croton oil to extensive areas of the face (Gross 1984; Truppman and Ellenby 1979; Warner and Harper

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1985). Cardiac arrhythmia and bradycardia have also been reported following accidental skin exposure to phenol (Horch et al. 1994), and in children with cerebral palsy treated with intramuscular injection with 5% phenol (Morrison et al. 1991). A relationship between cardiac arrhythmias and blood levels of phenol has not been observed (Gross 1984; Morrison et al. 1991). Exposures resulting in cardiac effects are likely to occur only during clinical procedures or when concentrated solutions of phenol are accidentally spilled on the skin. The mechanism for cardiac effects has not been elucidated. Cardiac arrhythmias have been demonstrated in rabbits exposed to 300 mg/kg or ≈67 mg/cm^2 of skin (Wexler et al. 1984). Following intermediate-duration inhalation exposure to relatively high concentrations of phenol, necrosis of the myocardium and inflammation have been observed in guinea pigs and rabbits (Deichmann et al. 1944). Following oral exposure of rodents, gross (Hsieh et al. 1992) or histopathologic changes (NCI 1980) in the heart have not been observed. Cardiovascular effects are unlikely to occur at concentrations of phenol that occur in the environment or near hazardous waste sites.

Gastrointestinal Effects. Signs of gastrointestinal irritation, including mouth sores, nausea, and diarrhea, have been reported in humans exposed to drinking water containing 5-126 mg/L (0.14-3.4 mg/kg/day) of phenol (Baker et al. 1978). No effects were observed in persons exposed to concentrations of 0.1 mg/L or less (oral dose of 0.003 mg/kg/day). The source of the phenol was a rail accident in which ≈38,000 L of 100% phenol were spilled on the soil and contaminated several local wells. Phenol intake in several families that drew drinking water from nearby wells was estimated to have been 10-240 mg/person/day for several weeks. Increased prevalence of nausea, vomiting, diarrhea, and abdominal pain was also reported following a spill of phenol into a drinking water source in Korea (Kim et al. 1994). Because the water was used after chlorination, chlorophenol may have contributed to the adverse effects. Nausea and vomiting have also been reported following accidental dermal exposure to phenol (Horch et al. 1994). Because gastrointestinal effects can occur following dermal exposure, it is likely that the effect may be a secondary neurological effect rather than just a result of direct irritation of the gastrointestinal tract.

Histopathological changes in the gastrointestinal tract have not been observed in rats or mice exposed to phenol in the drinking water for intermediate or chronic durations (NCI 1980). An *in vitro* study using antral mucosa isolated from the stomach of rabbits indicated that 5 millimolar (mM) phenol resulted in a gradual decrease in luminal acid loss, a gradual increase in tissue electrical resistance, and a gradual decease in short circuit current (Fuhro and Fromm 1978). This study indicates that phenol can have a direct effect on the gastrointestinal tract. Gastrointestinal effects are likely to occur at higher environmental exposures, which could occur during an accidental exposure or from drinking water contaminated by a large spill At the lower

doses resulting from more typical environmental exposures such as those near hazardous waste sites, gastrointestinal effects are not likely to occur.

Hematological Effects. A decrease in red blood cell counts was observed in persons exposed to a wood treatment liquid containing phenol, formaldehyde, and organic chlorohydrocarbons (Baj et al. 1994). Although only limited data were identified, hemolytic anemia and methemoglobinemia are considered to be well-documented complications of phenol poisoning in humans (ACGIH 1991).

Treatment-related decreases in red blood cell counts were observed in mice treated with phenol in the drinking water for 28 days (Hsieh et al. 1992). The EOAEL dose for this response was 4.7 mgL which the authors estimated to be a daily dose of 1.8 mg/kg. A reduction in the ratio of polychromatic to normochromatic red blood cells in the bone marrow was observed in pregnant mice treated by gavage with a single dose of phenol on gestation day 13 (Ciranni et al. 1988). The observation of hemoglobinuria and hematin casts in the distal convoluted tubules and tubular lumens in rats treated with a single dermal application of phenol (Conning and Hayes 1970) indicates red blood cell lysis and increased glomerular filtration of hemoglobin.

Hematological effects were not reported in monkeys, rats, or mice exposed to 5 ppm phenol in air for 90 days (Sandage 1961), or in rats exposed to 26 ppm continuously for 15 days (Dalin and Kristoffersson 1974). Studies in which the ratio of polychromatic to normochromatic red blood cells in the bone marrow of mice treated with one (Barale et al. 1990) or three (Chen and Eastmond 1995a) intraperitoneal injections of phenol did not show an adverse effect.

Hematological effects are likely to occur following exposure to high doses of phenol, which could occur during an accidental exposure. At the lower doses resulting from environmental exposure and exposure near hazardous waste sites, hematological effects are not likely to occur.

Musculoskeletal Effects. Muscle pains in the arms and legs were reported by a man who worked in a laboratory for 13.5 years where he distilled phenol several times a day (Merliss 1972). Because heavy odors were detected and phenol was spilled on his clothes resulting in skin irritation, dermal and inhalation exposures were involved. Histopathological changes in the bone were not observed in rats or mice provided with phenol in the drinking water for 13 or 103 weeks (NCI 1980). Musculoskeletal effects are unlikely to occur at the exposure levels found in the environment or near hazardous waste sites.

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Hepatic Effects. An increase in serum iron, which may reflect an adverse liver effect, was observed in workers exposed for 6 months to phenol in a wood treatment liquid (Baj et al. 1994). Elevated concentrations of hepatic enzymes in serum, and an enlarged and tender liver suggestive of liver injury, were reported in an individual who had been exposed repeatedly to phenol vapor for 13.5 years (Merliss 1972). Since phenol was also spilled on his clothes resulting in skin irritation, dermal and inhalation exposures were involved. A 2-fold increase in serum bilirubin was observed in a man who was accidentally splashed with a phenol solution over his face, chest wall, hand, and both arms (Horch et al. 1994). Changes in liver enzymes were not observed in persons exposed to phenol in drinking water for several weeks after an accidental spill (Baker et al. 1978). This study is not conclusive because the measurements were completed 7 months after the exposure.

Hepatotoxicity, characterized histologically by centrilobular necrosis, and elevated hepatic enzymes in serum were reported in separate studies in which laboratory animals were exposed to phenol in air at concentrations ≥26 ppm (Dalin and Kristoffersson 1974; Deichmann et al. 1944). Hepatic effects were not observed in monkeys, rats, or mice exposed to 5 ppm phenol in air continuously for 90 days (Sandage 1961). Hepatic effects have also not been observed in rodents following oral exposure to phenol (Berman et al. 1995; Hsieh et al. 1992; Jones-Price et al. 1983a, 1983b; NCI 1980).

Phenol is catabolized by liver microsomal monooxygenases to hydroxylated products (e.g., 1,4-dihydroxybenzene) that can undergo further conversion to a variety of electrophilic substances (e.g., benzoquinones). Such reactions may be involved in generating reactive toxic intermediates in the liver (Eastmond et al. 1986; Lunte and Kissinger 1983; Subrahmanyam and O'Brien 1985). Based on the available data, hepatic effects are unlikely to occur at the exposure levels found in the environment or near hazardous waste sites.

Renal Effects. Dark urine has been reported in persons occupationally exposed to phenol (inhalation and dermal) (ACGIH 1991; Merliss 1972) and following oral exposure (Baker et al. 1978; Kim et al. 1994). It has been stated that the dark urine is a result of oxidation products of phenol (Baker et al. 1978). The dark urine may also be a result of increased hemoglobin in the urine as suggested by the Merliss (1972) case report. In this case it took 2-3 months for the urine to clear after exposure was ended, which is not consistent with pharmacokinetic data that indicate that absorbed phenol is excreted in the urine in 1 day (Piotrowski 1971). A study in rats treated dermally with phenol, which found severe hemoglobinuria and hematin casts in

the tubules (Conning and Hayes 1970), suggests that hemoglobin or hemoglobin breakdown products could contribute to the dark urine observed in humans.

Edema in the convoluted tubules, cortical lesions, and glomerular degeneration were reported in guinea pigs and rabbits exposed to 26 ppm phenol in air (Deichmann et al. 1944). Histopathological changes in the kidneys were not observed in monkeys, rats, or mice exposed continuously to 5 ppm phenol in air for 90 days (Sandage 1961). Renal tubular necrosis, protein casts, and papillary hemorrhage were observed in the kidneys of rats treated once by gavage at a dose of 224 mg/kg (Berman et al. 1995). Changes in the kidneys were not observed after a single dose of 120 mg/kg or 14 daily doses of 40 mg/kg (Berman et al. 1995). Histopathological changes in the kidneys were not observed in rats or mice following intermediate- or chronic-duration oral exposure to phenol (Hsieh et al. 1992; NCI 1980). Direct infusion of 0.1, 1, or 5% phenol in saline into the renal circulation did not affect glomerular filtration rate or renal plasma blood flow (Coan et al. 1982). Concentration-dependent histological effects that were noted included basophilic and eosinophilic material in the lumin of proximal and distal tubules, vacuolization and dilation of proximal tubules, and necrotic glomeruli. Thus, phenol can be considered a direct-acting nephrotoxin when administered directly into the vasculature. Since this exposure route is not relevant to humans at or near hazardous waste sites, renal effects are not expected to occur.

Endocrine Effects. No studies regarding endocrine effects in humans were identified. Unspecified histological changes in the adrenal glands were observed in rats treated once by gavage at a dose of 224 mg/kg (Berman et al. 1995). Changes in the adrenal glands were not observed after a single dose of 120 mg/kg or 14 daily doses of 40 mg/kg (Berman et al. 1995). Histopathological changes in the pancreas, pituitary, adrenal glands, thyroid, or parathyroid were not observed in rats or mice following intermediate- or chronic-duration oral exposure to phenol (NCI 1980). Because endocrine gland function has not been examined in humans or animals following phenol exposure, the data are not sufficient to conclude whether phenol will result in endocrine effects at exposure levels in the environment or near hazardous waste sites.

Dermal *Effects.* In humans, application of concentrated solutions of phenol to the skin (>5%) results in inflammation and necrosis at the site of application, and this characteristic has resulted in the use of phenol for face peeling (Gross 1984; Truppman and Ellenby 1979; Warner and Harper 1985). Increases in skin rash, mouth sores, and throat sores have been reported in humans following drinking water exposures, which would include oral and dermal routes of exposures (Baker et al. 1978; Kim et al. 1994). Following accidental skin exposure, pain, redness, and edema occurred immediately (Horch et al. 1994; Merliss 1972). In an in

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vitro assay using human skin cultures, 10% phenol in water was considered corrosive (Perkins et al. 1996). In a review by Babich and Davis (1981), it is observed that dermal applications of phenol induce eczema, inflammation, discolorations, necrosis, sloughing, and gangrene.

The results of a study in pigs suggest that exposure to as little as 0.44 mg/kg/cm^2 can produce skin necrosis (Pullin et al. 1978). Skin irritation as indicated by thickening of the treated ear was observed in mice in which phenol was directly applied to the ear (Patrick et al. 1985). Erythema and increased skin permeability in guinea pigs (Steele and Wilhelm 1966), and necrosis of the skin in pigs (Hunter et al. 1992) have been reported following dermal exposure to phenol. Histopathological changes in the skin have not been reported in rats or mice following intermediate- or chronic-duration oral exposure to phenol (NCI 1980). Dermal effects are likely to occur at higher environmental exposures, which could occur during an accidental exposure or from drinking water contaminated by a large spill. At the lower doses resulting from more typical environmental exposures such as those near hazardous waste sites, dermal effects are not likely to occur.

Ocular Effects. Direct application of 5% phenol to the eyes of rabbits resulted in severe irritation, conjunctivitis, and corneal opacity (Murphy et al. 1982). No other reports of ocular effects in humans or animals were identified. Based on the limited data, ocular effects are unlikely to occur at the concentrations that occur in the environment or near hazardous waste sites.

Body Weight Effects. A man occupationally exposed (inhalation, dermal) to phenol for 13.5 years was described as emaciated, and the symptoms reported included loss of appetite and slow weight loss (Merliss 1972). No effects on body weight have been reported in animals exposed to phenol by inhalation (Dalin and Kristoffersson 1974; Sandage 1961). Following oral exposure, decreased maternal body weight gain has been reported in rats (Narotsky and Kavlock 1995) and mice (Jones-Price et al. 1983b) exposed during gestation. Decreased body weight gain associated with decreased water intake was observed in rats and mice exposed to phenol in drinking water for 13 weeks, and in rats but not mice exposed for 103 weeks (NCI 1980). Additional oral studies of phenol in rats (Berman et al. 1995; Jones-Price et al. 1983a; Moser et al. 1995) and mice (Hsieh et al. 1992) have not reported body weight effects. No studies regarding the effects of phenol on body weight following dermal exposure were identified. Based on the available data, effects on body weight are not likely to occur at exposure levels in the environment or near hazardous waste sites.

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Other Systemic Effects. Direct application of phenol to the tympanic membrane in the ear of rats resulted in inflammation (Schmidt and Hellstrom 1993). When phenol was placed in the ear of rats after tympanic membrane puncture, inflammation and a reduction in auditory brainstem response were observed (Schmidt et al. 1990). These studies indicate that direct application of phenol to the ear for treatment of ear infection should be used with caution.

Immunological and Lymphoreticular Effects. Occupational exposures to "inhaled formaldehyde, phenol and isomers of organic chlorohydrocarbons from Ksylamit ™ which is a widely used liquid wood preservative, were associated with immunological effects such as decreased levels of CD4, suppressed mitogen-induced lymphocyte proliferation, and significantly decreased natural killer cell cytotoxicity. However, it should be noted that in the report Ksylamit™ is indicated to consist of "a mixture of chlorinated benzenes, pentachlorophenol, alpha-chloronaphthalene, chloroparaffin and kerosene" and that the authors provide no discussion of how phenol and formaldehyde are produced through the use of such a mixture (Baj et al. 1994).

Increased susceptibility to *Streptococcus zooepidemicus* and bactericidal activity toward *Klebsiella pneumonia* were not observed in mice exposed by inhalation to 5 ppm phenol for 3 hours or for 3 hours/day for 5 days (Aranyi et al. 1986). Necrosis or atrophy of the spleen or thymus, which was not described further, was observed in rats given a single gavage dose of 240 mg/kg phenol (Berman et al. 1995). Effects on the spleen or thymus were not observed in rats given a single dose of 120 mg/kg or 14 daily doses of 40 mg/kg (Berman et al. 1995). Decreased antibody production was observed in mice treated with phenol in the drinking water at a dose of 6.2 mg/kg/day, with no immunological effects observed at 1.8 mg/kg/day (Hsieh et al. 1992). Histopathologic changes in the spleen or thymus were not observed in rats or mice exposed to phenol in the drinking water for 13 or 103 weeks (NCI 1980).

Using a series of *in vitro* assays, Wilmer et al. (1994) determined that exposure of epidermal keratinocytes to phenol had a profound effect on the cell's expression, production, and release of a number of proinflammatory cytokines and their precursor mRNAs. The pattern of cytokine effect for phenol was complex and different from those observed with other contact irritants. In order to determine if the pattern was related to histological differences *in vivo,* 10 µL phenol in acetone at concentrations ranging from 30 to 50% (doses ranged from 233 mg/kg to 1,398 mg/kg) was applied once to the surface of mouse ears and the skin examined for swelling and histopathologic changes at 3 and 24 hours. The results were moderate but significant ($p < 0.05$) dose-related increases in ear thickness at both time points, although the swelling was

greatest at 3 hours and somewhat diminished (by about 10%) at 24 hours. Histopathologic examination revealed that the treatment induced an extensive, albeit discontinuous, epidermal necrosis which in some areas extended into the subepidermis and resembled local ischemia. Macrophage infiltration of the epidermis was mild to moderate, whereas edema was moderate. Although these data clearly indicate the immunotoxicity of phenol in relatively high doses, they are not sufficient to conclude whether or not phenol will result in immunological/lymphoreticular effects at exposure levels found in the environment or near hazardous waste sites.

Neurological Effects. An increase in the number of headaches was reported by persons exposed to phenol in drinking water following an accident (Kim et al. 1994). Muscle tremors, loss of coordination, paralysis, and convulsions are indicative of phenol poisoning in laboratory animals following all routes of exposure (Conning and Hayes 1970; Deichmann et al. 1944; Itoh 1995; Jones-Price et al. 1983b; Liao and Qehme 1981; Moser et al. 1995; Pullin et al. 1978). Inhalation exposure of guinea pigs at 26-52 ppm (Deichmann et al. 1944), oral exposure of rats at 120 mg/kg (Moser et al. 1995), and dermal exposure of rats at 107.1 mg/kg produced these effects (Conning and Hayes 1970).

The mechanism for the neurological effects of phenol has not been elucidated, although effects on the neuromuscular junction (Blaber and Gallagher I971) and central nervous system have been implicated (Suzuki and Kisara 1985). Intra-arterial injection of phenol (0.25 mg) directly into the hindlimb of a cat facilitated synaptic transmission and contraction of electrically-stimulated skeletal muscle, but did not elicit contractions in the unstimulated muscle (Blaber and Gallagher 1971). In this same preparation, phenol antagonized neuromuscular blockade by tubocurarine, suggesting the possibility of a presynaptic mechanism of action at the neuromuscular junction. Tremors induced by subcutaneous injection of a 1% (w/v) solution of phenol in mice were enhanced by central but not peripheral nerve monoamine depleters, suggesting an involvement of the central monoamine pool in phenol-induced tremor (Suzuki and Kisara 1985). Changes in serum electrolytes may also contribute to the neurological symptoms observed in animals. In one study, serum magnesium and potassium levels were found to be elevated in rats after 15 days of continuous exposure to 26-52 ppm in air; during this period, the rats showed signs of impaired coordination (Dalin and Kristoffersson 1974). Elevated serum potassium and magnesium could cause or contribute to centrally or peripherally mediated muscle tremors; however, a cause and effect relationship has not been established. Changes in neurotransmitter levels in the brains of mice treated with phenol have also been reported (Hsieh et al. 1992) and may contribute to the neurological effects of phenol.

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Based on the available data, obvious neurological effects are not likely to occur at exposure levels found in the environment or near hazardous waste sites The data are not sufficient to conclude whether more subtle function changes in the nervous system may occur.

Reproductive Effects. Studies regarding reproductive effects in humans following exposure to phenol were not identified. In a multi-generation study in rats treated with phenol in the drinking water, many young died at a dose of 914 mg/kg/day, while stunted growtb of the offspring was observed at 800 mg/kg/day (Heller and Purse11 1938). Few details of this study were provided. No effects on reproduction were noted in rats (Jones-Price et al. 1983a) or mice (Jones-Price et al. 1983b) treated by gavage with phenol on gestation days 6-15. Histopathological changes in reproductive organs were not observed in rats or mice treated with phenol in the drinking water for 13 or 103 weeks (NCI 1980). Based on the limited available data, reproductive effects are unlikely to occur in humans following exposure to phenol at concentrations found in the environment or near hazardous waste sites.

Developmental Effects. Studies regarding developmental effects in humans following exposure to phenol were not identified. Gavage treatment of rats (Jones-Price et al. 1983a; Narotsky and Kavlock 1995) and mice (Jones-Price et al. 1983b) with phenol during gestation has resulted in decreased fetal body weight, a decrease in the number of liveborn pups, and an increase in cleft palate of mice. With the exception of a study in rats, which noted a decrease in fetal body weight (Jones-Price et al. 1983a), the developmental effects were associated with maternal toxicity which included severe respiratory effects (Narotsky and Kavlock 1995) and decreased maternal weight gain (Jones-Price et al. 1983b; Narotsky and Kavlock 1995). The lowest dose associated with maternal and developmental effects was 53.3 mg/kg/day given to rats (Narotsky and Kavlock 1995). The results of a modified frog embryo teratogenesis assay-Xenopus (FETAX) showed malformations only at concentrations of phenol resulting in lethality, suggesting that phenol does not have a high potential for teratogenic effects (Bernardini et al. 1996). Based on the limited available data, developmental effects are unlikely to occur in humans following exposure to phenol at concentrations found in the environment or near hazardous waste sites.

Genotoxic Effects. Phenol has been evaluated for genotoxicity in both *in vivo* (Table 2-4) and *in vitro* (Table 2-5) test systems. Increases in chromosomal aberrations have been reported in spermatocytes (Bulsiewicz 1977), bone marrow, and fetal liver (Ciranni et al. 1988) from mice treated with phenol. Other studies have not reported chromosomal aberrations in bone marrow from mice treated with phenol (Barale et al. 1990; Chen and Eastmond 1995a; Pashin et al. 1987) or in Drosophila (Gocke et al. 1981; Sturtevant

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1952). Negative results were reported in a micronucleus assay in bone marrow isolated from mice treated with phenol (Gocke et al. 1981). Phenol has tested positive for increased DNA synthesis in tubular renal and liver epithelial cells from mice treated with phenol (Amlacher and Rudolph 1981), with negative results for DNA synthesis reported in rat testes (Skare and Schrotel 1984) and rat liver (Miyagawa et al. 1995).

Both negative (Florin et al. 1980; Haworth et al. 1983; Nagel et al. 1982; Pool and Lin 1982) and positive (Demerec et al. 1951; Gocke et al. 1981) results for gene mutations in bacteria have been reported following phenol exposure. A single study of gene mutation in Chinese hamster ovary cells was positive (Pas&in and Bahitova 1982). *In vitro* studies regarding chromosomal aberrations in eukaryotic cells have been positive in *Aspergillus* (Crebelli et al. 1987) and in human lymphocytes (Erexson et al. 1985; Morimoto and Wolff 1980; Morimoto et al. 1983), and negative in human lymphocytes (Jansson et al. 1986), mouse lymphoma cells (Pellack-Walker and Blumer 1986), and Chinese hamster ovary cells (Sze et al. 1996). *In vitro* assays for DNA synthesis have been negative in rat liver mitochondria (Schwartz et al. 1985), and positive in human fibroblasts (Poirier et al. 1975) and HeLa cells (Painter and Howard 1982). The mixed results in both the *in vivo* and *in vitro* assays indicate that under certain conditions, especially at higher doses, phenol has the potential to be genotoxic. However, at the exposure levels likely to occur near hazardous waste sites, phenol is not anticipated to be genotoxic.

Cancer. A small non-significant excess of respiratory cancers among phenol-exposed wood industry workers was not clearly related to phenol exposure (Kauppinen et al. 1986). Although small non-significant excesses of Hodgkin's disease and of lung, esophageal, and kidney cancers were noted, mortality from cancer was not clearly related to phenol exposure in phenol production workers (Dosemeci et al. 1991).

Phenol has been tested in animals for carcinogenicity by the oral and dermal routes, but results are equivocal. In a chronic NCI cancer bioassay (NCI 1980), a significant incidence of tumors (pheochromocytomas of the adrenal gland, leukemia, or lymphomas) occurred only in male rats exposed to the lowest dose level (2,500 ppm, 277 mg/kg/day) of phenol but not in male or female mice or male rats exposed to a higher dose level (5,000 ppm, 624 mg/kg/day). Since tumors occurred only in males in one of the two species tested, and since a positive dose-response relationship was not established, this study does not provide sufficient evidence to conclude that phenol is carcinogenic when administered by the oral route. Dermal application of phenol has been shown to result in tumors in mice; phenol is a tumor promoter when it is applied after the application of the tumor initiator DMBA (Boutwell and Bosch 1959; Salaman and Glendenning 1957; Wynder and Hoffmann 1961). However, this effect occurs at dose levels of phenol that produce severe skin

Table 2-4. Genotoxicity of Phenol *In Vivo*

Species (test system)	End point	Results	Reference
Mammalian cells:			
Mouse bone marrow	Chromosomal aberration	–	Barale et al. 1990; Chen and Eastmond 1995a; Pashin et al. 1987
Mouse spermatocytes	Chromosomal aberration	+	Bulsiewicz 1977
Bone marrow from pregnant mice	Chromosomal aberration	+	Ciranni et al. 1988
Mouse fetal liver cells	Chromosomal aberration	+	Ciranni et al. 1988
Mouse bone marrow	Micronucleus	–	Gocke et al. 1981
Mouse tubular renal and liver epithelial	DNA synthesis	+	Amlacher and Rudolph 1981
Rat testes	DNA synthesis	–	Skare and Schrotel 1984
Rat liver	DNA synthesis	–	Miyagawa et al. 1995
Insects:			
Drosophila	Chromosomal aberration	–	Gocke et al. 1981; Sturtevant 1952

DNA = deoxyribonucleic acid; – = negative results; + = positive results

Table 2-5. Genotoxicity of Phenol *In Vitro*

Species (test system)	End point	Results: With activation	Results: Without activation	Reference
Prokaryotic organisms:				
Salmonella	Gene mutation	–	–	Florin et al. 1980; Haworth et al. 1983; Pool and Lin 1982;
Salmonella	Gene mutation	+	–	Gocke et al. 1981
Escherichia coli	Gene mutation	–	–	Nagel et al. 1982
E. coli	Gene mutation	No data	+	Demerec et al. 1951
Eukaryotic organisms:				
Aspergillus	Chromosomal aberration	No data	+	Crebelli et al. 1987
V79 Chinese hamster cells	Gene mutation	+	–	Paschin and Bahitova 1982
Chinese hamster ovary cells	Micronuclei	+	+	Miller et al. 1995
Chinese hamster ovary cells (DNA strand breaks)	Chromosomal aberration	No data	–	Sze et al. 1996
Mouse lymphoma (DNA strand breaks)	Chromosomal aberration	No data	–	Pellack-Walker and Blumer 1986
Rat liver mitochondria	DNA synthesis	No data	–	Schwartz et al. 1985
Human lymphocytes	Chromosomal aberration	+	+	Morimoto and Wolff 1980; Morimoto et al. 1983
Human lymphocytes	Chromosomal aberration	No data	–	Jansson et al. 1986
Human lymphocytes	Chromosomal aberration	No data	+	Erexson et al. 1985

Table 2-5 Genotoxicity of Phenol *In Vitro* (*continued*)

Species (test system)	End point	Results		Reference
		With activation	Without activation	
Human diploid fibroblasts	DNA synthesis	No data	+	Poirier et al. 1975
HeLa cells	DNA synthesis	+	No data	Painter and Howard 1982

DNA = deoxyribonucleic acid; – = negative results; + = positive results

lesions, and in one study (Boutwell and Bosch 1959), phenol was administered in benzene, which is also a dermal irritant. Dermal application of phenol partially inhibits B[a]P-induced tumor formation when it is applied simultaneously with B[a]P (Van Duuren et al. 1971,1973).

Based on the inadequate evidence for the carcinogenicity of phenol in humans and animals, IARC considers phenol not classifiable as to its carcinogenicity in humans (IARC 1989). Based on a complete lack of human carcinogenicity data, and inadequate animal data, EPA placed phenol in group D, not classifiable as to human carcinogenicity. Therefore, an increase in cancer cases would not be expected to be observed in populations exposed to phenol at concentrations found in the environment or near hazardous waste sites.

2.6 CHILDREN'S SUSCEPTIBILITY

This section discusses potential health effects from exposures during the period from conception to maturity at 18 years of age in humans, when all biological systems will have fully developed. Potential effects on offspring resulting from exposures of parental germ cells are considered, as well as any indirect effects on the fetus and neonate due to maternal exposure during gestation and lactation. Relevant animal and *in vitro* models are also discussed.

Children are not small adults. They differ from adults in their exposures and may differ in their susceptibility to hazardous chemicals. Children's unique physiology and behavior can influence the extent of their exposure. Exposures of children are discussed in section 5.6 Exposures of Children.

Children sometimes differ from adults in their susceptibility to hazardous chemicals, but whether there is a difference depends on the chemical (Guzelian et al. 1992; NRC 1993). Children may be more or less susceptible than adults to health effects and the relationship may change with developmental age (Guzelian et al. 1992; NRC 1993). Vulnerability often depends on developmental stage. There are critical periods of structural and functional development during both pre-natal and post-natal life and a particular structure or function will be most sensitive to disruption during its critical period(s). Damage may not be evident until a later stage of development. There are often differences in pharmacokinetics and metabolism between children and adults. For example, absorption may be different in neonates because of the immaturity of their gastrointestinal tract and their larger skin surface area in proportion to body weight (Morselli et al. 1980; NRC 1993); the gastrointestinal absorption of lead is greatest in infants and young children (Ziegler et al. 1978). Distribution of xenobiotics may be different; for example, infants have a larger proportion of their

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bodies as extracellular water, and their brains and livers are proportionately larger (Widdowson and Dickerson 1964; Foman et al. 1982; Owen and Brozek 1966; Altman and Dittmer 1974; Foman 1966). The infant also has an immature blood-brain barrier (Adinolfi 1985; Johanson 1980) and probably an immature blood-testis barrier (Setchell and Waites 1975). Many xenobiotic metabolizing enzymes have distinctive developmental patterns and at various stages of growth and development, levels of particular enzymes may be higher or lower than those of adults, and sometimes, unique enzymes may exist at particular developmental stages (Leeder and Kearns 1997; Komori et al. 1990; Vieira et al. 1996; NRC 1993). Whether differences in xenobiotic metabolism make the child more or less susceptible also depends on whether the relevant enzymes are involved in activation of the parent compound to its toxic form or in detoxification. There may also be differences in excretion, particularly in the newborn who has a low glomerular filtration rate and has not developed efficient tubular secretion and resorption capacities (Altman and Dittmer 1974; West et al. 1948; NRC 1993). Children and adults may differ in their capacity to repair damage from chemical insults. Children also have a longer lifetime in which to express damage from chemicals; this potential is particularly relevant to cancer.

Certain characteristics of the developing human may increase exposure or susceptibility while others may decrease susceptibility to the same chemical. For example, the fact that infants breathe more air per kilogram of body weight than adults may be somewhat counterbalanced by their alveoli being less developed, so there is a disproportionately smaller surface area for absorption (NRC 1993).

Based on a very limited data set, it is likely that most of the effects of phenol exposure, including cardiac arrhythmias and central nervous system depression, observed in adults will be observed in children if exposures are comparable. The data are insufficient to determine whether children will be especially sensitive to such effects, however.

IARC (1989), citing Hinkel and Kintzel(1968), indicated that a newborn infant whose umbilicus had been bound with a bandage containing 2% phenol, died after 11 hours. Another newborn whose skin ulcer was treated with a solution of 30% phenol:60% camphor developed circulatory failure, cerebral intoxication, and methemoglobinemia, but recovered after a blood transfusion. Rogers et al. (1978) evaluated the percutaneous absorption of phenol in 16 infants, aged 2-5 months, who were treated for seborrhoeic eczema with Magenta Paint B.P.C., a medicine containing 4% phenol. The treatment consisted of twice daily painting of the napkin and skin folds (representing about 11-15% of the body surface) with the Magenta paint over 48 hours, with an average of 32 mL of paint (approximately 1,300 mg of phenol) applied to each child. Phenol was detected

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in the urine of four of the infants; however, no information on concentration was presented. Liver function tests run on 8 of the 16 treated infants showed no abnormalities. The study was initiated because of the observation of signs of central nervous system depression in a 6-month-old who had been treated over a much larger area (all of the body except the face), and because of other observations that children with fair complexions or those who received treatment shortly after bathing became 'mildly shocked and drowsy.

In a 5-year (1987-1991) retrospective review of acute exposures to a phenol-containing disinfectant (Creolin Disinfectant™ [26% phenol]) reported to a regional poison control center, Spiller et al. (1993) identified 96 patients, 16 of which were lost to follow-up. There were 60 oral-only exposures, 7 dermal-only, 12 oral/dermal exposures, and 1 inhalation exposure. Sixty (75%) of the patients were under 5 years of age. It was not possible to determine from the information presented the degree of concordance between the 60 patients with oral-only exposures and the 60 under the age of 5, but it is clear that oral exposure of young children is the predominant characteristic of this population of exposed individuals. In this regard, children have clearly been demonstrated to be at greater risk of exposure to phenol via the accidental ingestion of phenol-containing disinfectants.

There are also several reports in the literature indicating that children are susceptible to the effects of phenol, but the findings are mixed with regard to any special sensitivity. In 1 report, a 10 year-old male developed cardiac arrhythmias following a chemical peeling procedure initiated to remove a 12x17 cm hairy nevus of the left scapula and nape. The procedure was performed under general anesthesia (initial conditions: nitrous oxide 60%/halothane 3%; maintenance: 90%/1%), with continuous electrocardiogram monitoring. An hour into the procedure, which involved the application of a solution of phenol (60% phenol, 0.8% croton oil in hexachlorophene soap and water) to the entire surface of the nevus, multifocal and coupled premature ventricular complexes developed. Two intravenous doses of 50 mg lidocaine were ineffective at regulating the arrhythmias; however, 250 mg of bretylium sulfate given by infusion was successful (Warner and Harper, 1985). Although this was a severe reaction, it is difficult to determine, based on a sample size of one, whether it reflects a special sensitivity based on age. In an additional case report, another 10 year-old boy was hospitalized with serious bums; during the next 2.5 days his burns were treated by applying 7.5 L of antiseptic solution containing 2% phenol; his urine became dark, respiration became labored, he fell into a coma, and died. Post mortem analysis of urine revealed 200 mg/L of conjugated phenol (Cronin and Brauer 1949).

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Wood (1978), in a review of the use of phenol as a neurolytic agent, summarized the results of a number of studies including one in which children with cerebral palsy were given nerve blocks with 3% phenol in water as a treatment for spasticity. Out of 150 blocks on 46 children, 9 were associated with complications, 8 with muscle weakness, and 1 with painful paresthesia. This degree of complication was twice that reported by another group who reported on 98 blocks, presumably in adults, with a complication rate of 3% with all complications being transient paresthesia. The first group concluded that in children the risk was too great for the benefit of the procedure. These two studies in combination suggest that children may be especially sensitive to phenol given by injection. Interestingly, a later study (Morrison et al. 1991) involving 24 pediatric patients similarly treated for spasticity with injections of 5% phenol in water at the motor point of insertion during halothane anesthesia concluded that there was no increase in the incidence of complications. In this study the complications of concern were cardiac arrhythmias and the incidence was 19%, yet the authors concluded that the procedure appeared "appropriate to perform in the day-surgery context." The difference in these studies is likely due to the fact that the earlier study evaluated the incidence of delayed complications, whereas the Morrison et al (1991) work evaluated the incidence of an immediate complication, e.g., cardiac arrhythmias. There was no indication in the Morrison et al. (1991) study that delayed complications such as subsequent muscle weakness or paresthesia were evaluated.

A second series of reports in the literature purport to discuss the toxicity of phenol to newborns. These, however, deal with an excessive level of hyperbilirubinemia, or jaundice, in newborns in hospital nurseries where a phenolic disinfectant detergent was used to clean the nursery and its equipment (bassinets and mattresses) (Doan et al. 1979, Wysowski et al. 1978). Review of these reports indicated that the detergent did not contain phenol *per se*, rather it contained more complex phenolics such as o-benzyl-p-chlorophenol and p-tertiary amylphenol.

In animals, several studies suggest a variable toxicity of phenol depending on age. Deichmann and Wither-up (1944) compared the response to oral and subcutaneous administration of phenol in 3 age groups of rats: 10 days old, 5 weeks old, and adults. At a dose of 600 mg/kg orally, death occurred in 90% of 10 day-old rats, in 30% of 5-week-old rats, and in 60% of adult rats. Similarly, 3,000 mg/kg administered subcutaneously caused death in 65% of 10 day-old, 25% of 5-week-old, and 45% of adult animals.

There is some evidence of developmental toxicity, although in some instances the effects noted have shown a typical dose-response relationship, while in others an inverse dose-response relationship has been observed. In a study of the developmental toxicity of substituted phenols, Kavlock (1990) examined the effect of 0,

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100, 333, 667, and 1,000 mg/kg phenol given by gavage on day 11 of gestation. Twenty-seven chemicals were tested in this study. In order for the data to be comparable, a single vehicle was used which consisted of a 4:4:1:1 mixture of water, Tween 20, propylene glycol, and ethanol. Because of the massive quantities of data such a study generates, the author focused his analytic efforts on five principal parameters, four of which were sampled at two time points. The 5 parameters were maternal weight change (at 24 and 72 hours postdosing), litter size (postnatal day [PD] 1 and 6), perinatal loss, pup weight (in g on PD 1 and 6), and litter biomass (in g on PD 1 and 6).

Within these five parameters, a significant impact of phenol dosing was seen only on maternal weight change, and only at the two highest doses. However, at these same doses, a syndrome of malformations involving the limbs and tail was seen. At a dose of 667 mg/kg, pups in 21.4% of the litters were affected. (At a dose of 1,000 mg/kg, pups in 27.3% of the litters were affected.) The effect on tails was one of shortening or crimping (i.e., 'kinky' tails). The hindlimb effect consisted of paralysis and/or palsy. In animals with palsy, the limb function would alternate between normal strides and a several second-long periods of tetany. Because limb function matures postnatally, this effect was not evident in the newborn but required 7-10 days to become obvious. In the case of phenol, the syndrome did not interfere with postnatal growth and viability; thus, by the statistical criteria used in the report to categorize developmental potency, phenol was not considered an active developmental toxicant. In a subsequent study with Fischer 344 rats given phenol by gavage, Narotsky and Kavlock (1995) found a significant impact of phenol on litter size with full resorption occurring in 1 of 14 low-dose and 2 of 15 high-dose litters. In addition, another high-dose litter showed excessive perinatal mortality and kinked tails in two of the surviving four pups; this finding was not analyzed for significance but was consistent with earlier observations (Kavlock 1990) and may reflect a teratogenic effect of phenol. These findings may be related to maternal toxicity since all of the dams of these litters showed severe respiratory distress; however, other dams with similar respiratory effects delivered apparently normal litters.

In a multi-generational study of the effect of various levels of phenol administered orally in water, Heller and Pursell (1938) saw no effect on growth, reproduction, or rearing of young over 5 generations of rats given concentrations of ~1,000 mg/L (estimated dose of 114 mg/kg/day), or over 3 generations of rats given concentrations of ~5,000 ppm (estimated dose 571 mg/kg/day). In a study by Jones-Price et al. (1983a), CD rat dams given doses as high as 120 mg/kg phenol showed no maternal toxicity at any dose. There was, however, a dose-related decrease in the average live fetal body weight per litter as compared to controls, but the percent of resorptions per litter decreased with increasing dose. In a parallel study in CD-1 mice, dams

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given 0,70, 140, or 280 mg/kg/day showed significant toxicity at the high dose. There were no significant changes in incidence of resorptions or a dead, or malformed fetuses. There was a significant dose-related decrease in the average live fetal body weight per litter, however.

In rats, the ability of the liver to sulfonate phenol develops with age. Analysis of 105,000 g hepatic supernatants indicated that fetal rats show very low activity (about 3% of the average of 7-week old male and female values which show a male to female ratio of almost 2). By post-natal day 2, the activity increases more than 10 fold in both sexes, a level that is maintained through day 24 (Iwasaki et al. 1993).

Although no reports were found that specifically evaluated age-related changes in the phase I and phase II metabolic transformations of phenol, in general it is known that there is a reduced capacity to metabolize xenobiotics in the first 15 days of life, and that the different enzyme systems have different time courses of development thereafter (Morselli et al. 1980). Thus for example, glucuronide conjugation reactions are considerably reduced in the young and reach adult values only after the age of 3 in humans, whereas sulfate conjugations and oxidative reactions catalyzed by the cytochrome P450 enzymes apparently develop more rapidly (Benet et al. 1995; Morselli et al. 1980). Thus, there could be age-related differences in the balance among metabolites, particularly at high doses where the glucuronide metabolites begin to dominate.

No information was found on the placental transfer and distribution of phenol, however, Ghantous and Danielsson (1986) examined this question for benzene, the principal metabolite of which is phenol. Mice at gestation day 11,14, and 17, were exposed by inhalation to ^{14}C benzene and the distribution of benzene and its volatile and non-volatile metabolites examined using whole body autoradiaography and assessment of tissue concentrations of ^{14}C (day 17 only). The authors indicated that the exposure regimen (50 μCi of ^{14}C benzene in maize oil, volatilized by gentle heating) would theoretically produce 2,000 ppm in the inhalation chamber. Measurements of the difference between the amount added to the chamber and the amount inhaled by the animals indicated an uptake of 90% (i.e., 45 μCi). These authors did not specfically characterize the metabolites, but were able to show that the ^{14}C labeled volatile and non-volatile activity crossed the placental barrier. There was no evidence of preferential accumulation. Indeed, the concentration of volatile and nonvolatile radioactivity in fetal tissues was much lower than that observed in the corresponding maternal tissues. As a metric of the relative accumulation, the authors noted that compared to maternal brain tissue, fetal uptake of benzene was only 8%.

No information was found on the accumulation of phenol in breast milk.

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2.7 BIOMARKERS OF EXPOSURE AND EFFECT

Biomarkers are broadly defined as indicators signaling events in biologic systems or samples. They have been classified as markers of exposure, markers of effect, and markers of susceptibility (NAS/NRC 1989).

Due to an incomplete understanding of the use and interpretation of biomarkers, implementation of biomarkers as tools of exposure in the general population is very limited. A biomarker of exposure is a xenobiotic substance or its metabolite(s), or the product of an interaction between a xenobiotic agent and some target molecule(s) or cell(s) that is measured within a compartment of an organism (NAS/NRC 1989). The preferred biomarkers of exposure are generally the substance itself or substance-specific metabolites in readily obtainable body fluid(s) or excreta. However, several factors can confound the use and interpretation of biomarkers of exposure. The body burden of a substance may be the result of exposures from more than one source. The substance being measured may be a metabolite of another xenobiotic substance (e.g., high urinary levels of phenol can result from exposure to several different aromatic compounds). Depending on the properties of the substance (e.g., biologic half-life) and environmental conditions (e.g., duration and route of exposure), the substance and all of its metabolites may have left the body by the time samples can be taken. It may be difficult to identify individuals exposed to hazardous substances that are commonly found in body tissues and fluids (e.g., essential mineral nutrients such as copper, zinc, and selenium). Biomarkers of exposure to phenol are discussed in Section 2.7.1.

Biomarkers of effect are defined as any measurable biochemical physiologic, or other alteration within an organism that, depending on magnitude, can be recognized as an established or potential health impairment or disease (NAS/NRC 1989). This definition encompasses biochemical or cellular signals of tissue dysfunction (e.g., increased liver enzyme activity or pathologic changes in female genital epithelial cells), as well as physiologic signs of dysfunction such as increased blood pressure or decreased lung capacity. Note that these markers are not often substance specific. They also may not be directly adverse, but can indicate potential health impairment (e.g., DNA adducts). Biomarkers of effects caused by phenol are discussed in Section 2.7.2.

A biomarker of susceptibility is an indicator of an inherent or acquired limitation of an organism's ability to respond to the challenge of exposure to a specific xenobiotic substance. It can be an intrinsic genetic or other characteristic or a preexisting disease that results in an increase in absorbed dose, a decrease in the

biologically effective dose, or a target tissue response. If biomarkers of susceptibility exist, they are discussed in Section 2.9, Populations That Are Unusually Susceptible.

2.7.1 Biomarkers Used to Identify or Quantify Exposure to Phenol

Biological monitoring for exposure to phenol is possible by measuring blood or urine levels of the parent compound. However, it should be noted that phenol and metabolites of phenol may also come from other sources. For example, phenol is a metabolite of benzene and of protein metabolism. Urine samples taken from male workers employed in the distillation of high-temperature phenolic fractions of tar revealed a phenol excretion rate of 4.20 mg/hour compared to a control rate of 0.53 mg/hour for non-exposed workers (Bieniek 1994). Samples were taken 4 hours into the workers' workday, but the worker exposure levels were not reported.

The biological exposure index (BEI) for occupational exposure to 5 ppm phenol is 250 mg total phenol in urine/g creatinine (ACGIH 1998). The urine should be collected at the end of the 8-hour work shift. The sample can be stored in the refrigerator for 4 days or frozen for at least 3 months before analysis. ACGIH (1998) warns that the test is nonspecific and should not be used when workers are exposed to benzene or to household products or medications that contain phenol. Dermal exposure may result in overestimation of inhalation exposure.

Phenol can also be measured in the urine after oral exposure, although a dose-response relationship between oral exposure to phenol and phenol in the urine has not been established. In persons not exposed to phenol or benzene, the total phenol concentration in the urine does not exceed 20 mg/L and is usually <10 mg/L (ACGIH 1998).

2.7.2 Biomarkers Used to Characterize Effects Caused by Phenol

Specific biomarkers used to characterize effects caused by phenol have not been identified. Dark urine has been reported in persons exposed to phenol (orally, dermally, or by inhalation) (ACGIH 1991; Baker et al. 1978; Cronin and Bainer 1949; Kim et al. 1994; Merliss 1972) and following oral exposure. The dark urine may be a result of an oxidation product of phenol or hemoglobin or hemoglobin breakdown products. Further research is required to identify the cause of the dark urine. If it is the result of an oxidation product of phenol, it should be considered a biomarker of exposure.

Phenol can result in hemolytic anemia. Therefore, red blood cell counts may serve as a useful biomarker of effect following exposure to phenol. Measurement of liver enzymes in the serum following phenol exposure would also be useful to determine if liver effects have occurred.

For more information on biomarkers for renal and hepatic effects of chemicals see ATSDR/CDC Subcommittee Report on Biological Indicators of Organ Damage (1990) and for information on biomarkers for neurological effects see OTA (1990).

2.8 INTERACTIONS WITH OTHER CHEMICALS

Phenol is a tumor promoter in laboratory animals In mice, dermal exposure to phenol in benzene (Boutwell and Bosch 1959) or in acetone (Salaman and Glendenning 1957; Wynder and Hoffmann 1961) increased the incidence of tumors resulting from dermal exposure to the tumor initiator, DMBA. When injected with mixtures of phenol and hydroquinone, a hydrolyzed metabolite of phenol, mice exhibited significantly depressed bone marrow erythropoiesis compared to injection with phenol alone (Chen and Eastmond 1995a). The involvement of peripheral acetylcholine in phenol-induced tremors was implicated by studies in which mice were injected with phenol and pentobarbital, an inhibitor of acetylcholine release (Itoh 1995).

2.9 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

A susceptible population will exhibit a different or enhanced response to phenol than will most persons exposed to the same level of phenol in the environment. Reasons may include genetic makeup, age, health and nutritional status, and exposure to other toxic substances (e.g., cigarette smoke). These parameters may result in reduced detoxification or excretion of phenol, or compromised function of target organs affected by phenol. Populations who are at greater risk due to their unusually high exposure to phenol are discussed in Section 5.7, Populations With Potentially High Exposure.

Potentially, individuals with low activities of the enzymes phenol sulfotransferase and glucuronyltransferase may be more susceptible to phenol toxicity. Persons with ulcerative colitis may have an impaired capacity to sulfate phenol (Ramakrishna et al. 1991), which may increase the amount of unchanged phenol that is absorbed following oral exposure. Neonates may also be more susceptible to toxicity from dermally-applied phenol because of increased skin permeability and proportionately greater surface area. A study in which 10-day old rats were more sensitive to lethality following oral exposure to phenol than 5-week-old or adult rats

(Deichmann and Witherup 1944) further suggests that the young may be more sensitive to phenol. (For a more detailed discussion please see Section 2.6.) Because phenol is a vesicant, individuals with sensitive skin or pulmonary incapacity may be more sensitive to phenol. Individuals with kidney or liver diseases that impair metabolism or excretion of phenol and phenol metabolites may be more susceptible to phenol.

2.10 METHODS FOR REDUCING TOXIC EFFECTS

This section will describe clinical practice and research concerning methods for reducing toxic effects of exposure to phenol. However, because some of the treatments discussed may be experimental and unproven, this section should not be used as a guide for treatment of exposures to phenol. When specific exposures have occurred, poison control centers and medical toxicologists should be consulted for medical advice. The following texts provide specific information about treatment following exposures to phenol: Bronstein AC, Currance PL. 1988. Emergency care for hazardous materials exposure. Washington, DC: CV Mosby Company; Ellenhorn MJ, Barceloux DG. 1988. Medical toxicology-diagnosis and treatment of human poisoning. New York, NY: Elsevier; Stutz DR, Ulin S. 1992. Hazardous materials injuries-a handbook for pre-hospital care. 3rd ed. Beltsville, MD: Bradford Communications Corp.

2.10.1 Reducing Peak Absorption Following Exposure

Human exposure to phenol may occur by inhalation, ingestion, or dermal contact. Mitigation methods for reducing exposure to phenol include the general recommendation of separating contaminated food, water, air, and clothing from the exposed individual. Externally, phenol can produce mild irritation; acute exposure may produce dermatitis and abnormal pigmentation (HSDB 1998). Dermal exposure to relatively low concentrations of phenol (5-6%) over a sufficient surface area can result in death. Therefore, speed in removing phenol from the skin is important (HSDB 1998). Because a study has shown that dilution in water increases the dermal absorption of phenol (Conning and Hayes 1970), it has been recommended that polyethylene be used to remove dermal contamination with phenol (Ellenhorn and Barceloux 1988). Because water is readily available, others believe that its use is more appropriate for the decontamination of skin following phenol exposure (Pullin et al. 1978).

2.10.2 Reducing Body Burden

Phenol is excreted in the breath, urine, and feces. Mitigation strategies to increase urinary output and dilute the chemical once it is in the bloodstream may be useful. One method for this may be increased hydration of the individual in order to stimulate diuresis. Information on the distribution of phenol is limited and provides little insight on how distribution might be altered to facilitate any attempts at mitigation of effects.

2.10.3 Interfering with the Mechanism of Action for Toxic Effects

The mechanism of action of phenol in the body is not well understood. Reports of cardiac arrhythmias resulting from phenol exposure are not uncommon (Gross 1984; Horch et al. 1994; Truppman and Ellenby 1979; Warner and Harper 1985). Methods to interfere with the mechanism of action for phenol were not identified.

2.11 ADEQUACY OF THE DATABASE

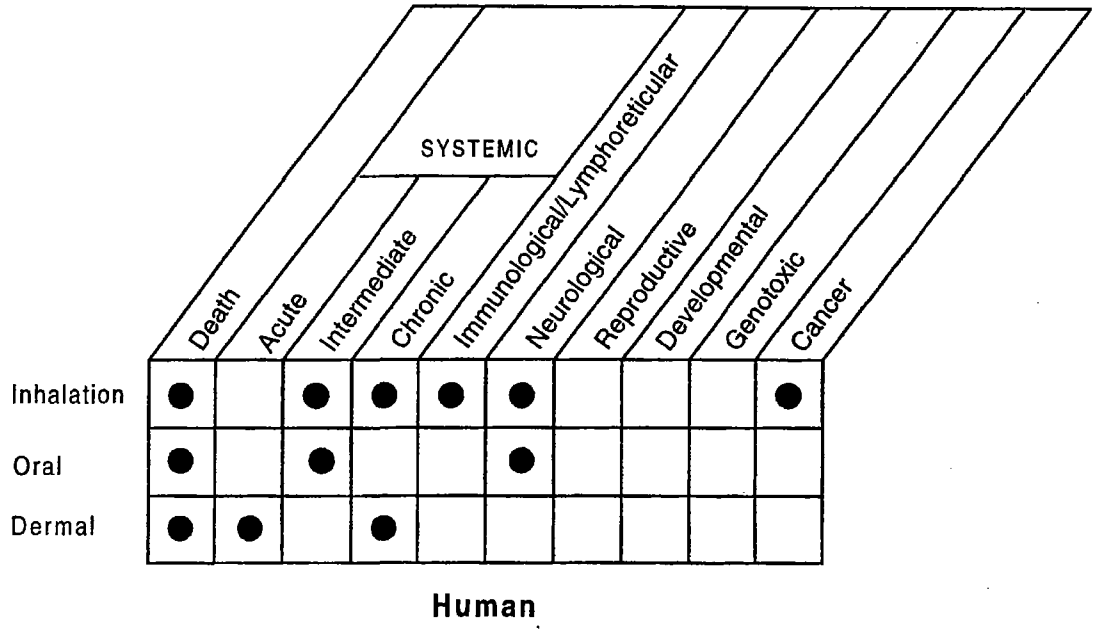
Section 104(I)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of phenol is available. Where adequate information is not available, ATSDR, in conjunction with the National Toxicology Program (NTP), is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of phenol.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

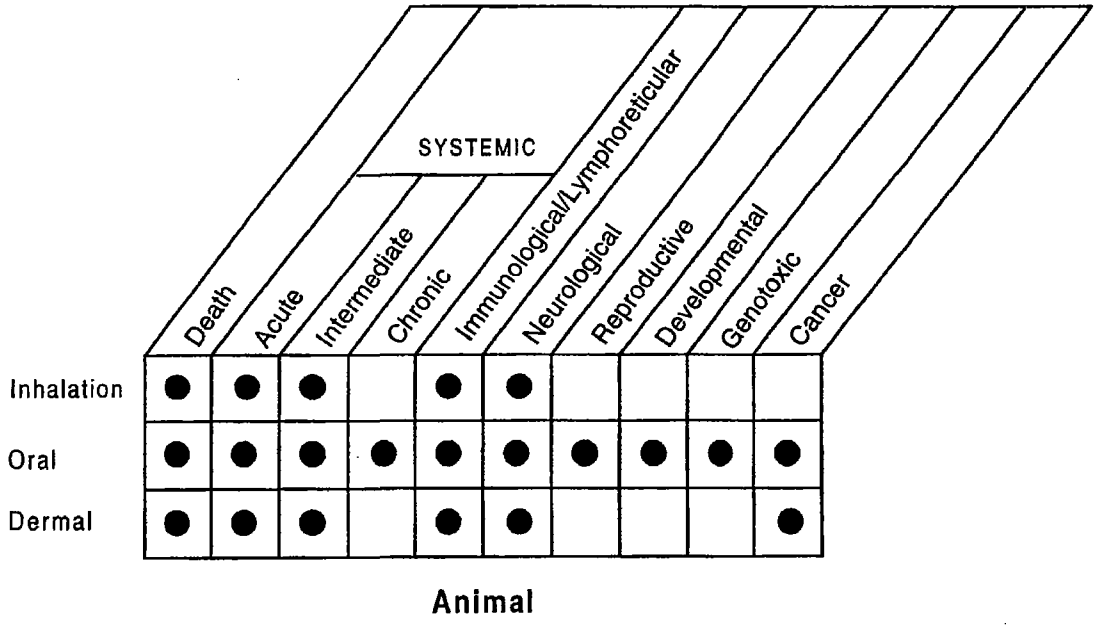
2.11.1 Existing Information on Health Effects of Phenol

The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to phenol are summarized in Figure 2-5. The purpose of this figure is to illustrate the existing information concerning

FIGURE 2-5. Existing Information on Health Effects of Phenol



Human



Animal

● Existing Studies

the health effects of phenol. Each dot in the figure indicates that one or more studies provide information associated with that particular effect. The dot does not necessarily imply anything about the quality of the study or studies, nor should missing information in this figure be interpreted as a "data need." A data need, as defined in ATSDR's *Decision Guide for Identifying Substance-Specific Data Needs Related to Toxicological Profiles* (ATSDR 1989), is substance-specific information necessary to conduct comprehensive public health assessments. Generally, ATSDR defines a data gap more broadly as any substance-specific information missing from the scientific literature.

Information regarding human health effects of exposure to phenol is almost exclusively limited to acute effects of dermal and oral exposure derived from the case report literature (Baj et al. 1994; Griffiths 1973; Gross 1984; Horch et al. 1994; Lewin and Cleary 1982; Merliss 1972; Stajduhar-Caric 1968; Truppman and Ellenby 1979; Warner and Harper 1985). In all of these cases, death or very serious effects were observed (e.g., cardiac arrhythmias), and most cases involved massive exposure levels. Two intermediate-duration exposure studies were found concerning health effects in small populations exposed to phenol in contaminated drinking water (Baker et al. 1978; Kim et al. 1994). One study regarding cancer following occupational exposure to phenol did not indicate an exposure-related effect (Dosemeci et al. 1991).

Data on toxicity of phenol in laboratory animals have been reported for acute and intermediate exposure by the inhalation, oral, and dermal routes. One immunotoxicity study was reported for the inhalation route; rats were exposed to phenol and challenged with infectious bacteria (Aranyi et al. 1986). Several studies provide data on neurologic effects of phenol administered by the inhalation, oral, and dermal routes. Data are extensive regarding genotoxicity of phenol in bacterial systems and mammalian systems (see Table 2-5). Data regarding the oral carcinogenicity of phenol in rats and mice have been reported (NCI 1980), as well as data on the dermal carcinogenicity, and the tumor-promoting and tumor-inhibiting activities of phenol (Boutwell and Bosch 1959; Salaman and Glendenning 1957; Van Duuren and Goldschmidt 1976; Wynder and Hoffmann 1961).

2.11.2 Identification of Data Needs

Acute-Duration Exposure. Phenol is a direct irritant that acts at the site of contact following acute exposure (Conning and Hayes 1970; De Ceaurriz et al. 1981; Hunter et al. 1992; Murphy et al. 1982; Patrick et al. 1985; Pullin et al. 1978; Steele and Wilhelm 1966). Cardiac arrhythmias are the most prominent effect observed in humans during accidental exposure and medical treatments with phenol (Gross 1984; Horch et al.

1994; Truppman and Ellenby 1979; Warner and Harper 1985). Other effects observed in animals following acute exposure to phenol include difficulty breathing (Narotsky and Kavlock 1995; Pullin et al. 1978), hematological effects (Ciranni et al. 1988), kidney effects (Berman et al. 1995; Conning and Hayes 1970), unspecified histopathological changes in the adrenal glands (Berman et al. 1995), decreased maternal weight gain in rats exposed during gestation (Jones-Price et al. 1983b); Narotsky and Kavlock 1995), necrosis or atrophy of the spleen or thymus (Berman et al. 1995), and nervous system effects including muscle twitching, convulsions, and coma (Jones-Price et al. 1983b; Liao and Oehme 1981; Moser et al. 1995). Fetotoxic effects include decreased fetal body weight (Jones-Price et al. 1983a, 1983b) and a decrease in the number of liveborn pups associated with maternal toxicity (Narotsky and Kavlock 1995). The lowest dose resulting in adverse effects following oral exposure was 40 mg/kg/day, a dose associated with difficulty in breathing and a decrease in maternal body weight gain (Narotsky and Kavlock 1995).

The available data were not sufficient for the development of acute-duration inhalation or oral MRLs. Additional data are necessary to further define the dose response of phenol following inhalation, oral, and dermal exposure. Because the oral toxicity of phenol varies with the concentration of the dose, studies using varying concentrations would be useful.

Intermediate-Duration Exposure. Adverse effects have been reported following intermediate-duration occupational exposure to phenol (Baj et al. 1994) and intermediate-duration exposure of humans to phenol in the drinking water (Baker et al. 1978; Kim et al. 1994). The effects reported include decreased red blood cell counts (Baj et al. 1994), gastrointestinal effects, dark urine, and direct skin effects (Baker et al. 1978; Kim et al. 1994).

Intermediate-duration inhalation studies were all single concentration studies at concentrations that resulted in serious effects (26-52 ppm) (Deichmann et al. 1944), or no effects (5 ppm) (Sandage 1961). Therefore, an intermediate-duration inhalation MIX was not derived for phenol. The serious effects noted included pneumonia, necrosis of the myocardium, fatty degeneration of the liver, glomerular degeneration, and hindlimb paralysis (Deichmann et al. 1944). Additional inhalation studies that examine the concentrationrelated response to phenol following intermediate-duration exposure would be useful.

Following intermediate-duration oral exposure to phenol, a decrease in red blood cell counts occurred in mice treated with phenol in drinking water at a dose of 1.8 mg/kg/day for 28 days (Hsieh et al. 1992). Other effects reported in animals following intermediate-duration oral exposure to phenol included decreased body

weight gain associated with decreased water intake (NCI 1980), decreased production of antibodies, and decreases in neurotransmitter levels in the brain (Hsieh et al. 1992). The decreased red blood cell counts in the EIsieh et al. (1992) study are considered a less serious effect from which a LOAEL of 1.8 mg/kg/day for intermediate exposure can be derived.

Skin ulcerations were reported in mice treated dermally with 20% phenol in acetone once each week for 24-32 weeks (Salaman and Glendenning 1957). Because humans are more likely to be dermally exposed to phenol in water, additional intermediate-duration studies examining the effects of dermal exposure to different concentrations of phenol in water are necessary. Additional intermediate-duration studies should include hematological effects as an endpoint.

Chronic-Duration Exposure and Cancer. Mortality was not increased in workers occupationally exposed to phenol (Dosemeci et al. 1991). Effects reported in a case of chronic phenol poisoning, in which exposure was by both the inhalation and dermal routes, included muscle pains in the arms and legs, enlarged and tender liver with increased levels of liver enzymes in the serum, dark urine, and emaciation (Merliss 1972).

No chronic-duration inhalation studies in animals were identified. The only systemic effect in a chronicduration oral study of phenol was decreased body weight gain in rats associated with decreased water intake (NCI 1980). This study did not include tests for neurologic impairment or hematologic studies, both critical effects of phenol exposure. Skin damage has been reported in mice treated dermally with phenol in benzene for chronic durations (Boutwell and Bosch 1959). Because of the limited chronic data available, chronicduration MRLs for phenol were not derived. A chronic-duration inhalation study of phenol in animals would be useful to help predict effects in humans exposed to phenol by inhalation. Additional chronic studies of phenol including neurological function tests and hematologic studies are necessary. Because drinking water is a likely route of exposure for humans, drinking water studies would be more relevant than gavage studies for predicting human health effects. A chronic-duration dermal study of phenol in water is also necessary to predict human health effects following dermal exposure to phenol.

In the occupational studies of phenol, chronic exposure was not clearly related to a carcinogenic effect (Dosemeci et al. 1991; Kauppinen et al. 1986). Phenol was also not clearly carcinogenic in an oral carcinogenicity study in rats and mice (NCI 1980). Additional carcinogenicity studies of inhalation exposure are needed

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Skin studies have indicated that phenol can act as a promotor following treatment with a polyaromatic hydrocarbon (Boutwell and Bosch 1959; Salaman and Glendenning 1957). These studies are limited because phenol was administered in benzene (Boutwell and Bosch 1959) or acetone (Salaman and Glendenning 1957). An additional dermal carcinogenicity study in which phenol is administered in water is necessary to predict the carcinogenicity of phenol following dermal exposure.

Genotoxicity. Phenol has been tested extensively for genotoxicity in a variety of in viva (Amlacher and Rudolph 1981; Barale et al. 1990; Bulsiewicz 1977; Chen and Eastmond 1995a; Ciranni et al. 1988; Gocke et al. 1981; Miyagawa et al. 1995; Pashin et al. 1987; Skare and Schrotel 1984; Sturtevant 1952) and *in vitro* (Crebelli et al. 1987; Demerec et al. 1951; Erexson et al. 1985; Florin et al. 1980; Gocke et al. 1981; Haworth et al. 1983; Jansson et al. 1986; Morimoto and Wolff 1980; Morimoto et al. 1983; Nagel et al. 1982; Painter and Howard 1982; Paschin and Bahitova 1982; Pellack-Walker and Blumer 1986; Poirier et al. 1975; Pool and Lin 1982; Schwartz et al. 1985; Sze et al. 1996) tests. The results of these assays have been eqivocal. Phenol appears to be potentially genotoxic, although this may be more a result of the action of its metabolites than the parent compound. Additional genotoxicity studies of phenol do not seem to be necessary.

Reproductive Toxicity. No studies regarding reproductive effects in humans following exposure to phenol were identified. Only one multigeneration reproductive study in rats has been reported (Heller and Pursell 1938). This study lacked controls, and the methods used to evaluate reproductive performance were not sensitive enough to detect possible reproductive effects (e.g., controlled evaluations of breeding performance). Effects on reproduction were not observed in rats or mice treated by gavage with phenol on gestation days 6-15 (Jones-Price et al. 1983a, 1983b). Histopathological changes in reproductive organs were not observed in rats or mice treated with phenol in the drinking water for 13 or 103 weeks (NCI 1980). Additional studies concerning reproductive effects following any route of exposure were not identified. Controlled multi-generation studies of phenol in rodents by inhalation and oral exposure are necessary to determine if phenol has the potential for causing reproductive effects in humans.

Developmental Toxicity. No studies regarding developmental effects in humans following exposure to phenol were identified. Phenol has been evaluated for developmental effects in rats and mice, but only by the oral route and then only by gavage (Jones-Price et al. 1983a, 1983b; Kavlock 1990; Narotsky and Kavlock 1995). Additional studies examining developmental effects in animals exposed to phenol are necessary.

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Ideally, a multi-generation study by an oral route such as food or drinking water and by inhalation are needed to determine if environmental exposures to phenol place the fetus, infants, or children at additional risk.

Immunotoxicity. Immunological effects were reported in workers exposed to a mixture of phenol, formaldehyde, and organic chlorohydrocarbons for 6 months, although there is some question whether the exposure was due to phenol or a substituted phenol (Baj et al. 1994). Increased susceptibility to bacteria was not observed in mice exposed by inhalation to phenol (Aranyi et al. 1986). Necrosis or atrophy of the spleen or thymus, which was not described further, was observed in rats given a single gavage dose of phenol (Berman et al. 1995). Effects on the spleen or thymus were not observed in rats given 14 daily doses of phenol (Berman et al. 1995). Decreased antibody production was observed in mice treated with phenol in the drinking water (Hsieh et al. 1992). Histopathologic changes in the spleen or thymus were not observed in rats or mice exposed to phenol in the drinking water for 13 or 103 weeks (NCI 1980). Effects on the immune system have not been studied following dermal exposure to phenol, and no studies regarding the ability of phenol to induce sensitivity were identified. Because immunologic effects have been noted in some studies, additional studies regarding immunological effects following inhalation or oral exposure to phenol are needed to further define the dose-response curve.

Neurotoxicity. An increase in the number of headaches was reported by persons exposed to phenol in drinking water following an accident (Kim et al. 1994). Neurological effects (muscle tremor, loss of coordination) have been reported in laboratory animals following exposure by all routes (Conning and Hayes 1970; Deichmann et al. 1944; Itoh 1995; Jones-Price et al. 1983b; Liao and Oehme 1981; Moser et al. 1995; Pullin et al. 1978). However, these studies used only a single dose level, and sensitive methods for evaluating neurotoxicity were not included in the studies. The dose-effect relationship for the neurological effect has not been established, and additional studies by all routes of exposure are needed.

Epidemiological and Human Dosimetry Studies. Retrospective epidemiological studies on small groups of individuals revealed an increased incidence of gastrointestinal symptoms, dark urine, and skin effects associated with drinking water contaminated with phenol (Baker et al. 1978; Kim et al. 1994). The exposure routes in these studies probably included dermal and inhalation, in addition to oral.

A study of workers from phenol production facilities did not find an association between phenol and mortality from various causes, including cancer (Dosemeci et al. 1991). Urinary levels of total phenol have been shown

to correlate with atmospheric phenol concentration when there is limited dermal exposure, and no exposure to benzene (ACGIH 1991; Ohtsuji and Jkeda 1972).

Levels of total urinary phenol (phenol plus phenol conjugates) measured at the end of the workshift correlated with atmospheric phenol concentrations, suggesting that this measurement may be useful in predicting recent exposure to phenol vapor.

Additional epidemiological studies might focus on the effects of low levels of phenol in the air, water, or soil near hazardous waste sites. These studies should carefully consider possible confounding factors including exposure to multiple chemicals, smoking and drinking habits, age, and gender. The endpoints that need to be carefully considered are hematological, kidney and liver, cardiovasculars, developmental, neurological, and genotoxic effects. A dosimetric model which predicts total exposure to phenol from contaminated water is needed. This model should consider inhalation, oral, and dermal exposure. This model is needed to predict the concentration of phenol in water that is safe for human exposure.

Biomarkers of Exposure and Effect

Exposure. Measurement of total phenol in the urine is the most useful biomarker following inhalation exposure to phenol (ACGIH 1991). The test is nonspecific and should not be used when workers are exposed to benzene, to household products, or to medications containing phenol. Dermal exposure may also result in overestimation of inhalation exposure. h-r persons not exposed to phenol or benzene, the total phenol concentration in the urine does not exceed 20 mg/L and is usually <10 mg/L (ACGIH 1991). Phenol can also be measured in the urine after oral exposure, although a dose-response relationship between oral exposure to phenol and phenol in the urine has not been established. Benzene metabolism yields not only phenol, 1,4-dihydroxybenzene, and their sulfates and glucuronides, but also the benzene-specific *t,t*-muconic acid. For both *t,t*-muconic acid and *S*-phenylmercapturic acid, significant correlations were shown with benzene concentrations in air and in blood (Popp et al. 1994; Stommel et al. 1989). Thus, determination of urinary concentrations of these metabolites allows delineation of the portion of metabolites stemming from phenols and the portion derived from benzene exposure. Further research on the relationship between exposure doses and urinary levels of phenol is needed.

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Effect. Specific biomarkers used to characterize effects caused by phenol have not been identified. Dark urine has been reported in persons occupationally exposed to phenol (inhalation, dermal) (ACGIH 1991; Merliss 1972), and following oral exposure (Baker et al. 1978; Kim et al. 1994). The dark urine may be a result of an oxidation product of phenol or hemoglobin. Further research is required to identify the cause of the dark urine.

Absorption, Distribution, Metabolism, and Excretion. The toxicokinetics of phenol have been studied extensively in laboratory animals and humans. Phenol is readily absorbed from the lungs, gastrointestinal tract, and skin. A study that examined the absorption of phenol vapor through the skin indicates that it is readily absorbed and clothing does not serve as a barrier (Piotrowski 1971). Dermal absorption is considered the primary route of entry for vapor, liquid, and solid phenol (ACGIH 1991). Conjugation of phenol with glucuronic acid and conjugation with sulfate are the main detoxification pathways. Conjugation occurs predominantly in the lungs, gastrointestinal tract, liver, and kidneys. The skin has relatively low potential to detoxify phenol. Therefore, absorption through the skin may represent the greatest hazard from phenol because it readily passes through the skin and because there is no first-pass metabolic effect as is observed following oral exposure. Further studies regarding the metabolism of phenol following dermal exposure are needed. *In vitro* studies of phenol metabolism have demonstrated that reactive intermediates are produced during the metabolism of phenol (Eastmond et al. 1986; Eunte and Kissinger 1983; Subrahmanyam and O'Brien 1985). These reactive compounds may be involved in mediating phenol toxicity. Further investigation of these compounds in tissues suspected of being targets for phenol toxicity (i.e., the lungs, skin, liver, kidney, and heart) are needed to provide information for extrapolating from animals to humans.

There is no PBPK model specifically designed for phenol, although phenol, as a major metabolite of benzene has been considered in the two PBPK models of benzene discussed in this profile (Bois et al. 1991; Medinsky et al. 1995). Neither of these models adequately explains the differences in carcinogenicity observed between benzene and phenol, and both models need additional refinements in order to incorporate all the observations and be validated by one another. Additional work on one or both of these models is needed.

Comparative Toxicokinetics. The metabolism and excretion of orally administered phenol in 18 animal species have been compared to metabolism and excretion in humans (Capel et al. 1972). The rat was the most similar to the human with respect to the fraction of administered dose excreted in urine in 24 hours (95%) and the number and relative abundance of the 4 principal metabolites excreted in urine (sulfate and

glucuronide conjugates of phenol and 1,4-dihydroxybenzene). The rat excreted a larger fraction of the orally administered dose than the guinea pig or the rabbit (Capel et al. 1972) and appears to be the least susceptible of the three species to respiratory, cardiovascular, hepatic, renal, and neurological effects of inhaled phenol (Deichmann et al. 1944). More rapid metabolism and excretion of absorbed phenol may account for the lower sensitivity of the rat to systemic effects of phenol. More information on the relative rates of metabolism of phenol in various species is needed to identify the most appropriate animal model for studying potential health effects in humans.

Methods for Reducing Toxic Effects. Removing a person from phenol exposure is the most important method for reducing toxic effects of phenol. This is especially important following dermal exposure, after which speed in removing phenol from the skin is important (HSDB 1998). Because a study has shown that dilution in water increases the dermal absorption of phenol (Conning and Hayes 1970), it has been recommended that polyethylene be used to remove dermal contamination with phenol (Ellenhorn and Barceloux 1988). Because water is readily available, others believe that its use is more appropriate for the decontamination of skin following phenol exposure (Pullin et al. 1978). Further research on the best way to remove phenol from the skin without increasing absorption is needed. The general recommendations for reducing the absorption of phenol following acute oral exposure are well established and have a proven efficiency (HSDB 1998). No additional investigations are considered necessary at this time.

No clinical treatments, other than supportive measures, are currently available to enhance elimination of phenol following exposure. Studies designed to assess the potential risks or benefits of increasing ventilation to enhance pulmonary elimination or of stimulating excretion of phenol and its metabolic products are needed.

Children's Susceptibility. Data needs relating to prenatal developmental exposures are discussed above in the Developmental Toxicity subsection.

Deichman and Witherup (1944) found that 10day-old rats were more sensitive to lethality following oral exposure to phenol than 5-week-old or adult rats; however, this work has never been repeated and there was little other information evaluating the toxicity of phenol at various ages. Such studies need to be conducted in order to follow up this earlier observation and determine if children of certain ages may be more at risk than others.

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There was no information found that specifically evaluated age-related changes in the phase I and phase II metabolic transformations of phenol. However, in general it is known that there is a reduced capacity to metabolize xenobiotics in the first 15 days of life, and that the different enzyme systems have different time courses of development thereafter (Morselli et al. 1980). For example, glucuronide conjugation reactions are considerably reduced in the young, and reach adult values only after the age of 3 in humans, whereas sulfate conjugations and oxidative reactions catalyzed by the cytochrome P450 enzymes apparently develop more rapidly (Benet et al. 1995; Morselli et al. 1980). Thus, there could be age-related differences in the balance among metabolites, particularly at high doses where the glucuronide metabolites begin to dominate. Studies are needed to examine whether age affects the metabolism of phenol, and particularly whether it changes the balance between phase I and phase II metabolism at either high or low doses.

There was no information found on the placental transfer of phenol or on the concentrations of phenol present in breast milk. There is evidence that benzene and its (not specifically identified) metabolites do cross the placenta, although there is no evidence of selective accumulation (Ghantous and Danielsson 1986). Additional studies of this issue are needed to determine if phenol and its metabolites are among the metabolites of benzene that cross the placenta, and if so whether phenol behaves like benzene in the lack of accumulation. Information is also needed on the content of phenol in breast milk under various conditions, e.g, smoking versus non-smoking mothers, in order to determine if breast milk could ever be a source of phenol exposure for children.

Child health data needs relating to exposure are discussed in 5.8.1 Data Needs: Exposures of Children.

2.11.3 Ongoing Studies

Ongoing studies regarding the toxicity and pharmacokinetics of phenol were not identified.

3. CHEMICAL AND PHYSICAL INFORMATION

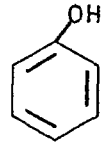
3.1 CHEMICAL IDENTITY

Information regarding the chemical identity of phenol is located in Table 3-1.

3.2 PHYSICAL AND CHEMICAL PROPERTIES

Information regarding the physical and chemical properties of phenol is located in Table 3-2.

TABLE 3-1. Chemical Identity of Phenol

Characteristic	Information	Reference
Chemical name	Phenol	Lide 1993
Synonym(s)	Benzenol, hydroxybenzene, monophenol, oxybenzene, phenyl alcohol, phenyl hydrate, phenyl hydroxide, phenylic acid, phenylic alcohol	Lewis 1996
Registered trade name(s)	Carbolic acid, phenic acid, phenic alcohol	Gardner et al. 1978
Chemical formula	C_6H_6O	Lide 1993
Chemical structure		Budavari et al. 1989
Identification numbers:		
CAS registry	108-95-2	OHM/TADS 1998
NIOSH RTECS	SJ3325000	RTECS 1998
EPA hazardous waste	U188	EPA 1998b
OHM/TADS	7216849	OHM/TADS 1998
DOT/UN/NA/IMO shipping	IMO 6.1 UN 1671 (solid) UN 2312 (molten) UN 2821 (solution)	HSDB 1997
HSDB	113	HSDB 1998
NCI	C50124	Lewis 1996

CAS = Chemical Abstracts Services; DOT/UN/NA/IMO = Department of Transportation/United Nations/North America/International Maritime Dangerous Goods Code; EPA = Environmental Protection Agency; HSDB = Hazardous Substances Data Bank; NCI = National Cancer Institute; NIOSH = National Institute for Occupational Safety and Health; OHM/TADS = Oil and Hazardous Materials/ Technical Assistance Data System; RTECS = Registry of Toxic Effects of Chemical Substances

TABLE 3-2. Physical and Chemical Identity of Phenol

Property	Information	Reference
Molecular weight	94.11	Lide 1993
Color	Colorless to light pink	HSDB 1998
Physical state	Crystalline solid liquid (w/8% H_2O)	
Melting point	43°C	Lide 1993
Boiling point	181.8°C	Lide 1993
Density:		
At 20°C	1.0545@45°C/4°C	Lide 1993
Vapor density	3.24	Lewis 1996
Odor	Distinct aromatic, somewhat sickening, sweet and acrid odor	HSDB 1998
Odor threshold:		
Water	7.9 ppm (w/v)	Amoore and Hautala 1983
	1 ppm (w/v)	Baker et al. 1978
Air	0.040 ppm (v/v)	Amoore and Hautala 1983
Solubility:		
Water at 25°C	87 g/L	Lide 1993
Organic solvent(s)	Very soluble in alcohol, chloroform, ether, benzine, acetone, water	Lide 1993
Partition coefficients:		
Log K_{ow}	1.46	HSDB 1998
Log K_{oc}	1.21–1.96	Artiola-Fortuny and Fuller 1982; Boyd 1982; Briggs 1981; Sacan and Balcioglu 1996; Scott et al. 1983
Vapor pressure:		
at 25°C	0.3513	HSDB 1998
Henry's law constant:	4.0×10^{-7} m^3/mol	Lide 1993
Autoignition temperature	715°C	Lewis 1996
Flashpoint, open cup	85°C	HSDB 1998
Flashpoint, closed cup	79°C	NIOSH 1997
Flammability limits (in air, by % v)	1.7%–8.6%	NIOSH 1997
Conversion factors:		
ppm (v/v) to mg/m^3 in air (20°C)	ppm (v/v) × 3.92 = mg/m^3	
mg/m^3 to ppm (v/v) in air (20°C)	mg/m^3 × 0.255 = ppm (v/v)	

atm = atmosphere; v = volume; w = weight

4. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL

4.1 PRODUCTION

Table 4-1 lists the number of facilities in each state that manufacture or process phenol, the intended use, and the range of maximum amounts of phenol that are stored onsite. The data listed in Table 4-1 are derived from the Toxics Release Inventory (TRI) (TRI96 1998). Only certain types of facilities were required to report. Therefore, this is not an exhaustive list.

Phenol has been obtained by distillation from petroleum and synthesis by oxidation of cumene or toluene, and by vapor-phase hydrolysis of chlorobenzene (USITC 1987). In 1995, 95% of U.S. phenol production was based on oxidation of cumene except at one company that used toluene oxidation and a few companies that distilled phenol from petroleum (CMR 1996). In 1995 the total annual capacity of phenol production approached 4.5 billion pounds (CMR 1996).

4.2 IMPORT/EXPORT

According to the National Trade Data Bank (1996), imports of phenol were 28.7 million kg (63.1 million pounds) and exports of phenol were 138.2 million kg (304 million pounds) in 1995.

4.3 USE

The two major uses of phenol in 1995 were the production of bisphenol-A (35%) and the production of phenolic resins (34%) (CMR 1996). The largest use for bisphenol-A is as an intermediate in the production of epoxy resins (Thurman 1982). Phenol-formaldehyde resins comprise over 95% of this market (Thurman 1982). The plywood adhesive industry required 26% of the total production of phenolic resins in 1977. These low-cost, versatile, thermoset resins have other major uses in the construction, automotive, and appliance industries (Thurman 1982).

Other major uses of phenol include the production of caprolactam (15%), aniline (5%), alkylphenols (5%), xylenols (5%), and miscellaneous uses (1%) (CMR 1996). Phenol is used as a slimicide (a chemical toxic to bacteria and fungi characteristic of aqueous slimes) and as a general disinfectant in solution or mixed with

Table 4-1. Facilities that Manufacture or Process Phenol

State[a]	Number of Facilities	Range of Maxumum Amounts on Site in Pounds[b]	Activities and Uses[c]
AL	31	0–49,999,999	1, 5, 6, 7, 8, 9, 12, 13
AR	14	0–9,999,999	1, 2, 5, 6, 7, 8, 9, 11, 13
AZ	4	100–99,999	8, 12, 13
CA	24	100–9,999,999	1, 2, 3, 5, 6, 7, 8, 9, 11, 12, 13
CO	1	1,000–9,999	12
CT	8	100–99,999	7, 8, 9, 12, 13
DE	1	10,000–99,999	7
FL	10	100–999,999	1, 6, 7, 9, 13
GA	27	0–999,999	1, 2, 3, 5, 6, 7, 8, 9, 11, 13
IA	8	0–99,999	7, 9, 11, 12
ID	1	100–999	1, 6
IL	36	0–9,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13
IN	33	100–49,999,999	1, 2, 3, 4, 5, 7, 8, 9, 11, 12, 13
KS	8	0–9,999,999	1, 4, 5, 6, 7, 8, 9, 12
KY	11	100–9,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12
LA	28	100–99,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13
MA	8	1,000–99,999	7, 8, 9, 12
MD	2	100–99,999	1, 6, 7, 8, 9
ME	7	100–99,999	1, 2, 5, 6, 7, 8, 13
MI	32	0–9,999,999	1, 5, 6, 7, 8, 9, 11, 12, 13
MN	10	1,000–9,999,999	1, 5, 6, 7, 8, 9, 12
MO	10	0–999,999	7, 8, 10, 11, 12, 13
MS	19	0–999,999	1, 5, 6, 7, 9, 12, 13
MT	2	1,000–999,999	1, 6, 7
NC	26	100–9,999,999	1, 5, 6, 7, 8, 9, 11, 12, 13
NE	3	1,000–99,999	7, 9, 12
NH	3	100–99,999	1, 6, 12
NJ	9	0–9,999,999	1, 3, 5, 6, 7, 8, 13
NY	21	100–9,999,999	1, 2, 3, 5, 6, 7, 8, 9, 12, 13
OH	57	0–49,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13
OK	8	100–99,999	1, 5, 6, 8, 9, 11, 12, 13
OR	18	100–9,999,999	1, 6, 7, 8, 9, 12
PA	33	0–99,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13
PR	1	1,000–9,999	9
RI	2	1,000–99,999	7, 8
SC	25	0–9,999,999	1, 5, 6, 7, 8, 10, 11, 13
TN	17	100–99,999	1, 5, 6, 7, 8, 9, 11, 12, 13
TX	66	100–99,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13
UT	3	1,000–999,999	1, 3, 5, 6, 7, 11, 13
VA	18	0–49,999,999	1, 2, 3, 5, 6, 7, 8, 9, 11, 12, 13
VI	1	1,000–9,999	1, 2, 3, 4, 5, 7
VT	1	1,000–9,999	2, 3, 9, 11

Table 4–1. Facilities that Manufacture or Process Phenol (*continued*)

State[a]	Number of Facilities	Range of Maxumum Amounts on Site in Pounds[b]	Activities and Uses[c]
WA	12	0–9,999,999	1, 3, 4, 5, 6, 7, 8
WI	30	100–9,999,999	1, 5, 6, 7, 8 , 9, 11, 12, 13
WV	7	1,000–9,999,999	1, 3, 5, 6, 7, 8, 9
WY	2	100–99,999	1, 4, 5, 6

Source: TRI96 1998

a Post office state abbreviations used

b Range represents maximum amounts on site reported by facilities in each state

c Activities/Uses:

1. Produce
2. Import
3. Onsite
4. Sale/Distribution
5. Byproduct
6. Impurity
7. Reactant
8. Formulation Component
9. Article Component
10. Repackaging
11. Chemical Processing Aid use/processing
12. Manufacturing Aid
13. Ancillary/Other Uses

slaked lime for toilets, stables, cesspools, floors, drains, and other areas (Budavari et al. 1989; Hawley 1981). Phenol is used in medicinal preparations including ointments, ear and nose drops, cold sore lotions, mouthwashes, gargles, toothache drops, analgesic rubs (Douglas 1972), throat lozenges (EPA 1980), and antiseptic lotions (Musto et al. 1977).

4.4 DISPOSAL

Phenol is listed as a toxic substance under Section 313 of the Emergency Planning and Community Right to Know Act (EPCRA) under Title III of the Superfund Amendments and Reauthorization Act (SARA) (EPA 1998c). Disposal of wastes containing phenol is controlled by a number of federal regulations (see Chapter 7).

Phenol may be disposed of by controlled burning or by feeding dilute amounts to sewage organisms. Because shock loadings will be fatal to organisms, sludge acclimation is generally required for efficient digestion by bacteria. Potassium permanganate (100–500 ppm) can be used to disrupt the structure of phenol, forming aliphatic acids (OHM/TADS 1988). Phenol can be recovered economically from solutions of greater than 1% phenol by steam stripping, distillation, or adsorption onto carbon (OHM/TADS 1988).

According to the TRI, about 8.5 million pounds (3.8 million kg) of phenol were transferred to landfills and/or other treatment facilities, and about 3.3 million pounds (1.5 million kg) were sent to publicly-owned treatment works (POTWs) in 1996 (see Table 5-1) (TRI96 1998).

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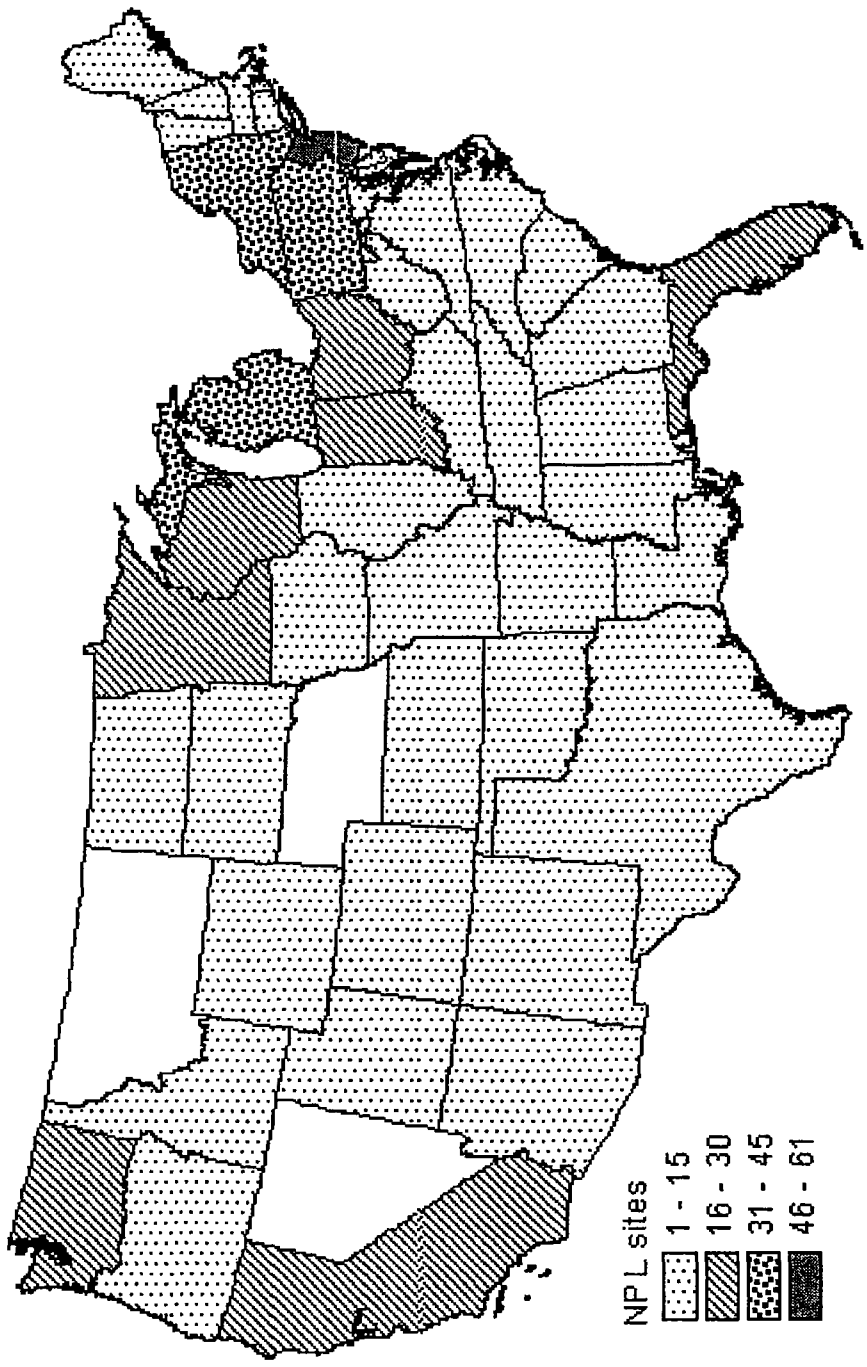
5.1 OVERVIEW

Phenol has been identified in at least 481 of the 1,467 current or former EPA National Priorities List (NPL) hazardous wastes sites (HazDat 1998). However, the number of sites evaluated for phenol is not known. The frequency of these sites within the United States can be seen in Figure 5-1. Of these sites, 477 are located in the United States and 4 are located in the Commonwealth of Puerto Rico.

Phenol is released primarily to the air and water as a result of its manufacture and use and as a result of wood burning and auto exhaust. Phenol mainly enters the water from industrial effluent discharges. Phenol disappears rapidly in air by gas-phase hydroxyl radical reaction (estimated half-life 14.6 hours), but may persist in water for a somewhat longer period. Half-lives for biodegradation range from less than 1 day in samples of lake water to 9 days in estuarine water; a typical half-life for photooxidation by photochemically produced peroxyl radicals is approximately 19 hours. In soil, phenol will generally biodegrade rapidly; however, biodegradation of phenol in water or soil may be hindered or precluded by the presence of high, toxic concentrations of phenol or other chemicals, or by other factors such as a lack of nutrients or microorganisms capable of degrading phenol. If biodegradation is sufficiently slow, phenol in sunlit water will undergo photooxidation with photochemically produced peroxyl radicals, and phenol in soil will leach to groundwater. Since plants can metabolize phenol readily, exposure through eating food derived from plants grown in phenol-containing soil is probably minimal. Phenol may remain in air, water, and soil for much longer periods if it is continually or consistently released to these media from point sources.

Phenol has been measured in effluents (up to 53 ppm), ambient water (from 1.5 to >100 ppb), drinking water (not quantified), groundwater (from 1.9 to >10 ppb), rain (0.075–1.2 ppb), sediment (>10 ppb), and ambient air (0.03–44 ppb). Occupational exposures occur through inhalation and dermal exposure; air concentrations monitored in various workplaces range from 0.1 to 12.5 mg/m^3 (0.03–32 ppm). Occupational as well as consumer exposure may also occur through dermal contact with phenol or phenol-containing products.

Figure 5-1. Frequency of NPL Sites with Phenol Contamination



* Derived from HazDat 1998

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5.2 RELEASES TO THE ENVIRONMENT

According to the TRI, in 1996, a total of about 23.5 million pounds (10.6 million kg) of phenol was released to the environment from 689 large processing facilities (TRI96 1998). Table 5-1 lists amounts released from these facilities. In addition, an estimated 3.3 million pounds (1.5 million kg) were released by manufacturing and processing facilities to publicly owned treatment works (POTWs) and an estimated 8.5 million pounds (3.8 million kg) were transferred offsite (TRI96 1998). The TRI data should be used with caution because only certain types of facilities are required to report This is not an exhaustive list.

Phenol has been identified in a variety of environmental media (air surface water, groundwater, soil, and sediment) collected at 481 of the 1,467 NPL hazardous waste sites (HazDat 1998).

5.2.1 Air

According to the TRI, in 1996, the estimated releases of phenol of 9.5 million pounds (4.3 million kg) to air from 635 large processing facilities accounted for about 5% of total environmental releases (TRI96 1998). Table 5-l lists amounts released from these facilities. The TRI data should be used with caution, however, since only certain types of facilities are required to report. This is not an exhaustive list.

During manufacturing, phenol is released primarily to the atmosphere from storage tank vents and during transport loading (Delaney and Hughes 1979). Other major sources of release to the atmosphere are residential wood burning and automobile exhaust (Scow et al. 1981). Volatilization from environmental waters and soils has been shown to be a slow process (see Section 5.3.1) and is not expected to be a significant source of atmospheric phenol. Phenol has been detected at a concentration of 0.36 ppb in the emissions of a waste incinerator plant in Germany (Jay and Stieglitz 1995). Phenol is also found in cigarette smoke and in plastics (Graedel 1978), but no data are available to determine the extent of exposure to phenol from these sources.

5.2.2 Water

According to the TRI, in 1996, the estimated releases of phenol of 72,55 pounds (32,650 kg) to water from 220 large processing facilities accounted for about 0.3% of total environmental releases (TR196 1998).

Table 5-1. Releases to the Environment from Facilities that Manufacture or Process Phenol

State[b]	Number of Facilities	Total of reported amounts released in pounds per year[a]						
		Air[c]	Water	Land	Underground Injection	POTW[d] Transfer	Off-site Waste Transfer	Total Environment[e]
AL	30	396,256	5,344	13,899	0	4,055	39,513	459,067
AR	14	59,333	1,071	327	1,392	0	6,133	68,256
AZ	4	3,668	0	0	0	0	13,756	17,424
CA	25	100,792	2,714	0	0	426,725	144,299	674,530
CO	1	0	0	0	0	0	3,345	3,345
CT	8	16,581	0	0	0	5,987	47,591	70,159
DE	1	63	0	0	0	5	0	68
FL	9	130,619	404	10	0	3,900	136,647	271,580
GA	26	283,854	1,166	3,325	0	6,799	110,232	405,376
IA	8	59,447	552	2,262	0	0	748,476	810,737
ID	1	755	5	5	0	0	0	765
IL	36	672,577	1,878	3,215	0	1,430,152	602,140	2,709,962
IN	33	1,194,276	9,329	3,372	110,000	1,579	380,631	1,699,187
KS	8	194,981	1,720	232	548	4,114	24,601	226,196
KY	11	235,558	855	7,502	0	152,690	629,679	1,026,284
LA	28	263,918	3,431	850	130,311	0	466,678	865,188
MA	7	59,264	0	0	0	338	14,141	73,743
MD	2	45,805	0	0	0	4,400	16,300	66,505
ME	7	37,555	302	118	0	2	737	38,714
MI	33	193,425	7,652	9,642	0	65,089	211,701	487,509
MN	10	135,671	1,293	3	0	250	12,319	149,536
MO	10	84,683	1	0	0	605	95,795	181,084
MS	18	144,137	2,738	543	0	224	818	148,460
MT	2	1,380	250	0	0	0	5	1,635
NC	26	335,372	1,095	765	0	737	114,352	452,321
NE	3	56,207	0	0	0	0	2,044	58,251
NH	3	2,114	0	1	0	0	16,573	18,688
NJ	9	51,810	6,287	230	0	317,750	81,035	457,112
NY	21	151,883	555	0	0	37,294	1,030,762	1,220,494

Table 5-1. Releases to the Environment from Facilities that Manufacture or Process Phenol (*continued*)

State[b]	Number of Facilities	Total of reported amounts released in pounds per year[a]						
		Air[c]	Water	Land	Underground Injection	POTW[d] Transfer	Off-site Waste Transfer	Total Environment[e]
OH	55	1,237,909	2,288	18,125	460,000	43,438	1,681,659	3,443,419
OK	7	37,511	471	19	0	0	12,455	50,456
OR	18	73,458	625	1	0	2,984	21,868	98,936
PA	32	364,657	2,625	1,021	0	213,875	192,753	774,931
PR	1	640	0	0	0	0	255	895
RI	1	197	0	0	0	2,316	1,642	4,155
SC	24	1,415,260	6,381	8,622	0	807	119,508	1,550,578
TN	17	326,085	345	1,028	0	60,316	57,481	445,255
TX	66	532,158	5,889	2,940	1,343,119	436,982	718,088	3,039,176
UT	3	6,407	32	12,000	0	0	198	18,637
VA	18	250,313	295	68,894	0	26,471	11,531	357,504
VI	1	54,876	1,504	44	0	0	0	56,424
VT	1	9,722	0	0	0	0	0	9,722
WA	12	172,668	1,833	29	0	750	5,454	180,734
WI	30	65,344	990	0	0	29,655	423,747	519,736
WV	7	87,398	635	25	0	0	283,914	371,972
WY	2	5,915	0	10	0	0	0	5,925

Source: TRI96 1998

[a]Data in TRI are maximum amounts released by each facility

[b]Post office state abbreviations used

[c]The sum of fugitive and stack releases are included in releases to air by a given facility

[d]POTW= publicly owned treatment works

[e]The sum of all releases of the chemical to air, land, and water, and underground injection wells; and transfers off-site by a given facility

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Table 5-1 lists amounts released from these facilities. The TRI data should be used with caution, however, since only certain types of facilities are required to report This is not an exhaustive list.

The most common anthropogenic sources of phenol in natural water include coal tar (Thurman 1982) and waste water from manufacturing industries such as resins, plastics, fibers, adhesives, iron, steel, aluminum, leather, rubber (EPA 1981), and effluents from synthetic fuel manufacturing (Parkhurst et al. 1979). Phenol is also released from paper pulp mills (Keith 1976) and wood treatment facilities (Goerlitz et al. 1985). Other releases of phenol result from commercial use of phenol and phenol-containing products, including slimicides, general disinfectants (Hawley 1981; Budavari et al. 1989), and medicinal preparations such as ointments, ear and nose drops, cold sore lotions, mouthwashes, gargles, toothache drops, analgesic rubs (Douglas 1972), throat lozenges (EPA 1980), and antiseptic lotions (Musto et al. 1977). It has been estimated that 3.8 kg/day of phenol are released to Newark Bay, in New Jersey, from municipal treatment facilities (Crawford et al. 1995). Two natural sources of phenol in aquatic media are animal wastes and decomposition of organic wastes (EPA 1980). No data are available to determine the extent of exposure from these sources.

5.2.3 Soil

According to the TRI, in 1996, the estimated releases of phenol of 159,059 pounds (71,577 kg) to soil from 102 large processing facilities accounted for about 0.7% of total environmental releases (TR196 1998). Table 5-1 lists amounts released from these facilities. The TRI data should be used with caution, however, since only certain types of facilities are required to report. This is not an exhaustive list

Phenol may be released to the soil during its manufacturing process, loading and transport when spills occur, and when it leaches from hazardous waste sites and landfills (Xing et al. 1994). Generally, data on concentrations of phenol found in soil at sites other than hazardous waste sites are lacking. This may be due in part to a rapid rate of biodegradation and leaching (see Sections 5.3.1 and 5.3.2.3). Phenol can be expected to be found in soils that receive continuous or consistent releases from a point source. Phenol that leaches through soil to groundwater spends at least some time in that soil as it travels to the groundwater. Phenol has been found in groundwater, mainly at or near hazardous waste sites.

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5.3 ENVIRONMENTAL FATE

5.3.1 Transport and Partitioning

Phenol is released into the air and discharged into water from both manufacturing and use. Based on its high water solubility (see Table 3-2) and the fact that it has been detected in rainwater, some phenol may wash out of the atmosphere; however, it is probable that only limited amounts wash out because of the short atmospheric half-life of phenol. During the day, when photochemically produced hydroxyl radical concentrations are highest in the atmosphere, very Little atmospheric transport of phenol is likely to occur.

In water, neither volatilization nor sorption to sediments and suspended particulates is expected to be an important transport mechanism. Using the Henry's Law constant, a half-life of 88 days was calculated for evaporation from a model river 1 m deep with a current of 1 m/second, and with a wind velocity of 3 m/second (Lyman et al. 1982). The biological treatment of waste water containing phenol has shown that less than 1% of phenol is removed by stripping (Kincannon et al. 1983; Petrasek et al. 1983).

Phenol has been reported in sediments at up to 608 ppm dry weight; however, it is not known whether the location of the site where this concentration was reported is at or near a point source of release, such as a hazardous waste dump. The average concentration (6.1 ppb dry weight) of the sediment concentration contained in the STORET database (EPA 1988b) and the concentration found in the Pacific Ocean near Los Angeles (10 ppb dry weight) is probably more representative of ambient sediment phenol concentrations. The concentrations of the overlying waters were not reported. The moderately low soil sorption partition coefficient (1.21-1 .96) suggests that sorption to sediment is not an important transport process. There is very little sorption of phenol onto aquifer materials (Ehrlich et al. 1982), suggesting that phenol sorption to sediments may also be minimal. Based on the soil adsorption coefficient, phenol released to soil is expected to leach to groundwater; however, the rate of phenol biodegradation in the soil may be so rapid, except in cases of large releases such as spills or continuous releases such as leaching from landfill sites, that the probability of groundwater contamination may be low (Ehrlich et al. 1982). Phenol has been detected in groundwater as a result of leaching through soil from a spill of phenol (Delfino and Dube 1976), from landfill sites (Clark and Piskin 1977), and from hazardous waste sites (Plumb 1987). The sorption coefficient for phenol by soils increases with increasing soil organic matter which may indicate that soil organic matter may be the primary phenol sorbent in soil (Xing et al. 1994).

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Phenol is not expected to bioconcentrate significantly in aquatic organisms. Reported log bioconcentration factors (BCF) in fish for phenol include 0.28 for goldfish, (Kobayashi et al. 1979) and 1.3 for golden orfe (Freitag et al. 1984). The highest mean level of phenol detected in bottom fish from Commencement Bay in Tacoma, WA, was 0.14 ppm (Nicola et al. 1987). The levels of phenol in the water or sediments were not stated.

Since the pK_a of phenol is 9.686 at 20°C it will exist in a partially dissociated state in water and moist soil. Therefore, its transport in these media in the environment would be affected by the pH of the medium.

Although it has been shown that plants readily uptake phenol (Cataldo et al. 1987), bioaccumulation does not take place due to a high rate of respiratory decomposition of phenol to CO_2.

5.3.2 Transformation and Degradation

5.3.2.1 Air

Because phenol absorbs light in the region of 290-330 nm (Sadtler 1960), it might photodegrade directly in the atmosphere. The gas-phase reaction of phenol with photochemically produced hydroxyl radicals is probably a major removal mechanism in the atmosphere. An estimated half-life for phenol for this reaction is 0.61 days (Hendry and Kenley 1979). The reaction of phenol with nitrate radicals during the night may constitute a significant removal process. This is based on a rate constant of 3.8×10^{12} cm^3/molecule second for this reaction, corresponding to a half-life of 15 minutes at an atmospheric concentration of 2×10^8 nitrate radicals per cm^3 (Atkinson et al. 1987). The reaction of phenol with nitrate radicals present in the atmosphere during smog episodes may decrease the half-life of phenol in polluted atmospheres. The above data indicate that phenol has a short half-life in the atmosphere, probably less than 1 day.

5.3.2.2 Water

Because phenol absorbs light in the region of 290-330 nm (Sadtler 1960), it might photodegrade directly in surface waters. As a class, phenols react relatively rapidly in sunlit natural water via reaction with photochemically produced hydroxyl radicals and peroxyl radicals; typical half-lives for hydroxyl and peroxyl radical reactions are on the order of 100 and 19.2 hours of sunlight, respectively (Mill and Mabey 1985). The estimated half-life for the reaction of phenol with photochemically produced singlet oxygen in sunlit

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surface waters contaminated by humic substances is 83 days (assuming Switzerland summer sunlight and a singlet oxygen concentration of $4x10^{-14}$ molar [M]) (Scully and Hoigne 1987). The rate constant for the reaction of phenol with ozone in water has been reported to range from $1.5x10^{-5}$ to $6x10^{-5}$ $milliseconds^{-1}$ (Beltran and Alvarez 1996).

Phenol is readily biodegradable in natural water, provided the concentration is not high enough to cause significant inhibition. Complete degradation in less than 1 day has been reported in water from three lakes; the rates of degradation increase with increasing concentration of phenol and increasing trophic levels of water, and are affected by the concentration of organic and inorganic nutrients in the water (Rubin and Alexander 1983). Complete removal of phenol in river water has been reported after 2 days at 20 °C and after 4 days at 4 °C (Ludzack and Ettinger 1960). The degradation of phenol is somewhat slower in salt water, and a half-life of 9 days has been reported in an estuarine river (Lee and Ryan 1979). Rapid degradation of phenol also has been reported in various sewage and water treatment processes. Removal in aerobic activated sludge reactors is frequently >90% with a retention time of 8 hours (Stover and Kincannon 1983). In aerobic reactors using municipal seed (conventional activated sludge organisms) and in reactors using an industrial seed (mixture of organisms), it was noted that concentrations as low as 50 mg/L inhibited organism respiration rates, but complete inhibition was not observed at concentrations as high as 200 mg/L (Davis et al. 1981). Utilization is also very high in anaerobic reactors, although acclimation periods are longer and degradation usually takes about 2 weeks (Boyd et al. 1983; Healy and Young 1978). One method of phenol breakdown is accomplished by the bacterium *Pseudomonas* sp. CF600, which uses a set of enzymes encoded by the plasmid *dmp* operon (Powlowski and Shingler 1994). The use of sequence batch reactors (SBR) in treating sludge contaminated with phenolic compounds has proven effective in breaking down the compounds biologically with no evidence of phenol volatility (Al-Harazin et al. 1991). Levels as high as a 1-time treatment of 1,600 mg/L can be broken down by 75% with a 1-day retention time. lower concentrations as high as 800 mg/L can be broken down to less than 0.5 mg/L with a 1-day retention time. The alga *Ochromonas dunica* has also been shown to degrade phenol (Semple and Cain 1996). When grown in the dark with 0.1-1 mM phenol as the sole carbon source, phenol was removed within 3 days. Because of biodegradation, groundwater is generally free of phenol even though it is highly mobile in soil (HSDB 1997). However, monitoring data in Section 5.4.2 contain groundwater concentrations in areas of large phenol releases.

While the evidence presented in the literature cited above suggests that phenol can be rapidly and virtually completely degraded under both natural water and sewage treatment plant conditions, monitoring data

presented in Section 5.4 below indicate that phenol, despite this apparent biodegradability, is still present in the environment. This suggests that the exact conditions under which phenol is rapidly degraded are not present in all instances. In some situations, the concentration of phenol may be too high or the populations of microorganisms may not be present in sufficient concentration for significant biodegradation to occur.

5.3.2.3 Sediment and Soil

Available data indicate that phenol biodegrades in soil under both aerobic and anaerobic soil conditions. The half-life of phenol in soil is generally less than 5 days (Baker and Mayfield 1980; HSDB 1998), but acidic soils and some surface soils may have half-lives of between 20 and 25 days (HSDB 1998). Mineralization in an alkaline, para-brown soil under aerobic conditions was 45.5, 48, and 65% after 3,7, and 70 days, respectively (Haider et al. 1974). Half-lives for degradation of low concentrations of phenol in two silt loam soils were 2.70 and 3.51 hours (Scott et al. 1983). Plants have been shown to be capable of metabolizing phenol readily (Cataldo et al. 1987).

While degradation is slower under anaerobic conditions, evidence presented in the literature suggests that phenol can be rapidly and virtually completely degraded in soil under both aerobic and anaerobic conditions (HSDB 1998).

Phenol is not expected to adsorb to sediment in the water column (HSDB 1998).

5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

Reliable evaluation of the potential for human exposure to phenol depends in part on the reliability of supporting analytical data from environmental samples and biological specimens. In reviewing data on phenol levels monitored or estimated in the environment, it should also be noted that the amount of chemical identified analytically is not necessarily equivalent to the amount that is bioavailable.

5.4.1 Air

There are very few monitoring data concerning the presence of phenol in ambient air. Phenol was found at a median concentration of 30 parts per trillion (ppt) in seven samples from 1 U.S. urban/suburban site in 1974 and at an overall median concentration of 5,000 ppt in 83 samples from 7 source-dominated sites between

1974 and 1978 (Brodzinsky and Singh 1982). The individual medians of the 7 source sites ranged from 520 to 44,000 ppt (Brodzinsky and Singh 1982). During a smog episode in West Covina, CA, in July of 1973, phenol concentrations ranged from 16 to 91 ppt, with a mean concentration of 60 ppt (Cronn et al. 1977). Phenol was detected, but not quantified, in air above the Niagara River in September of 1982 (Hoff and Chan 1987). Phenol concentrations in 2 urban areas ranged from 13 to 91 ppt and from <5 to 75 ppb with 50% of all measurements less than 8 ppb (Scow et al. 1981). Phenol was found at approximately 1 ppb in the ambient air near a fishmeal factory in Japan (Hoshika et al. 1981).

Phenol and other volatile organic compounds were measured in the air of 50 homes or apartments in Finland (Kostiainen 1995). The average concentration was 0.23 ppb, with a range of 0-0.77 ppb. Phenol levels were not significantly higher in houses in which people complained of symptoms that resembled those of a sick building syndrome.

5.4.2 Water

Phenol has been detected in surface waters, rainwater, sediments, drinking water, groundwater, industrial effluents, urban runoff, and at hazardous waste sites. Background levels of phenol from relatively pristine sites can be as high as 1 ppb for unpolluted groundwater and have been reported to range from 0.0 1 to 1 ppb in unpolluted rivers (Thurman 1985). Phenol has been detected in Lake Huron water at 3-24 ppb (Konasewich et al. 1978) and industrial rivers in the United States at 0-5 ppb (Sheldon and Hites 1978, 1979). The annual mean concentration of phenol in water from the lower Mississippi River was 1.5 ppb (EPA 1980). River water in an unspecified location in the United States was reported to contain 10-100 ppb of phenol (Jungclaus et al. 1978). Phenol was detected, but not quantified, in a Niagara River watershed (Elder et al. 1981) and in 2 of 110 raw water samples analyzed during the National Organic Monitoring Survey (EPA 1980). In the STORET database, 7% of 2,181 data points for U.S. surface waters were positive for the presence of phenol; the mean and range of the reported concentrations were 533 ppb and 0.002-46,700 ppb, respectively (EPA 1988c).

In general, higher levels of phenol appear to be found in lakes and rivers that serve as water sources and discharge receivers for industrial and population centers, probably as a result of industrial activity and commercial use of phenol-containing products. For example, the presence of higher levels of phenol in the Delaware River near Philadelphia is the result of industrial effluents discharged into the sewer system (Sheldon and Hites 1979).

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The presence of phenol in drinking water probably results from using contaminated surface water or groundwater as a source. Its presence in groundwater is probably the result of release to soil, often industrial releases or leachate from waste dumps, and the subsequent leaching of phenol through the soil to the groundwater. Phenol has been detected, but not quantified, in drinking water in the United States from 5 of 14 drinking water treatment plants (Fielding et al. 1981). It was detected in drinking water in Great Britain between March and December of 1976 in 2 of 4 sites (groundwater source) and in 30% of an unspecified number of sites (surface water source) (Fielding et al. 1981). Phenol levels in tap water, spring water, and mineral water in Italy were 0.58, 0.051, and 0.161 µg/L, respectively (Achilli et al. 1995). Phenol was detected at a maximum concentration of 1,130 ppm in 9 wells in Wisconsin after a spill, and was detected for at least 1.5 years after the spill (Delfino and Dube 1976). It was found at concentrations up to 10.4 ppm in groundwater from a sand aquifer adjacent to waste ponds at a wood-preserving facility in Florida (Goerlitz et al. 1985), and was detected at 6.5-10,000 ppb in 2 aquifers 15 months after the completion of a coal gasification project (Stuermer et al. 1982). Phenol was detected at a maximum concentration of 1.9 ppm in leachates from landfill sites in Illinois (Clark and Piskin 1977). Near a landfill in central Florida, phenol was found in groundwater and surface water at about 17 and 15 ppb, respectively (Chen and Zoltek 1995). In the STORET database, 18.3% of 3,443 data points for U.S. groundwaters are positive for the presence of phenol; the mean and range of the reported concentrations are 1.499 ppm (mean) and from not detected to 420 ppm (range) (EPA 1988c). Phenol was detected, but not quantified, in the groundwater at 13.6% of 178 CERCLA hazardous waste sites (Plumb 1987).

Phenol was detected during seven rain events in Portland, OR between February and April of 1984. Concentrations in rain ranged from more than 75 to 1,200 ppt, and averaged above 280 ppt. Gas-phase concentrations ranged from 220 (56.1 ppt) to 410 ng/m^3 (105 ppt) and averaged 320 ng/m^3 (82 ppt) (Leuenberger et al. 1985).

Phenol has been detected in the effluent discharges of a variety of industries. It was found in petroleum refinery waste water at concentrations of 33.5 ppm (Pfeffer 1979) and 100 ppb (Paterson et al. 1996), in the treated and untreated effluent from a coal conversion plant at 4 and 4,780 ppm, respectively (Parkhurst et al. 1979), and in shale oil waste water at a maximum of 4.5 ppm (Hawthorne and Sievers 1984). It has also been detected in the effluent from a chemical specialties manufacturing plant at 0.01-0.30 ppm (Jungclaus et al. 1978), in effluent from paper mills at 5-8 ppb (Keith 1976; Paterson et al. 1996), and at 0.3 ppm in a 24-hour composite sample from a plant on the Delaware River, 2 and 4 miles downriver from a sewage treatment plant (Sheldon and Hites 1979).

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Phenol has also been found in the primary and secondary effluent from the los Angeles City Treatment Plant at concentrations of 32 and <10 ppb, respectively (Young et al. 1983). It was found in 3 of 86 samples of runoff from 2 of 15 cities at 3-10 ppb by the U.S. Nationwide Urban Runoff Program as of July of 1982 (Cole et al. 1984). In the STORET database, 50% of 525 data points for U.S. industrial effluents were positive for the presence of phenol. The mean and range of the reported concentrations were 215 and 1.0-29,000 ppb, respectively (EPA 1988c).

5.4.3 Sediment and Soil

Very few data concerning the presence of phenol in soils were found. Phenol generally does not adsorb very strongly to soils and tends to leach rapidly through soil, which may account for the lack of monitoring data, since any phenol released to soils is likely to leach to groundwater.

Sediment collected 6 km northwest of the los Angeles County waste-water treatment plant discharge zone at Palos Verdes, CA, contained 10 ppb (dry weight) phenol (Gossett et al. 1983). In the STORET database, 9.7% of 1,158 data points for U.S. sediment were positive for the presence of phenol. The mean and range of the reported concentrations (dry weight) were 6.1 ppm (mean) and from not detected to 608 ppm (range) (EPA 1988c).

5.4.4 Other Environmental Media

Phenol has been reported at concentrations of 7 and 28.6 ppm in smoked summer sausage and smoked pork belly, respectively (EPA 1980), and was identified but not quantified in mountain cheese (Dumont and Adda 1978), fried bacon (Ho et al. 1983), fried chicken (Tang et al. 1983), and black fermented tea (Kaiser 1967). Phenol has also been found in honey at concentrations ranging from 0 (detection limit 0.1 ppm) to 19 ppm (Spoms 1981). It was present each time the honey was collected with phenol-treated boards.

Phenol has been found in bottomfish from 5 sites in Commencement Bay in Tacoma, WA, at a highest maximum average and overall maximum concentration of 0.14 and 0.22 ppm, respectively (Nicola et al. 1987). Phenol has been reported to be a natural component of animal matter; it has been found at 0-1.6 ppm in rabbit muscle tissue (EPA 1980).

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Phenol is also found in medicinal preparations including ointments, ear and nose drops, cold sore lotions, mouthwashes, gargles, toothache drops, and analgesic rubs (Douglas 1972). A commercial antiseptic lotion was reported to contain 1.4% phenol (Musto et al. 1977). Package labeling information indicates that commercial throat lozenges contain up to 29 mg of phenol per lozenge (PDR 1998). Other consumer products such as disinfectants and cleaners may contain concentrations of phenol ranging from 0.45-26% (CA EPA 1998; Forum for Scientific Excellence, Inc. 1990). It has been found that the smoke of 1 nonfilter cigarette contains 60-140 μg of phenol, 19-35 μg for a filter-tipped cigarette, and 24-107 μg in cigars (IARC 1986; NCI 1998).

5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

Data concerning concentrations of phenol in ambient air are insufficient to estimate the potential for exposure by inhalation. However, it is known that the smoke of 1 nonfilter cigarette contains 60-140 μg phenol, while levels of phenol range from 19-35 μg in the smoke of filter-tipped cigarettes, and from 24-107 μg in the smoke of cigars (IARC 1986; NCI 1998). Indoor environments polluted with tobacco smoke contain measurable amounts of phenol (Guerin et al. 1982).

Phenol concentrations in surface and drinking waters are expected to vary with location and proximity to varying industrial and municipal discharges. Considering the lack of quantitative, current monitoring data and the probable seasonal, spatial, and temporal variations in the concentrations of phenol at these sources, it is not possible to estimate accurately a potential daily dose of phenol from drinking contaminated water or from dermal exposure to contaminated water. Nonetheless, it is probable that only those systems that receive their water from contaminated surface water and groundwater contain phenol. Ingestion of phenol via consumption of food cannot be estimated from the available data.

Few data concerning occupational exposures to phenol were located. The average airborne concentrations of phenol to which workers were exposed at three locations within two wood creosote impregnation plants ranged from 0.03 to 0.5 ppm (Heikkila et al. 1987). A phenol concentration of approximately 0.5 ppm was measured in the workroom air at a casting factory in Osaka City, Japan (Kuwata et al. 1980), and concentrations as high as 3.2 ppm were measured in Japanese Bakelite factories (Ohtsuji and Ikeda 1972). Considering the lack of quantitative monitoring data for phenol in occupational atmospheres, it is not possible to estimate the potential for occupational exposure to phenol. The data, however, do show that exposure to phenol through breathing and dermal contact with contaminated workroom atmospheres is

possible. The National Occupational Exposure Survey (NOES) conducted by NIOSH estimated that 584,385 workers were exposed to phenol in the United States (NOES 1990). The NOES database does not contain information on the frequency, concentration, or duration of exposures. The survey provides only estimates of workers potentially exposed to chemicals in the workplace.

Exposure to phenol also occurs through the use and subsequent ingestion of phenol-containing products, including mouthwashes, gargles, toothache drops, (Douglas 1972), and throat lozenges (EPA 1980). Cepastat® lozenges, an over-the-counter remedy for sore throats, contain up to 29 mg phenol/lozenge (PDR 1998). If a patient (adults and children over 6) takes the maximum recommended dose of 300 mg phenol/day, this would result in an approximate dose of 4-8 mg/kg/day.

Dermal exposure also occurs through the use of phenol-containing ointments, ear and nose drops, analgesic rubs (Douglas 1972), and antiseptic lotions (Musto et al. 1977). It is not possible to estimate dose levels for these sources given the available data.

The estimated relative contributions of the various exposure routes and sources of total phenol exposure cannot be estimated using the available data. Nonetheless, for persons not exposed to phenol in the workplace, exposure will most likely result from: inhalation of contaminated ambient air, primarily in the vicinity of industries and municipalities that release significant amounts of phenol into the atmosphere; ingestion of drinking water from contaminated surface waters or groundwaters; ingestion of phenolcontaining products; and dermal exposure to contaminated water and to phenol-containing products. Dermal contact with phenol or ingestion of phenol-containing products probably constitutes the largest consumer exposure, although this exposure may occur on an acute basis. Inhalation and dermal exposures appear to be most significant in occupational settings. Total phenol exposure for workers exposed to phenol in the workplace is probably substantially higher than for those not exposed in the workplace.

5.6 EXPOSURES OF CHILDREN

This section focuses on exposures from conception to maturity at 18 years in humans and briefly considers potential pre-conception exposure to germ cells. Differences from adults in susceptibility to hazardous substances are discussed in 2.6 Children's Susceptibility.

5. POTENTIAL FOR HUMAN EXPOSURE

Children are not small adults. A child's exposure may differ from an adult's exposure in many ways. Children drink more fluids, eat more food, and breathe more air per kilogram of body weight, and have a larger skin surface in proportion to their body volume. A child's diet often differs from that of adults. The developing human's source of nutrition changes with age: from placental nourishment to breast milk or formula to the diet of older children who eat more of certain types of foods than adults. A child's behavior and lifestyle also influence exposure. Children crawl on the floor, they put things in their mouths, they may ingest inappropriate things such as dirt or paint chips, they spend more time outdoors. Children also are closer to the ground, and they do not have the judgement of adults in avoiding hazards (NRC 1993).

Oral, dermal, and combined oral-dermal exposures are the most likely routes by which children will be exposed to phenol. Oral exposure to low levels of phenol among children is likely because many consumer products contain phenol, particularly in medicines such as gargles, tooth drops, throat lozenges, ointments, and others (Douglas 1972; EPA 1980). Products other than medicines that contain phenols include general disinfectants, cleaners, and epoxies.

Accidental phenol poisoning from the ingestion of these products and these mentioned previously could result, depending on the product ingested, since the range of concentrations in consumer products range from 0.45-26% (CA EPA 1998; Douglas 1972; EPA 1980; Forum for Scientific Excellence, Inc. 1990; Musto 1977; Spiller et al. 1993). In the case of accidental ingestion, health effects may be the result of phenol and/or other chemical constituents depending on their concentrations in the product. In a study by Spiller et al. (1993), the mean age of accidental acute exposure cases to a disinfectant containing 26% phenol reported to regional poison control centers was 10 years, and 75% of the cases involved children less than 5 years old.

Some foods containing phenol have been identified (see Section 5.4.4) and could result in low levels of phenol exposure in children. In addition, phenol is produced endogenously as a breakdown product of protein metabolism; normal concentrations in urine generally do not exceed 20 mg/L (ACGIH 1991).

Since phenol can be readily absorbed through the skin (ACGIH 1991), children may be more susceptible to low levels of phenol exposure since they have a higher skin-surface-area to weight ratio. Since young children are more likely to come in contact with the floor and other low-lying areas, they may be exposed to phenol found in consumer products such as general disinfectants used to clean toilets, floors, drains, and other areas (Budavari 1989; CA EPA 1998; Hawley 1981).

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Exposure to phenol through inhalation is a less probable route than oral and dermal. It is known that both cigarettes and cigars contain small amounts (19-140 μg) of phenol (IARC 1986; NCI 1998), and smoking these products indoors produces a measurable amount of phenol (Guerin et al. 1982). If children are present in indoor environments polluted with tobacco smoke, they may be exposed to low levels of phenol.

5.7 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

Populations with potentially high exposure to phenol generally include those who are exposed to relatively highly contaminated environments over long periods of time. These include populations exposed to both identified and unidentified phenol-containing waste disposal sites and landfills. Populations residing in the vicinity of industries that manufacture or use phenol and large population centers may be exposed to potentially high levels of phenol. Persons who work at establishments that manufacture or use phenol have a risk for high exposure to phenol. Populations that regularly ingest food contaminated with phenol or that regularly ingest or come in contact with phenol-containing products are at risk for high exposure to phenol. Populations that live near a phenol spill site, especially those whose water supply sources are near the spill sites, have a risk for high exposure to phenol. Relatively high exposure may also result from exposure to emissions from municipal waste incinerators and cigarette smoke, although no quantitative data concerning phenol emission from these sources were located.

5.8 ADEQUACY OF THE DATABASE

Section 104(I)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of phenol is available. Where adequate information is not available, ATSDR, in conjunction with the NTP, is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of phenol.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

5. POTENTIAL FOR HUMAN EXPOSURE

5.8.1 Identification of Data Needs

Physical and Chemical Properties. Knowledge of physical and chemical properties is essential for estimating the partitioning of a chemical in the environment. Information about the physical and chemical properties of phenol is available (Hawley 1981; HSDB 1998; IARC 1989), and the database is adequate for the input requirements of environmental models that predict the behavior of a chemical under specific conditions.

Production, Import/Export, Use, Release, and Disposal. According to the Emergency Planning and Community Right-to-Know Act of 1986, 42 U.S.C. Section 11023, industries are required to submit chemical release and off-site transfer information to the EPA. The Toxics Release Inventory (TRI), which contains this information for 1996, became available in May of 1998. This database will be updated yearly and should provide a list of industrial production facilities and emissions.

Additional production data are available from the Chemical Marketing Reporter (CMR 1996), and import/export data for phenol are available on the National Trade Data Bank (NTDB 1996). Additional data are not needed at this time.

Environmental Fate. Based on the physical properties of phenol, volatilization and sorption of phenol to sediments are not expected to be important transport mechanisms (Lyman et al. 1982). The adsorption of phenol to soils has been shown to increase with increasing organic matter (Xing et al. 1994). Photochemical degradation of phenol is thought to be an important process both in air (Hendry and Kenley 1979) and water (Scully and Hoigne 1987). Phenol is also readily biodegradable (Ludzack and Ettinger 1960; Rubin and Alexander 1983; Scott et al. 1983; Stover and Kincannon 1983). Additional studies that examine the volatilization and sorption of phenol to soil and sediments are needed to help predict the environmental fate of phenol.

Bioavailability from Environmental Media. Data from monitoring studies indicate that phenol is present in the environment (Brodzinsky and Singh 1982; Gossett et al. 1983; Hoff and Ghan 1987; Konasewich et al. 1978; Scow et al. 1981; Sheldon and Hites 1978,1979; Thurman 1985) as well as in environmental organisms (Nicola et al. 1987). Exposure to phenol is most likely to be highest in areas at or near industrial centers and population centers where drinking and bathing water, ambient air, and certain foods, such as fish, are obtained from sources contaminated with phenol. Reliable data on the bioavailability

of phenol from inhaled air and from skin exposed to phenol vapor have been reported for humans (Piotrowski 1971). Studies of bioavailability of phenol from ingested soil and foods and dermal contact with contaminated water are needed for evaluating the hazards posed by ingesting materials that have been contaminated with phenol.

Food Chain Bioaccumulation. No studies were located regarding the food chain bioaccumulation of phenol from environmental media. Data from monitoring studies indicate that phenol is present in the environment as well as in environmental organisms (Nicola et al. 1987). The available bioaccumulation studies are concerned only with exposure of fish to aqueous concentrations of phenol. Although the results of these studies indicate a low potential for bioaccumulation (see Section 5.3.1), the detection of phenol in fish (see Section 5.4.4) indicates that phenol can be found in aquatic organisms; it is possible that food chain bioaccumulation may occur. A clearer understanding of the potential for bioaccumulation would aid in determining how levels in the environment affect the food chain and potentially impact human exposure levels. A study examining phenol levels in organisms from several trophic levels is needed.

Exposure Levels in Environmental Media. Phenol has been measured in air (Brodzinsky and Singh 1982; Cronn et al. 1977; Scow et al. 1981), water (EPA 1980; Sheldon and Hites 1978, 1979; Thurman 1985), and sediments (Gosset et al. 1983). Additional more recent monitoring data are needed to help estimate human exposure to phenol.

Reliable monitoring data for the levels of phenol in contaminated media at hazardous waste sites are needed so that the information obtained on levels of phenol in the environment can be used in combination with the known body burdens of phenol to assess the potential risk of adverse health effects in populations living in the vicinity of hazardous waste sites.

Exposure Levels in Humans. Data concerning exposure levels in humans are incomplete and not current (Heikkila et al. 1987; Kuwata et al. 1980; Qhtsuji and Ikeda 1972). A detailed recent database of exposure would be helpful in determining the current exposure levels, thereby allowing the estimation of the average daily dose associated with various scenarios such as living near a hazardous waste site or landfill, or with drinking water containing phenol. An environmental media monitoring program would provide the necessary information for estimating environmental exposures, while a detailed examination of the uses of phenol and the kinds of potential exposure in addition to workplace monitoring would probably provide adequate workplace information. The environmental media that would provide the most useful information

are air, groundwater, and surface and drinking water in urban and industrial locations, and air, groundwater, and surface water at hazardous waste sites. Performing the monitoring over a 1-year period would allow estimation of seasonal variations.

This information is necessary for assessing the need to conduct health studies on these populations.

Exposures of Children. Children are likely to be exposed to low levels of phenol from the use of many consumer products including medicines and cleaning agents (Budavari et al. 1989; Douglas 1972; EPA 1980; Hawley 1981). There are no known data that quantify the level of exposure to phenol in children. It is likely that young children may be exposed to low levels of phenol because they come into contact with the floor and other areas where disinfectants containing phenol might be used. More studies are needed to assess whether children differ in their weight-adjusted intake of phenol, as little or no information is known. Studies are needed to measure the baseline phenol level in children's urine in order to use phenol levels in urine as a biomarker of exposure.

Exposure Registries. No exposure registries for phenol were located. This substance is not currently one of the compounds for which a subregistry has been established in the National Exposure Registry. The substance will be considered in the future when chemical selection is made for subregistries to be established. The information that is amassed in the National Exposure Registry facilitates the epidemiological research needed to assess adverse health outcomes that may be related to exposure to this substance.

5.8.2 Ongoing Studies

As part of the Third National Health and Nutrition Evaluation Survey (NHANES III), the Environmental Health Laboratory Sciences Division of the National Center for Environmental Health, Centers for Disease Control and Prevention, will be analyzing human blood samples for phenol and other volatile organic compounds. These data will give an indication of the frequency of occurrence and background levels of these compounds in the general population.

No additional on-going studies regarding environmental fate or exposure data for phenol were located.

6. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting, and/or measuring, and/or monitoring phenol, its metabolites, and other biomarkers of exposure and effect to phenol. The intent is not to provide an exhaustive list of analytical methods. Rather, the intention is to identify well-established methods that are used as the standard methods of analysis. Many of the analytical methods used for environmental samples are the methods approved by federal agencies and organizations such as EPA and the National Institute for Occupational Safety and Health (NIOSH). Other methods presented in this chapter are those that are approved by groups such as the Association of Official Analytical Chemists (AOAC) and the American Public Health Association (APHA). Additionally, analytical methods are included that modify previously used methods to obtain lower detection limits, and/or to improve accuracy and precision.

6.1 BIOLOGICAL SAMPLES

Analytical methods for the detection of phenol in biological materials are summarized in Table 6- 1. Phenol is expected to be present in blood and urine in its free acid and conjugated forms (glucuronide and sulfate). The average urinary phenol concentration in unexposed individuals is 9.5±3.6 mgL when corrected to a standard specific gravity of 1.024 (Piotrowski 1971). In exposed individuals, the urinary phenol level may vary from 10 to 200 mg/L (Tesarova and Packova 1983). The two common methods for quantifying conjugated phenol are chemical and enzymatic hydrolysis of the conjugate to the free phenol form. The chemical method uses acidic hydrolysis (Baldwin et al. 1981; Needham et al. 1984). Both the nature of the acid (sulfuric versus perchloric) and the temperature should be controlled carefully to obtain a quantitative yield and to avoid thermal decomposition of other phenolic or related compounds that may interfere with phenol quantification (Baldwin et al. 1981; Rick et al. 1982). The best available method appears to be specific enzyme hydrolysis or hydrolysis at ambient temperature with sulfuric acid. Enzymatic hydrolysis with an extract of *Helix pomatia* has also been used to liberate phenol from its conjugates (Ahmed and Hale 1994).

TABLE 6-1. Analytical Methods for Determining Phenol in Biological Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Whole blood	Sample extracted with ethyl acetate, extract concentrated and analyzed (for free phenol), packed blood cells previously extracted for free phenol incubated with β-glucuronidase containing sulfatase at 37°C, extracted with ethyl acetate after addition of normal saline solution and extract concentrated and analyzed (for conjugated phenol)	GC-FID	<1 mg/mL	97% (free phenol); 103% (conjugated phenol)	O'Grodnick et al. 1983
	Sample with spiked internal standard extracted with ethyl acetate and extract concentrated and analyzed	GC-FID	0.1 mg/L	>90% at concentrations above 0.5 mg/L	Handson and Hanrahan 1983
Urine	Sample mixed with phosphoric acid, passed through a pre-column at 165°C for hydrolysis of conjugates (for free and conjugated phenol) and analyzed	GC-FID	NG	89% (for conjugates)	Baldwin et al. 1981
	Sample refluxed with $HClO_4$, solvent extracted, concentrated, and separated by TLC; spot developed by *p*-nitro-benzenediazonium fluoroborate, removed quantitatively and solvent extracted (for free and conjugated phenol) and analyzed	Spectrophotometry	NG	NG	Bienick and Wilczok 1986
	Acidified sample steam distilled, reacted with ammonia, *N*-chloro-succinimide, and sodium nitroprusside at basic pH (method probably for free phenol) and analyzed	Spectrophotometry	0.3 mg/L	>95%	Amlathe et al. 1987

TABLE 6-1. Analytical Methods for Determining Phenol in Biological Samples (*continued*)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Urine (continued)	Sample heated with HCl to 95°C; diethyl ether added; mixture cooled to 0°C and allowed to separate into two phases; clear ether layer used for analysis	GC-FID	0.5 µg/mL	94–95%	NIOSH 1994
	Sample incubated with glucuronidase and sulfatase at pH 5 and 37°C, H_2SO_4 added and steam distilled (total phenol) and analyzed	HPLC-electrochemical detector	2 ng/ injection	95–107%	Schaltenbrand and Coburn 1985
	Sample hydrolyzed at room temperature and extracted with methyl *tert*-butyl ether (total phenol) and analyzed	GC-FID	NG	NG	Rick et al. 1982
	Sample spiked with internal standard, hydrolyzed with H_2SO_4, and extracted with ethyl acetate (free and conjugated) and analyzed	GC-FID	NG	93–97% at 20–70 mg/L	Needham et al. 1984
	Sample spiked with internal standard, distilled with H_2SO_4 in a special apparatus, distillate directly injected into GC (free and conjugated)	GC-FID	0.1 mg/L	99% at 5.9 mg/L	Van Roosmalen et al. 1981

FID = flame ionization detector; GC = gas chromatography; H_2SO_4 = sulfuric acid; HCl = hydrochloric acid; $HClO_4$ = perchloric acid; HPLC = high performance liquid chromatography; NG = not given; TLC = thin layer chromatography

6. ANALYTICAL METHODS

High-performance liquid chromatographic separation with electrochemical detection may provide the best sensitivity for phenol quantification in biological samples. The use of gas chromatography with a flame ionization detector may be a more versatile method, if other non-ionic pollutants must be quantified. The advantages and disadvantages of different methods available for the quantification of phenol and metabolites in biological and environmental samples have been discussed by Tesarova and Packova (1983).

The level of phenol detected in blood or urine may not accurately reflect actual phenol exposure because phenol may also appear as a metabolite of benzene or other drugs. It has been shown that under certain acidic conditions used for the hydrolysis of conjugated phenols, acetyl salicylic acid (aspirin) may produce phenol (Baldwin et al. 1981) and yield spuriously higher values for phenol in blood and urine.

Por occupational exposure, it is recommended that urine samples be collected at the end of an 8-hour work shift (ACGIH 1991). Small amounts of thymol can be used as a preservative, and the urine can be stored for 4 days if refrigerated, or at least 3 months if frozen

6.2 ENVIRONMENTAL SAMPLES

Analytical methods for detecting phenol in environmental samples are summarized in Table 6-2. The accuracy and sensitivity of phenol determination in environmental samples depends on sample preconcentration and pretreatment and the analytical method employed. The recovery of phenol from air and water by the various preconcentration methods is usually low for samples containing low levels of phenol. The two preconcentration methods commonly used for phenols in water are adsorption on XAD resin and adsorption on carbon. Both can give low recoveries, as shown by Van Rossum and Webb (1978). Solvent extraction at acidic pH with subsequent solvent concentration also gives unsatisfactory recovery for phenol. Even during carefully controlled conditions, phenol losses of up to 60% may occur during solvent evaporation (Handson and Hanrahan 1983). The in situ acetylation with subsequent solvent extraction as developed by Sithole et al. (1986) is probably one of the most promising methods.

TABLE 6-2. Analytical Methods for Determining Phenol in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Urban air	Sample collected in bubbler containing NaOH, derivatized as nitrobenzeneazo compound	HPLC-UV	0.05 ppb for 150-L sample; 58–60% at 0.33–0.5 µg phenol	72.3% at 10–50 µg phenol	Kuwata et al. 1980
Occupational air	Sorption on activated carbon, desorption by solvent and derivatized to trimethylsilyl product	GC-FID	0.5 mg/m^3 (0.13 ppm)	96–102% at 2.5–100 mg/m^3	Yrjanheikki 1987
	Sorption on XAD-2, desorption by acetonitrile and concentrated if necessary	HPLC-electro-chemical detector and HPLC-UV	8 µg/m^3 (2.04 ppb) with 12 L air (electrochemical); 0.16 mg/m^3 (0.04 ppm) with 12 L air (UV)	NG	Nieminen and Heikkila 1986
	Sample collected with a thermal desorption tube using a sorbent capable of capturing a C_6 organic compound	GC-MS	100 ng/tube or less	NA	NIOSH 1994
Total particulate matter in cigarette smoke	Extract particulate matter with NaOH, buffer to a pH 4.6	HPLC-fluorescence spectrophotometer	0.3 mg/L	91% at 20–30 µg	Tomkins et al. 1984
Industrial emission, auto exhaust, and tobacco smoke	Sample collected in NaOH bubbler and derivatized to *p*-nitrobenzene-diazonium tetrafluoroborate	HPLC-UV	0.05 pbb for 150 L sample	NG	Kuwata et al. 1980

TABLE 6-2. Analytical Methods for Determining Phenol in Environmental Samples (*continued*)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Drinking water, waste water, natural water	Direct distillation or distillation of solvent-cleaned sample (if necessary) at acidic pH, react with 4-amino-antipyrine and potassium ferricyanide at pH 8, extract in chloroform	Spectrophotometric	1 µg/L for 500-mL sample	NG	APHA/AWWA/ WPCF 1985
Waste water and natural water	None	GC-FID	<1 mg/L	NG	APHA/AWWA/ WPCF 1985
Water	Direct distillation or distillation of solvent-cleaned sample at acidic pH, react with 4-amino antipyrine and potassium ferricyanide at pH 10 or extract colored complex in chloroform	Spectrophotometric (ASTM Method D-1783)	<5 µg/L (chloro-form extract); <0.1 mg/L (direct)	NG	ASTM 1978
Water, waste water	Acidified sample extracted with solvent, concentrated or derivatized to pentafluorobenzylbromide product	GC-FID; GC-ECD (for derivatized EPA Method 604)	0.14 µg/L (FID); 2.2 µg/L (ECD)	41% (FID); NG (ECD)	EPA 1982
	Sample extracted in acidic pH, extract concentrated	GC-MS (EPA Method 625); HRGC-MS (EPA Method 625.1)	1.5 µg/L (GC-MS); 1–10 µg/L (HRGC-MS)	36% (GC-MS) at 10–1,500 µg/L; 25% (GC-MS) at 8.3 µg/L; 42% (HRGC-MS) at 20 µg/L	Eichelberger et al. 1983; EPA 1982
Water	Sample passed through graphitized carbon black, eluted with methylene chloride	Ion-suppression; reversed phase LC with UV detection	50–100 ng/L	91–97%	Di Corcia et al. 1996

TABLE 6-2. Analytical Methods for Determining Phenol in Environmental Samples (*continued*)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Water	Sample passed though a mixed XAD-4/8 column, solvent eluted and concentrated	GC-MS	NG	46–70% (distilled water); 9% (tap water)	Van Rossum and Webb 1978
Waste water	Distillation of acidified solution, reacted with ammonia, *N*-chloro-succinimide, and sodium nitro-prusside at basic pH	Spectrophotometric	<0.3 mg/L	96.7% at 3 mg/L	Amlathe et al. 1987
Potable water and raw source water	Sample acetylated *in situ* by addition of acetic anhydride, solvent extracted and concentrated; alternatively, extracted acidic sample derivatized by pentafluorobenzyl bromide and cleaned up by column chromatography	HRGC-ECD (for pentafluorobenzyl derivative); HRGC-MS (for acetyl derivative)	<50 ng/L (penta-fluorobenzyl); <50 ng/L (acetyl derivative)	10–64% (penta-fluorobenzyl derivative); 70–132% (acetyl derivative)	Sithole et al. 1986
Sediment	Homogenized sample solvent extracted at acidic pH, fractionated by GPC and fractions concentrated	HRGC-MS	NG	112–128% at 400 ng/g	Lopez-Avila et al. 1983
Groundwater	Solvent extraction in acidic pH, extract concentrated	GC-MS (EPA-CLP Method)	10 µg/L	NG	EPA 1987
Soil, sediment	Sample mixed with anhydrous powdered Na_2SO_4, solvent extracted ultrasonically, extract subjected to GPC if necessary, extract concentrated	GC-MS (EPA-CLP Method)	330 µg/kg	NG	EPA 1987
Water and waste water	Phenols separated on a Nova-Pak Phenyl column eluted with ammonium acetate:acetonitrile	LC-ED	0.5 mg/L	91–100%	Paterson et al. 1996

TABLE 6-2. Analytical Methods for Determining Phenol in Environmental Samples (*continued*)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Groundwater	Solvent extraction, column chromatographic cleanup, concentration of extract	GC-MS (EPA Method 8250A)	1.5 mg/L	(0.43c+1.26)/c x 100 where c is the actual concentration	EPA 1994a
Soil, sludge, or solid waste	Extracted by soxhlet or sonication, extract subjected to column chromatographic cleanup and concentrated	GC-MS (EPA Method 8250A)	1.5 mg/kg	(0.43c+1.26)/c x 100 where c is the actual concentration	EPA 1994a
Groundwater	Solvent extraction, column chromatographic cleanup, concentration of extract	HRGC-MS (EPA Method 8270B)	10 µg/L	(0.43c+1.26)/c x 100 where c is the actual concentration	EPA 1994b
Soil, sludge, and solid waste	Extracted soxhlet or sonication, extract subjected to column chromatographic cleanup, concentrated	HRGC-MS (EPA Method 8270C)	660 µg/kg	(0.43c+1.26)/c x 100 where c is the actual concentration	EPA 1996b
Honey	Sample dissolved in water, steam distilled; distillate cleaned up by column chromatography	HPLC-UV	0.1 ppm (for 10 g sample)	98% at 111 µg added phenol	Sporns 1981

C_6 = 6 carbon; ECD = electron capture detector; ED = electrochemical detection; FID - flame ionization detector; GC = gas chromatography; GPC = gel permeation chromatography; HPLC = high performance liquid chromatography; HRGC = high resolution gas chromatography; LC = liquid chromatography; MS = mass spectrometry; Na_2SO_4 = sodium sulfate; NaOH = sodium hydroxide; NG = not given; UV = ultraviolet detection

6. ANALYTICAL METHODS

Capillary columns may provide the best method for the separation of phenols prior to their quantification (Eichelberger et al. 1983; Shafer et al. 1981; Sithole et al. 1986). Of the various methods available for detection, the two commonly used methods that are most sensitive are mass spectrometry and flame ionization detection. Although electron capture detectors provide good sensitivities for higher chlorine-substituted phenols, they are poor for phenol itself (Sithole et al. 1986). The best method for the quantification of phenol may be mass spectrometric detection in the selected ion mode, but the loss of qualitative information may be significant (Eichelberger et al. 1983).

6.3 ADEQUACY OF THE DATABASE

Section 104(I)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of phenol is available. Where adequate information is not available, ATSDR, in conjunction with the NTP, is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of phenol.

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6.3.1 Identification of Data Needs

Methods for Determining Biomarkers of Exposure and Effect. Measurement of total phenol in urine serves as a biomarker of exposure for persons occupationally exposed to phenol (ACGIH 1991). Specific biomarkers used to characterize effects caused by phenol have not been identified. Dark urine has been reported in persons occupationally exposed to phenol (inhalation, dermal) (ACGIH 1991; Merliss 1972) and following oral exposure (Baker et al. 1978; Kim et al. 1994). The dark urine may be a result of an oxidation product of phenol, or hemoglobin and hemoglobin breakdown products. Further research is required to identify the cause of the dark urine and relate it to exposure concentration.

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Methods for Determining Parent Compounds and Metabolites in Biological Materials. The analytical methods available (Amlathe et al. 1987; Baldwin et al. 1981; Bieniek and Wilczok 1986; Handson and Han&an 1983; Needham et al. 1984; O'Grodnick et al. 1983; Rick et al. 1982; Schaltenbrand and Coburn 1985; Van Roosmalen et al. 1981) are adequate for the quantification of phenol and its conjugates in biological samples. The study of the levels of parent compound in human blood, urine, or other biological matrices can be useful in deriving a correlation between the levels of this compound found in the environment and those found in human tissue or body fluid.

The changes in metabolite concentrations in human blood, urine, or other appropriate biological media over time may be useful in estimating phenol's rate of metabolism in humans. In some instances, the quantification of metabolites may be useful in correlating the exposure doses to the human body burden. Studies that correlate phenol exposure with levels of metabolites in human biological matrices are not available for this compound, although analytical methods for the quantification of the metabolites are available.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. The analytical methods available (Eichelberger et al. 1983; EPA 1982,1986b, 1987; Kuwata et al. 1980; Nieminen and Heikkila 1986; NIOSH 1994; Sithole et al. 1986; Tomkins et al. 1984; Van Rossum and Webb 1978; Yrjanheikki 1978) are adequate for the quantification of phenol in environmental materials Knowledge of the levels of this compound in environmental media, such as air, water, and food, can be used to indicate exposure of humans to this compound through the inhalation of air and ingestion of drinking water and foods containing phenol.

Although the products of environmental biotic and abiotic degradation of phenol have been identified adequately, no systematic study measuring the concentrations of the degradation products in the environment was found. Analytical methods are available for determining the levels of the degradation products such as hydroxylated phenol. Knowledge of the levels of degradation products would allow the development of a monitoring program designed to assess the ambient concentrations of phenol degradation products in the environment. Such a program could provide information concerning both human and environmental exposure to phenol since it might allow an estimation of the concentration of phenol in the environment prior to degradation.

6. ANALYTICAL METHODS

6.3.2 Ongoing Studies

The Environmental Health Laboratory Sciences Division of the National Center for Environmental Health, Centers for Disease Control and Prevention, is developing methods for the analysis of phenol and other volatile organic compounds in blood. These methods use purge and trap methodology, high resolution gas chromatography, and magnetic sector mass spectrometry, which gives detection limits in the low parts per trillion (ppt) range.

A search of federal research programs has indicated that no additional research is in progress for improving the method of phenol quantification in biological or environmental samples.

7. REGULATIONS AND ADVISORIES

International, national, and state regulations and guidelines pertinent to human exposure to phenol are summarized in Table 7-1. The IARC classification for phenol is Group 3, not classifiable with regard to its carcinogenicity to humans (IARC 1989).

The permissible exposure limit time-weighted average (PEL-TWA) is 5 ppm (OSHA 1997). ACGIH (1998) and NIOSH (1992) also recommend a TWA exposure limit of 5 ppm for occupational exposure.

Phenol is regulated by the Clean Water Effluent Guidelines for the following industrial point sources: electroplating, organic chemicals, steam electric, asbestos, timber products processing, metal finishing, paving and roofing, paint formulating, ink formullating, gum and wood, carbon black, metal molding and casting, aluminum forming, and electrical and electronic components (EPA 1988a). EPA has established a Reportable Quantity (RQ) of 1,000 pounds (EPA 1998b). The lifetime health advisory for phenol in water is 4 mg/L (EPA 1996a). The EPA cancer classification for phenol is D, not classifiable as to human carcinogenicity (IRIS 1998).

The EPA reference dose (RfD) of 0.6 mg/kg/day (IRIS 1998) is based on a NOAEL of 60 mg/kg/day for developmental effects (decreased fetal body weights) observed in rats at a dose of 120 mg/kg/day (Jones-Price et al. 1983a).

TABLE 7-1. Regulations and Guidelines Applicable to Phenol

Agency	Description	Information	References
INTERNATIONAL			
IARC	Carcinogenic classification	Group 3[a]	IARC 1989
NATIONAL			
Regulations:			
a. Air:			
OSHA	PEL-TWA	5 ppm (19 mg/m^3)	OSHA 1997 (29 CFR 1910.1000)
b. Other:			
EPA	Reportable quantity	454 kg (1,000 lbs)	EPA 1998b (40 CFR 302.4)
	Required reporting under Title III SARA	Yes	EPA 1998c (40 CFR 372)
	Designated as a hazardous substance	Yes	EPA 1998a (40 CFR 116.4)
FDA	Indirect food additive	Yes	FDA 1998b (21 CFR 175 subsections 300, 380, & 390) FDA 1998c (21 CFR 176.170) FDA 1998d (21 CFR 177 subsections 1210, 1580, 2410, & 2600)
Guidelines:			
a. Air:			
ACGIH	TLV-TWA	5 ppm (19 mg/m^3)	ACGIH 1998
EPA	RfC (inhalation)	None listed	IRIS 1998
NIOSH	REL (TWA)	5 ppm (19 mg/m^3)	NIOSH 1997
	REL (ceiling)	15.6 ppm (60 mg/m^3)	NIOSH 1997
b. Water:			
EPA	MCLG	None listed	EPA 1996c
	MCL	None listed	EPA 1996c
	Health advisories:		EPA 1996c
	1-day (child)	6 mg/L	
	1-day (adult)	None listed	
	10-day (child)	6 mg/L	
	10-day (adult)	None listed	
	Longer term (child)	6 mg/L	
	Longer term (adult)	20 mg/L	
	Lifetime	4 mg/L	
	DWEL	20 mg/L	EPA 1996c
	Ambient water quality criteria for protection of human health		IRIS 1996
	Water and fish	3.5 mg/L	
	Fish only	None	

TABLE 7-1. Regulations and Guidelines Applicable to Phenol (*continued*)

Agency	Description	Information	References
NATIONAL (Continued)			
	Ambient water quality criteria for aquatic organisms		IRIS 1996
	Freshwater (acute)	10 .2 mg/L	
	Freshwater (chronic)	2.56 mg/L	
	Marine (acute)	5.8 mg/L	
	Marine (chronic)	None listed	
b. Other:			
ACGIH	Biological exposure index	250 mg/ g creatinine	ACGIH 1998
EPA	RfD (oral)	0.6 mg/kg/day	IRIS 1998
EPA	CEGL	None listed	IRIS 1996
	Carcinogenic classification	Group D[c]	IRIS 1998
STATE			
Regulations:			
a. Air:	Acceptable ambient air concentrations		
Connecticut	(30 min)	1900 µg/m^3	CT Bureau Air Manage 1998
	(8 hour)	380 µg/m^3	CT Bureau Air Manage 1998
Louisiana	(8 hour)	452 µg/m^3	LA Air Qual. Div. 1998
Massachusetts	(24 hour)	52.33 µg/m^3	MA Div. Air Qual. Con. 1998
New Hampshire		63 µg/m^3	NH Air Res. Div. 1998
New York	(Short term)	4500 µg/m^3	NY Div. Air Res 1998
	(1 year)	9.6 µg/m^3	NY Div. Air Res 1998
North Dakota	(8 hour)	190 µg/m^3	ND Env. Health Sec. 1998a
South Carolina		190 µg/m^3	SC Bureau Air Qual. 1998
Vermont	(8 hour)	1900 µg/m^3	VT Air Pol. Control Div. 1998
Washington	(24 hour)	63 µg/m^3	WA Air Qual. Program 1998
b. Water:			
Kentucky	*Domestic Water Supply*	3.5 mg/L	KY Div. Water 1998
Louisiana	Drinking Water Supply	5 µg/L	LA Water Res. Div. 1998
Mississippi	Human Health (Water and Organisms)	300 µg/L	MS Sur. Water Div. 1998
Misouri	Drinking Water Supply	100 µg/L	MO Water Pol. Con. Pro. 1998
Nevada	Municipal or Domestic Supply	3.5 mg/L	NV Water Res. Div. 1998
New Hampshire	Human Health (Water and Organisms)	21 mg/L	NH Water Sup. Pol. Con. 1998
North Dakota	Human Health (Water and Organisms)	21 mg/L	ND Env. Health Sec. 1998b

TABLE 7-1. Regulations and Guidelines Applicable to Phenol (*continued*)

Agency	Description	Information	References
STATE (Continued)			
Oklahoma	Human Health (Water and Organisms)	20.9 mg/L	OK Water Qual. Div. 1998
Pennsylvania	Human Health (Water and Organisms)	300 µg/L	PA Bureau Water Sup. Com. Health 1998
Rhode Island	Human Health (Water and Organisms)	21 mg/L	RI Div. Water Res. 1998
South Dakota	Human Health (Water and Organisms)	21 mg/L	SD Office Drink. Water 1998
South Carolina	Human Health	3.5 mg/L	SC Div. Water Res. 1998
Tennessee	Human Health (Water and Organisms)	21 mg/L	TN Water Pol. Con. 1998
Utah	Domestic Purposes	21 mg/L	UT Div. Drink. Water 1998
Vermont	Human Health (Water and Organisms)	21 mg/L	VT Water Qual. Div. 1998
Virginia	Human Health (Water and Organisms)	21 mg/L	VA Dept. Env. Qual. 1998
Wyoming	Human Health	21 mg/L	WY Water Qual. Div. 1998

[a]Group 3: Not classifiable as to its carcinogenicity to humans
[b]Group A4: Not classifiable as a human carcinogen
[c]Group D: Not classifiable as to human carcinogenicity

ACGIH = American Conference of Governmental Industrial Hygienists; CEGL = continuous exposure guidance level; CFR = Code of Federal Regulations; DWEL = Drinking Water Equivalent Level; EPA = Environmental Protection Agency; IARC = International Agency for Research on Cancer; MCL = Maximum Concentration Level; MCLG = Maximum Concentration Level Goal; NIOSH = National Institute for Occupational Safety and Health; OSHA = Occupational Safety and Health Administration; PEL = Permissible Exposure Limit; REL = Recommended Exposure Limit; RfC = Reference Concentration; SARA = Superfund Amendments and Reauthorization Act; TLV = Threshold Limit Value; TWA = Time-Weighted Average

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9. GLOSSARY

Acute Exposure-Exposure to a chemical for a duration of 14 days or less, as specified in the Toxicological Profiles.

Adsorption Coefficient (K_{oc})-The ratio of the amount of a chemical adsorbed per unit weight of organic carbon in the soil or sediment to the concentration of the chemical in solution at equilibrium.

Adsorption Ratio (Kd)-The amount of a chemical adsorbed by a sediment or soil (i.e., the solid phase) divided by the amount of chemical in the solution phase, which is in equilibrium with the solid phase, at a fixed solid/solution ratio. It is generally expressed in micrograms of chemical sorbed per gram of soil or sediment.

Bioconcentration Factor (BCF)-The quotient of the concentration of a chemical in aquatic organisms at a specific time or during a discrete time period of exposure divided by the concentration in the surrounding water at the same time or during the same period.

Cancer Effect Level (CEL)-The lowest dose of chemical in a study, or group of studies, that produces significant increases in the incidence of cancer (or tumors) between the exposed population and its appropriate control.

Carcinogen-A chemical capable of inducing cancer.

Ceiling Value-A concentration of a substance that should not be exceeded, even instantaneously.

Chronic Exposure-Exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

Developmental Toxicity-The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.

Embryotoxicity and Fetotoxicity-Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the insult occurred. The terms, as used here, include malformations and variations, altered growth, and in utero death.

EPA Health Advisory-An estimate of acceptable drinking water levels for a chemical substance based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

Immediately Dangerous to Life or Health (IDLH)-The maximum environmental concentration of a contaminant from which one could escape within 30 min without any escape-impairing symptoms or irreversible health effects.

Intermediate Exposure-Exposure to a chemical for a duration of 15-364 days, as specified in the Toxicological Profiles.

9. GLOSSARY

Immunologic Toxicity-The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals.

in vitro-Isolated from the living organism and artificially maintained, as in a test tube.

In Vivo-Occurring within the living organism.

Lethal ConcentrationL_{lo} (LC_{Lo})-The lowest concentration of a chemical in air which has been reported to have caused death in humans or animals.

Lethal Concentration$_{(50)}$ (LC_{50})-A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

Lethal Dose$_{(lo)}$ (LD_{lo})-The lowest dose of a chemical introduced by a route other than inhalation that is expected to have caused death in humans or animals.

Lethal Dose$_{(50)}$ (LD_{50})-The dose of a chemical which has been calculated to cause death in 50% of a defined experimental animal population.

Lethal Time$_{(50)}$ (LT_{50})-A calculated period of time within which a specific concentration of a chemical is expected to cause death in 50% of a defined experimental animal population.

lowest-Observed-Adverse-Effect Level (LOAEL)-The lowest dose of chemical in a study, or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Malformations-Permanent structural changes that may adversely affect survival, development, or function.

Minimal Risk Level-An estimate of daily human exposure to a dose of a chemical that is likely to be without an appreciable risk of adverse noncancerous effects over a specified duration of exposure.

Mutagen-A substance that causes mutations. A mutation is a change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

Monte Carlo - A statistical technique commonly used to quantitatively characterize the uncertainty and variability in estimates of exposure or risk. The analysis uses statistical sampling techniques to obtain a probabilistic approximation to the solution of a mathematical equation or model.

Neurotoxicity-The occurrence of adverse effects on the nervous system following exposure to chemical.

No-Observed-Adverse-Effect Level (NOAEL)-The dose of chemical at which there were no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

Octanol-Water Partition Coefficient (K_{ow})-The equilibrium ratio of the concentrations of a chemical in n-octanol and water, in dilute solution.

9. GLOSSARY

Permissible Exposure Limit (PEL)-An allowable exposure level in workplace air averaged over an 8-hour Shift

q_1*-The upper-bound estimate of the low-dose slope of the dose-response curve as determined by the multistage procedure. The q_1* can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually μg/L for water, mg/kg/day for food, and $\mu g/m^3$ for air).

Reference Dose (RfD)-An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the NOAEL (from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used to estimate RfDs and an additional modifying factor, which is based on a professional judgment of the entire database on the chemical. The RfDs are not applicable to nonthreshold effects such as cancer.

Reportable Quantity (RQ)-The quantity of a hazardous substance that is considered reportable under CERCLA. Reportable quantities are (1) 1 pound or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Sect. 3 11 of the Clean Water Act. Quantities are measured over a 24-hour period.

Reproductive Toxicity-The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

Short-Term Exposure Limit (STEL)-The maximum concentration to which workers can be exposed for up to 15 min continually. No more than four excursions are allowed per day, and there must be at least 60 min between exposure periods. The daily TLV-TWA may not be exceeded.

Target Organ Toxicity-This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

Teratogen-A chemical that causes structural defects that affect the development of an organism.

Threshold Limit Value (TLV)-A concentration of a substance to which most workers can be exposed without adverse effect. The TLV may be expressed as a TWA, as a STEL, or as a CL.

Time-Weighted Average (TWA)-An allowable exposure concentration averaged over a normal 8-hour workday or 40-hour workweek.

Toxic Dose (TD_{50})-A calculated dose of a chemical, introduced by a route other than inhalation, which is expected to cause a specific toxic effect in 50% of a defined experimental animal population.

Uncertainty Factor (UF)-A factor used in operationally deriving the RfD from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of human, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using LOAEL data rather than NOAEL data. Usually each of these factors is set equal to 10.

APPENDIX A

ATSDR MINIMAL RISK LEVELS AND WORKSHEETS

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) [42 U.S.C. 9601 et seq.], as amended by the Superfund Amendments and Reauthorization Act (SARA) [Pub. L. 99–499], requires that the Agency for Toxic Substances and Disease Registry (ATSDR) develop jointly with the U.S. Environmental Protection Agency (EPA), in order of priority, a list of hazardous substances most commonly found at facilities on the CERCLA National Priorities List (NPL); prepare toxicological profiles for each substance included on the priority list of hazardous substances; and assure the initiation of a research program to fill identified data needs associated with the substances.

The toxicological profiles include an examination, summary, and interpretation of available toxicological information and epidemiologic evaluations of a hazardous substance. During the development of toxicological profiles, Minimal Risk Levels (MRLs) are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive health effect(s) for a specific duration for a given route of exposure. An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. MRLs are based on noncancer health effects only and are not based on a consideration of cancer effects. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors to identify contaminants and potential health effects that may be of concern at hazardous waste sites. It is important to note that MRLs are not intended to define clean-up or action levels.

MRLs are derived for hazardous substances using the no-observed-adverse-effect level/uncertainty factor approach. They are below levels that might cause adverse health effects in the people most sensitive to such chemical-induced effects. MRLs are derived for acute (1–14 days), intermediate (15–364 days), and chronic (365 days and longer) durations and for the oral and inhalation routes of exposure. Currently, MRLs for the dermal route of exposure are not derived because ATSDR has not yet identified a method suitable for this route of exposure. MRLs are generally based on the most sensitive chemical-induced end point considered to be of relevance to humans. Serious health effects (such as irreparable damage to the liver or kidneys, or birth defects) are not used as a basis for establishing MRLs. Exposure to a level above the MRL does not mean that adverse health effects will occur.

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MRLs are intended only to serve as a screening tool to help public health professionals decide where to look more closely. They may also be viewed as a mechanism to identify those hazardous waste sites that are not expected to cause adverse health effects. Most MRLs contain a degree of uncertainty because of the lack of precise toxicological information on the people who might be most sensitive (e.g., infants, elderly, nutritionally or immunologically compromised) to the effects of hazardous substances. ATSDR uses a conservative (i.e., protective) approach to address this uncertainty consistent with the public health principle of prevention. Although human data are preferred, MRLs often must be based on animal studies because relevant human studies are lacking. In the absence of evidence to the contrary, ATSDR assumes that humans are more sensitive to the effects of hazardous substance than animals and that certain persons may be particularly sensitive. Thus, the resulting MRL may be as much as a hundredfold below levels that have been shown to be nontoxic in laboratory animals.

Proposed MRLs undergo a rigorous review process: Health Effects/MRL Workgroup reviews within the Division of Toxicology, expert panel peer reviews, and agencywide MRL Workgroup reviews, with participation from other federal agencies and comments from the public. They are subject to change as new information becomes available concomitant with updating the toxicological profiles. Thus, MRLs in the most recent toxicological profiles supersede previously published levels. For additional information regarding MRLs, please contact the Division of Toxicology, Agency for Toxic Substances and Disease Registry, 1600 Clifton Road, Mailstop E-29, Atlanta, Georgia 30333.

APPENDIX B

USER'S GUIDE

Chapter 1

Public Health Statement

This chapter of the profile is a health effects summary written in non-technical language. Its intended audience is the general public especially people living in the vicinity of a hazardous waste site or chemical release. If the Public Health Statement were removed from the rest of the document, it would still communicate to the lay public essential information about the chemical.

The major headings in the Public Health Statement are useful to find specific topics of concern. The topics are written in a question and answer format. The answer to each question includes a sentence that will direct the reader to chapters in the profile that will provide more information on the given topic.

Chapter 2

Tables and Figures for Levels of Significant Exposure (LSE)

Tables (2-1) 2-2, and 2-3) and figures (2-1 and 2-2) are used to summarize health effects and illustrate graphically levels of exposure associated with those effects. These levels cover health effects observed at increasing dose concentrations and durations, differences in response by species, minimal risk levels (MRLs) to humans for noncancer end points, and EPA's estimated range associated with an upper- bound individual lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. Use the LSE tables and figures for a quick review of the health effects and to locate data for a specific exposure scenario. The LSE tables and figures should always be used in conjunction with the text. All entries in these tables and figures represent studies that provide reliable, quantitative estimates of No-Observed-Adverse- Effect Levels (NOAELs), lowest-Observed-Adverse-Effect Levels (LOAELs), or Cancer Effect Levels (CELs).

The legends presented below demonstrate the application of these tables and figures. Representative examples of LSE Table 2-1 and Figure 2-1 are shown. The numbers in the left column of the legends correspond to the numbers in the example table and figure.

LEGEND

See LSE Table 2-1

(1) Route of Exposure One of the first considerations when reviewing the toxicity of a substance using these tables and figures should be the relevant and appropriate route of exposure. When sufficient data

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exists, three LSE tables and two LSE figures are presented in the document. The three LSE tables present data on the three principal routes of exposure, i.e., inhalation, oral, and dermal (LSE Table 2-1, 2-2, and 2-3, respectively). LSE figures are limited to the inhalation (LSE Figure 2-1) and oral (LSE Figure 2-2) routes. Not all substances will have data on each route of exposure and will not therefore have all five of the tables and figures.

(2) Exposure Period Three exposure periods - acute (less than 15 days), intermediate (15-364 days), and chronic (365 days or more) are presented within each relevant route of exposure. In this example, an inhalation study of intermediate exposure duration is reported. For quick reference to health effects occurring from a known length of exposure, locate the applicable exposure period within the LSE table and figure.

(3) Health Effect The major categories of health effects included in LSE tables and figures are death, systemic, immunological, neurological, developmental, reproductive, and cancer. NOAELs and LOAELs can be reported in the tables and figures for all effects but cancer. Systemic effects are further defined in the "System" column of the LSE table (see key number 18).

(4) Key to Figure Each key number in the LSE table links study information to one or more data points using the same key number in the corresponding LSE figure. In this example, the study represented by key number 18 has been used to derive a NOAEL and a Less Serious LOAEL (also see the 2 "18r" data points in Figure 2-1).

(5) Species The test species, whether animal or human, are identified in this column. "Relevance to Public Health," covers the relevance of animal data to human toxicity and Section 2.3, "Toxicokinetics," contains any available information on comparative toxicokinetics. Although NOAELs and LOAELs are species specific, the levels are extrapolated to equivalent human doses to derive an MRL.

(6) Exposure Freauency/Duration The duration of the study and the weekly and daily exposure regimen are provided in this column. This permits comparison of NOAELs and LOAELs from different studies. In this case (key number 18), rats were exposed to 1,1,2,2-tetrachloroethane via inhalation for 6 hours per day, 5 days per week, for 3 weeks. For a more complete review of the dosing regimen refer to the appropriate sections of the text or the original reference paper, i.e., Nitschke et al. 1981.

(7) System This column further defines the systemic effects. These systems include: respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, and dermal/ocular. "Other" refers to any systemic effect (e.g., a decrease in body weight) not covered in these systems. In the example of key number 18, 1 systemic effect (respiratory) was investigated.

(8) NOAEL A No-Observed-Adverse-Effect Level (NOAEL) is the highest exposure level at which no harmful effects were seen in the organ system studied. Key number 18 reports a NOAEL of 3 ppm for

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the respiratory system which was used to derive an intermediate exposure, inhalation MRL of 0.005 ppm (see footnote "b").

(9) LOAEL A lowest-Observed-Adverse-Effect Level (LOAEL) is the lowest dose used in the study that caused a harmful health effect. LOAELs have been classified into "Less Serious" and "Serious" effects. These distinctions help readers identify the levels of exposure at which adverse health effects first appear and the gradation of effects with increasing dose. A brief description of the specific endpoint used to quantify the adverse effect accompanies the LOAEL. The respiratory effect reported in key number 18 (hyperplasia) is a Less serious LOAEL of lo ppm. MRLs are not derived from Serious LOAELs .

(10) Reference The complete reference citation is given in chapter 8 of the profile.

(11) CEL A Cancer Effect Level (CEL) is the lowest exposure level associated with the onset of carcinogenesis in experimental or epidemiologic studies. CELs are always considered serious effects. The LSE tables and figures do not contain NOAELs for cancer, but the text may report doses not causing measurable cancer increases.

(12) Footnotes Explanations of abbreviations or reference notes for data in the LSE tables are found in the footnotes. Footnote "b" indicates the NOAEL of 3 ppm in key number 18 was used to derive an MRL of 0.005 ppm.

LEGEND

See Figure 2-1

LSE figures graphically illustrate the data presented in the corresponding LSE tables. Figures help the reader quickly compare health effects according to exposure concentrations for particular exposure periods.

(13) Exposure Period The same exposure periods appear as in the LSE table. In this example, health effects observed within the intermediate and chronic exposure periods are illustrated.

(14) Health Effect These are the categories of health effects for which reliable quantitative data exists. The same health effects appear in the LSE table.

(15) Levels of Exposure concentrations or doses for each health effect in the LSE tables are graphically displayed in the LSE figures. Exposure concentration or dose is measured on the log scale "y" axis. Inhalation exposure is reported in mg/m^3 or ppm and oral exposure is reported in mg/kg/day.

(16) NOAEL In this example, 18r NOAEL is the critical endpoint for which an intermediate inhalation exposure MRL is based. As you can see from the LSE figure key, the open-circle symbol indicates to a

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NOAEL for the test species-rat. The key number 18 corresponds to the entry in the LSE table. The dashed descending arrow indicates the extrapolation from the exposure level of 3 ppm (see entry 18 in the Table) to the MRL of 0.005 ppm (see footnote "b" in the LSE table).

(17) CEL Key number 38r is 1 of 3 studies for which Cancer Effect Levels were derived. The diamond symbol refers to a Cancer Effect Level for the test species-mouse. The number 38 corresponds to the entry in the LSE table.

(18) Estimated Upper-Bound Human Cancer Risk Levels This is the range associated with the upper-bound for lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. These risk levels are derived from the EPA's Human Health Assessment Group's upper-bound estimates of the slope of the cancer dose response curve at low dose levels (q_1*).

(19) Key to LSE Figure The Key explains the abbreviations and symbols used in the figure.

The Relevance to Public Health section provides a health effects summary based on evaluations of existing toxicologic, epidemiologic, and toxicokinetic information This summary is designed to present interpretive, weight-of-evidence discussions for human health end points by addressing the following questions.

1 . What effects are known to occur in humans?

2 . What effects observed in animals are Likely to be of concern to humans?

3 . What exposure conditions are likely to be of concern to humans, especially around hazardous waste sites?

The section covers end points in the same order they appear within the Discussion of Health Effects by Route of Exposure section, by route (inhalation, oral, dermal) and within route by effect. Human data are presented first, then animal data. Both are organized by duration (acute, intermediate, chronic). *In vitro* data and data from parenteral routes (intramuscular, intravenous, subcutaneous, etc.) are also considered in this section. If data are located in the scientific literature, a table of genotoxicity information is included.

The carcinogenic potential of the profiled substance is qualitatively evaluated, when appropriate, using existing toxicokinetic, genotoxic, and carcinogenic data. ATSDR does not currently assess cancer potency or perform cancer risk assessments. Minimal risk levels (MRLs) for noncancer end points (if derived) and the end points from which they were derived are indicated and discussed.

Limitations to existing scientific literature that prevent a satisfactory evaluation of the relevance to public health are identified in the Data Needs section.

SAMPLE

1 →

TABLE 2-1. Levels of Significant Exposure to [Chemical x] – Inhalation

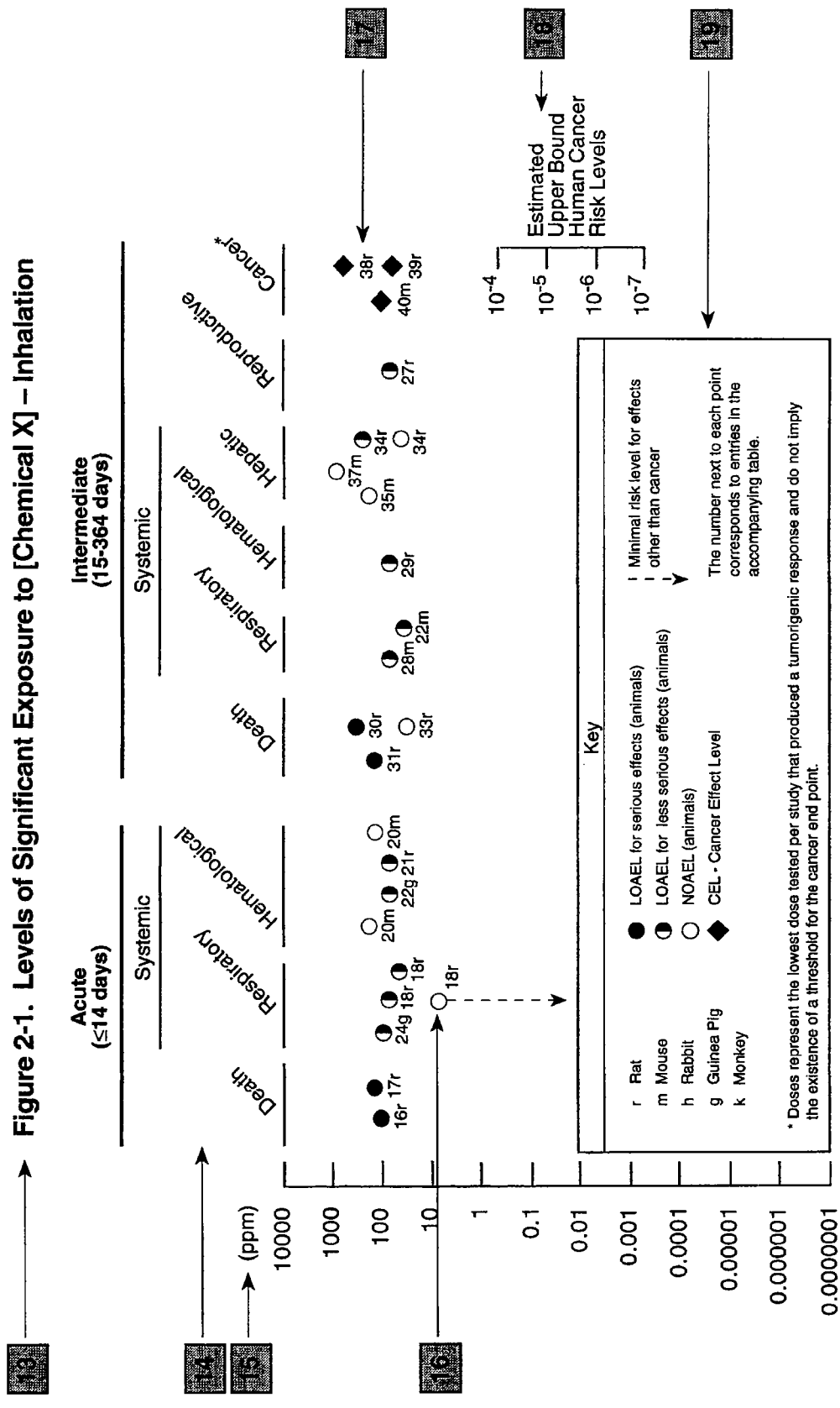
Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect) Less serious (ppm)		Reference
2 → INTERMEDIATE EXPOSURE							
	5	6	7	8	9		10
3 → Systemic	↓	↓	↓	↓	↓		↓
4 → 18	Rat	13 wk 5d/wk 6hr/d	Resp	3 [b]	10 (hyperplasia)		Nitschke et al. 1981
CHRONIC EXPOSURE							
					11		
Cancer					↓		
38	Rat	18 mo 5d/wk 7hr/d			20	(CEL, multiple organs)	Wong et al. 1982
39	Rat	89–104 wk 5d/wk 6hr/d			10	(CEL, lung tumors, nasal tumors)	NTP 1982
40	Mouse	79–103 wk 5d/wk 6hr/d			10	(CEL, lung tumors, hemangiosarcomas)	NTP 1982

[a] The number corresponds to entries in Figure 2-1.

12 → [b] an uncertainty factor of 100 (10 for extrapolation from animal to humans, 10 for human variability).

SAMPLE

Figure 2-1. Levels of Significant Exposure to [Chemical X] – Inhalation



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Chapter 2 (Section 2.5)

Relevance to Public Health

Interpretation of Minimal Risk Levels

Where sufficient toxicologic information is available, we have derived minimal risk levels (MRLs) for inhalation and oral routes of entry at each duration of exposure (acute, intermediate, and chronic). These MRLs are not meant to support regulatory action; but to acquaint health professionals with exposure levels at which adverse health effects are not expected to occur in humans. They should help physicians and public health officials determine the safety of a community living near a chemical emission, given the concentration of a contaminant in air or the estimated daily dose in water. MRLs are based largely on toxicological studies in animals and on reports of human occupational exposure.

MRL users should be familiar with the toxicologic information on which the number is based. Chapter 2.5, "Relevance to Public Health," contains basic information known about the substance. Other sections such as 2.8, "Interactions with Other Substances," and 2.9, "Populations that are Unusually Susceptible" provide important supplemental information.

MRL users should also understand the MRL derivation methodology. MRLs are derived using a modified version of the risk assessment methodology the Environmental Protection Agency (EPA) provides (Barnes and Dourson 1988) to determine reference doses for lifetime exposure (RfDs).

To derive an MRL, ATSDR generally selects the most sensitive endpoint which, in its best judgement, represents the most sensitive human health effect for a given exposure route and duration. ATSDR cannot make this judgement or derive an MRL unless information (quantitative or qualitative) is available for all potential systemic, neurological, and developmental effects. If this information and reliable quantitative data on the chosen endpoint are available, ATSDR derives an MRL using the most sensitive species (when information from multiple species is available) with the highest NOAEL that does not exceed any adverse effect levels. When a NOAEL is not available, a lowest-observed-adverse-effect level (LOAEL) can be used to derive an MRL, and an uncertainty factor (UP) of lo must be employed. Additional uncertainty factors of lo must be used both for human variability to protect sensitive subpopulations (people who are most susceptible to the health effects caused by the substance) and for interspecies variability (extrapolation from animals to humans). In deriving an MRL, these individual uncertainty factors are multiplied together. The product is then divided into the inhalation concentration or oral dosage selected from the study. Uncertainty factors used in developing a substance-specific MRL are provided in the footnotes of the LSE Tables.

APPENDIX C

ACRONYMS, ABBREVIATIONS, AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
ADME	Absorption, Distribution, Metabolism, and Excretion
AML	acute myeloid leukemia
atm	atmosphere
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
BEI	Biological Exposure Index
BSC	Board of Scientific Counselors
C	Centigrade
CDC	Centers for Disease Control
CEL	Cancer Effect Level
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
Ci	curie
CLP	Contract Laboratory Program
cm	centimeter
CML	chronic myeloid leukemia
CNS	central nervous system
d	day
DHEW	Department of Health, Education, and Welfare
DHHS	Department of Health and Human Services
DOL	Department of Labor
ECG	electrocardiogram
EEG	electroencephalogram
EPA	Environmental Protection Agency
EKG	see ECG
F	Fahrenheit
F_1	first filial generation
FAO	Food and Agricultural Organization of the United Nations
FEMA	Federal Emergency Management Agency
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
fpm	feet per minute
ft	foot
FR	*Federal Register*
g	gram
GC	gas chromatography
gen	generation
HPLC	high-performance liquid chromatography
hr	hour
IDLH	Immediately Dangerous to Life and Health

IARC	International Agency for Research on Cancer
ILO	International Labor Organization
in	inch
Kd	adsorption ratio
kg	kilogram
kkg	metric ton
K_{oc}	organic carbon partition coefficient
K_{ow}	octanol-water partition coefficient
L	liter
LC	liquid chromatography
LC_{Lo}	lethal concentration, low
LC_{50}	lethal concentration, 50% kill
LD_{Lo}	lethal dose, low
LD_{50}	lethal dose, 50% kill
LOAEL	lowest-observed-adverse-effect level
LSE	Levels of Significant Exposure
m	meter
MA	trans,trans-muconic acid
mCi	millicurie
mg	milligram
min	minute
mL	milliliter
mm	millimeter
mm Hg	millimeters of mercury
mmol	millimole
mo	month
mppcf	millions of particles per cubic foot
MRL	Minimal Risk Level
MS	mass spectrometry
NCE	normochromatic erythrocytes
NG	not given
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute for Occupational Safety and Health
NIOSHTIC	NIOSH's Computerized Information Retrieval System
ng	nanogram
nm	nanometer
NHANES	National Health and Nutrition Examination Survey
nmol	nanomole
NOAEL	no-observed-adverse-effect level
NOES	National Occupational Exposure Survey
NOHS	National Occupational Hazard Survey
NPL	National Priorities List
NRC	National Research Council
NTIS	National Technical Information Service
NTP	National Toxicology Program
OSHA	Occupational Safety and Health Administration

APPENDIX C

PEL	permissible exposure limit
PCE	polychromatic erythrocytes
pg	picogram
pmol	picomole
PHS	Public Health Service
PMR	proportionate mortality ratio
ppb	parts per billion
ppm	parts per million
ppt	parts per trillion
REL	recommended exposure limit
RfD	Reference Dose
RTECS	Registry of Toxic Effects of Chemical Substances
sec	second
SCE	sister chromatid exchange
SIC	Standard Industrial Classification
SMR	standard mortality ratio
STEL	short term exposure limit
STORET	STORAGE and RETRIEVAL
TLV	threshold limit value
TSCA	Toxic Substances Control Act
TRI	Toxics Release Inventory
TWA	time-weighted average
UMDNJ	University of Medicine and Dentistry New Jersey
U.S.	United States
UF	uncertainty factor
yr	year
WHO	World Health Organization
wk	week

>	greater than
≥	greater than or equal to
=	equal to
<	less than
≤	less than or equal to
%	percent
α	alpha
β	beta
δ	delta
γ	gamma
µm	micrometer
µg	microgram

Attachment C2

Agency for Toxic Substances and Disease Registry Toxicological Profiles

TOXICOLOGICAL PROFILE FOR NAPHTHALENE, 1-METHYLNAPHTHALENE, AND 2-METHYLNAPHTHALENE

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry

August 2005

DISCLAIMER

The use of company or product name(s) is for identification only and does not imply endorsement by the Agency for Toxic Substances and Disease Registry.

UPDATE STATEMENT

A Toxicological Profile for Naphthalene, 1-Methylnaphthalene, and 2-Methylnaphthalene, Draft for Public Comment was released in September 2003. This edition supersedes any previously released draft or final profile.

Toxicological profiles are revised and republished as necessary. For information regarding the update status of previously released profiles, contact ATSDR at:

Agency for Toxic Substances and Disease Registry
Division of Toxicology/Toxicology Information Branch
1600 Clifton Road NE
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FOREWORD

This toxicological profile is prepared in accordance with guidelines* developed by the Agency for Toxic Substances and Disease Registry (ATSDR) and the Environmental Protection Agency (EPA). The original guidelines were published in the *Federal Register* on April 17, 1987. Each profile will be revised and republished as necessary.

The ATSDR toxicological profile succinctly characterizes the toxicologic and adverse health effects information for the hazardous substance described therein. Each peer-reviewed profile identifies and reviews the key literature that describes a hazardous substance's toxicologic properties. Other pertinent literature is also presented, but is described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

The focus of the profiles is on health and toxicologic information; therefore, each toxicological profile begins with a public health statement that describes, in nontechnical language, a substance's relevant toxicological properties. Following the public health statement is information concerning levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Data needs that are of significance to protection of public health are identified by ATSDR and EPA.

Each profile includes the following:

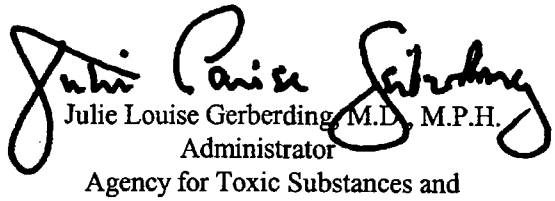
(A) The examination, summary, and interpretation of available toxicologic information and epidemiologic evaluations on a hazardous substance to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects;

(B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure that present a significant risk to human health of acute, subacute, and chronic health effects; and

(C) Where appropriate, identification of toxicologic testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

The principal audiences for the toxicological profiles are health professionals at the Federal, State, and local levels; interested private sector organizations and groups; and members of the public.

This profile reflects ATSDR's assessment of all relevant toxicologic testing and information that has been peer-reviewed. Staff of the Centers for Disease Control and Prevention and other Federal scientists have also reviewed the profile. In addition, this profile has been peer-reviewed by a nongovernmental panel and was made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.



Julie Louise Gerberding, M.D., M.P.H.
Administrator
Agency for Toxic Substances and
Disease Registry

*Legislative Background

The toxicological profiles are developed in response to the Superfund Amendments and Reauthorization Act (SARA) of 1986 (Public Law 99-499) which amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law directed ATSDR to prepare toxicological profiles for hazardous substances most commonly found at facilities on the CERCLA National Priorities List and that pose the most significant potential threat to human health, as determined by ATSDR and the EPA. The availability of the revised priority list of 275 hazardous substances was announced in the *Federal Register* on November 7, 2003 (68 FR 63098) . For prior versions of the list of substances, see *Federal Register* notices dated April 17, 1987 (52 FR 12866); October 20, 1988 (53 FR 41280); October 26, 1989 (54 FR 43619); October 17,1990 (55 FR 42067); October 17, 1991 (56 FR 52166); October 28, 1992 (57 FR 48801); February 28, 1994 (59 FR 9486); April 29, 1996 (61 FR 18744); November 17, 1997 (62 FR 61332); October 21, 1999(64 FR 56792) and October 25, 2001 (66 FR 54014). Section 104(i)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list.

QUICK REFERENCE FOR HEALTH CARE PROVIDERS

Toxicological Profiles are a unique compilation of toxicological information on a given hazardous substance. Each profile reflects a comprehensive and extensive evaluation, summary, and interpretation of available toxicologic and epidemiologic information on a substance. Health care providers treating patients potentially exposed to hazardous substances will find the following information helpful for fast answers to often-asked questions.

Primary Chapters/Sections of Interest

Chapter 1: Public Health Statement: The Public Health Statement can be a useful tool for educating patients about possible exposure to a hazardous substance. It explains a substance's relevant toxicologic properties in a nontechnical, question-and-answer format, and it includes a review of the general health effects observed following exposure.

Chapter 2: Relevance to Public Health: The Relevance to Public Health Section evaluates, interprets, and assesses the significance of toxicity data to human health.

Chapter 3: Health Effects: Specific health effects of a given hazardous compound are reported by type of health effect (death, systemic, immunologic, reproductive), by route of exposure, and by length of exposure (acute, intermediate, and chronic). In addition, both human and animal studies are reported in this section.
NOTE: Not all health effects reported in this section are necessarily observed in the clinical setting. Please refer to the Public Health Statement to identify general health effects observed following exposure.

Pediatrics: Four new sections have been added to each Toxicological Profile to address child health issues:

Section 1.6	**How Can (Chemical X) Affect Children?**
Section 1.7	**How Can Families Reduce the Risk of Exposure to (Chemical X)?**
Section 3.7	**Children's Susceptibility**
Section 6.6	**Exposures of Children**

Other Sections of Interest:

Section 3.8	**Biomarkers of Exposure and Effect**
Section 3.11	**Methods for Reducing Toxic Effects**

ATSDR Information Center

Phone:	1-888-42-ATSDR or (404) 498-0110	***Fax***:	(770) 488-4178
E-mail:	atsdric@cdc.gov	***Internet***:	http://www.atsdr.cdc.gov

The following additional material can be ordered through the ATSDR Information Center:

Case Studies in Environmental Medicine: Taking an Exposure History—The importance of taking an exposure history and how to conduct one are described, and an example of a thorough exposure history is provided. Other case studies of interest include *Reproductive and Developmental*

Hazards; Skin Lesions and Environmental Exposures; *Cholinesterase-Inhibiting Pesticide Toxicity*; and numerous chemical-specific case studies.

Managing Hazardous Materials Incidents is a three-volume set of recommendations for on-scene (prehospital) and hospital medical management of patients exposed during a hazardous materials incident. Volumes I and II are planning guides to assist first responders and hospital emergency department personnel in planning for incidents that involve hazardous materials. Volume III—*Medical Management Guidelines for Acute Chemical Exposures*—is a guide for health care professionals treating patients exposed to hazardous materials.

Fact Sheets (ToxFAQs) provide answers to frequently asked questions about toxic substances.

Other Agencies and Organizations

The National Center for Environmental Health (NCEH) focuses on preventing or controlling disease, injury, and disability related to the interactions between people and their environment outside the workplace. Contact: NCEH, Mailstop F-29, 4770 Buford Highway, NE, Atlanta, GA 30341-3724 • Phone: 770-488-7000 • FAX: 770-488-7015.

The National Institute for Occupational Safety and Health (NIOSH) conducts research on occupational diseases and injuries, responds to requests for assistance by investigating problems of health and safety in the workplace, recommends standards to the Occupational Safety and Health Administration (OSHA) and the Mine Safety and Health Administration (MSHA), and trains professionals in occupational safety and health. Contact: NIOSH, 200 Independence Avenue, SW, Washington, DC 20201 • Phone: 800-356-4674 or NIOSH Technical Information Branch, Robert A. Taft Laboratory, Mailstop C-19, 4676 Columbia Parkway, Cincinnati, OH 45226-1998 • Phone: 800-35-NIOSH.

The National Institute of Environmental Health Sciences (NIEHS) is the principal federal agency for biomedical research on the effects of chemical, physical, and biologic environmental agents on human health and well-being. Contact: NIEHS, PO Box 12233, 104 T.W. Alexander Drive, Research Triangle Park, NC 27709 • Phone: 919-541-3212.

Referrals

The Association of Occupational and Environmental Clinics (AOEC) has developed a network of clinics in the United States to provide expertise in occupational and environmental issues. Contact: AOEC, 1010 Vermont Avenue, NW, #513, Washington, DC 20005 • Phone: 202-347-4976 • FAX: 202-347-4950 • e-mail: AOEC@AOEC.ORG • Web Page: http://www.aoec.org/.

The American College of Occupational and Environmental Medicine (ACOEM) is an association of physicians and other health care providers specializing in the field of occupational and environmental medicine. Contact: ACOEM, 25 Northwest Point Boulevard, Suite 700, Elk Grove Village, IL 60007-1030 • Phone: 847-818-1800 • FAX: 847-818-9266.

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THE PROFILE HAS UNDERGONE THE FOLLOWING ATSDR INTERNAL REVIEWS:

1. Health Effects Review. The Health Effects Review Committee examines the health effects chapter of each profile for consistency and accuracy in interpreting health effects and classifying end points.

2. Minimal Risk Level Review. The Minimal Risk Level Workgroup considers issues relevant to substance-specific Minimal Risk Levels (MRLs), reviews the health effects database of each profile, and makes recommendations for derivation of MRLs.

3. Data Needs Review. The Research Implementation Branch reviews data needs sections to assure consistency across profiles and adherence to instructions in the Guidance.

4. Green Border Review. Green Border review assures the consistency with ATSDR policy.

PEER REVIEW

A peer review panel was assembled for naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene. The panel consisted of the following members:

1. Martin Alexander, Ph.D., Cornell University, Ithaca, New York;

2. Susan Borghoff, Ph.D., DABT, CIIT Centers for Health Research, Research Triangle Park, North Carolina; and

3. G.A. Shakeel Ansari, Ph.D., The University of Texas Medical Branch, Galveston, Texas.

These experts collectively have knowledge of naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in Section 104(I)(13) of the Comprehensive Environmental Response, Compensation, and Liability Act, as amended.

Scientists from the Agency for Toxic Substances and Disease Registry (ATSDR) have reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound.

The citation of the peer review panel should not be understood to imply its approval of the profile's final content. The responsibility for the content of this profile lies with the ATSDR.

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1. PUBLIC HEALTH STATEMENT

This public health statement tells you about naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene and the effects of exposure to these chemicals.

The Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. These sites are then placed on the National Priorities List (NPL) and are targeted for long-term federal clean-up activities. Naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene have been found in at least 654, 36, and 412, respectively, of the 1,662 current or former NPL sites. Although the total number of NPL sites evaluated for these substances is not known, the possibility exists that the number of sites at which naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene are found may increase in the future as more sites are evaluated. This information is important because these sites may be sources of exposure and exposure to these substances may harm you.

When a substance is released either from a large area, such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment. Such a release does not always lead to exposure. You can be exposed to a substance only when you come in contact with it. You may be exposed by breathing, eating, or drinking the substance, or by skin contact.

If you are exposed to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene, many factors will determine whether you will be harmed. These factors include the dose (how much), the duration (how long), and how you come in contact with them. You must also consider any other chemicals you are exposed to and your age, sex, diet, family traits, lifestyle, and state of health.

1.1 WHAT ARE NAPHTHALENE, 1-METHYLNAPHTHALENE, AND 2-METHYLNAPHTHALENE?

Naphthalene is a white solid that evaporates easily. It is also called mothballs, moth flakes, white tar, and tar camphor. When mixed with air, naphthalene vapors easily burn. Fossil fuels, such as petroleum and coal, naturally contain naphthalene. Burning tobacco or wood produces

naphthalene. The major commercial use of naphthalene is to make other chemicals used in making polyvinyl chloride (PVC) plastics. The major consumer products made from naphthalene are moth repellents, in the form of mothballs or crystals, and toilet deodorant blocks. It is also used for making dyes, resins, leather tanning agents, and the insecticide carbaryl.

Naphthalene has a strong but not unpleasant smell. Its taste is unknown, but it must not be unpleasant since children have eaten mothballs and deodorant blocks. You can smell naphthalene in the air at a concentration of 84 parts naphthalene per one billion parts (ppb) of air. You can smell it in water when 21 ppb are present.

1-Methylnaphthalene is a naphthalene-related compound that is also called alpha methyl-naphthalene. It is a clear liquid. Its taste and odor have not been described, but you can smell it in water when only 7.5 ppb are present.

Another naphthalene-related compound, 2-methylnaphthalene, is also called beta methyl-naphthalene. It is a solid like naphthalene. The taste and odor of 2-methylnaphthalene have not been described. Its presence can be detected at a concentration of 10 ppb in air and 10 ppb in water.

1-Methylnaphthalene and 2-methylnaphthalene are used to make other chemicals such as dyes, and resins. 2-Methylnaphthalene is also used to make vitamin K. All three chemicals are present in cigarette smoke, wood smoke, tar, asphalt, and at some hazardous waste sites.

See Chapters 4, 5, and 6 for more information on the properties and uses of naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene.

1.2 WHAT HAPPENS TO NAPHTHALENE, 1-METHYLNAPHTHALENE, AND 2-METHYLNAPHTHALENE WHEN THEY ENTER THE ENVIRONMENT?

Naphthalene enters the environment from industrial uses, from its use as a moth repellent, from the burning of wood or tobacco, and from accidental spills. Naphthalene at hazardous waste

sites and landfills can dissolve in water and be present in drinking water. Naphthalene can become weakly attached to soil or pass through the soil particles into underground water.

Most of the naphthalene entering the environment is from the burning of woods and fossil fuels in the home. The second greatest release of naphthalene is through the use of moth repellents. Only about 10% of the naphthalene entering the environment is from coal production and distillation. Less than 1% of the naphthalene released to the atmosphere can be attributed to the losses from naphthalene production. Cigarette smoking also releases small amounts of naphthalene into the air.

Naphthalene evaporates easily. That is why you can smell mothballs. In the air, moisture and sunlight make it break down, often within 1 day. Naphthalene can change to 1-naphthol or 2-naphthol. These chemicals have some of the toxic properties of naphthalene. Some naphthalene will dissolve in water in rivers, lakes, or wells. Naphthalene in water is destroyed by bacteria or evaporates into the air. Most naphthalene will be gone from water in rivers or lakes within 2 weeks.

Naphthalene binds weakly to soils and sediments. It easily passes through sandy soils to reach underground water. In soil, some microorganisms break down naphthalene. When near the surface of the soil, naphthalene will evaporate into air. Microorganisms present in the soil will break down most of the naphthalene in 1–3 months.

Naphthalene does not accumulate in the flesh of animals and fish that you might eat. If dairy cows are exposed to naphthalene, some naphthalene will be in their milk; if laying hens are exposed, some naphthalene will be in their eggs. Naphthalene and the methylnaphthalenes have been found in very small amounts in some samples of fish and shellfish from polluted waters.

Scientists know very little about what happens to 1-methylnaphthalene and 2-methylnaphthalene in the environment. These compounds are similar to naphthalene and should act like it in air, water, or soil.

See Chapters 5 and 6 for more information on what happens to naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene in the environment.

1.3 HOW MIGHT I BE EXPOSED TO NAPHTHALENE, 1-METHYLNAPHTHALENE, AND 2-METHYLNAPHTHALENE?

You are most likely to be exposed to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene from the air. Outdoor air contains low amounts of these chemicals. Burning of wood or fossil fuels and industrial discharges adds these chemicals to the environment. Automobile exhaust contributes naphthalene among other chemicals to air pollution in the cities. Typical air concentrations for naphthalene are low, 0.2 ppb or less. Studies of outdoor air reported concentrations of 0.09 ppb 1-methylnaphthalene and 0.011 ppb 2-methylnaphthalene. In homes or businesses where cigarettes are smoked, wood is burned, or moth repellents are used, the levels of naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene in the air are higher. Studies of indoor air typically report that average indoor air concentrations of these contaminants are less than 1 ppb.

You are not likely to be exposed to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene by eating foods or drinking beverages. These materials are unlikely to come in contact with naphthalene or methylnaphthalenes during production or processing. Naphthalene and the methylnaphthalenes are also unlikely to be present in tap water.

If you live near a hazardous waste site and have a well used for drinking water, you might be exposed to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene. For this to happen, the chemicals must pass through the soil and dissolve in the underground water that supplies your well. Children might also contact these chemicals by playing in or eating the dirt near a waste site.

Work using or making moth repellents, coal tar products, dyes, or inks could expose you to naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene in the air. Working in the wood-preserving, leather tanning, or asphalt industries could expose you to naphthalene.

Using moth repellents containing naphthalene in your home will expose you to naphthalene vapors. Your skin can come in contact with naphthalene via the use of naphthalene-treated clothing, blankets, or coverlets. You can breathe in the naphthalene vapors that are present in clothes and linen stored with moth-balls. Smoke from cigarettes can also expose you to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene. The highest airborne naphthalene concentrations in indoor air occur in the homes of cigarette smokers.

See Chapter 6 for more information on how you might be exposed to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene.

1.4 HOW CAN NAPHTHALENE, 1-METHYLNAPHTHALENE, AND 2-METHYLNAPHTHALENE ENTER AND LEAVE MY BODY?

Naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene can enter your body if you breathe air that contains these chemicals, if you smoke, if you eat mothballs, if you drink water that contains these chemicals, or if they touch your skin. These chemicals are most likely to enter your body through the air you breath into your lungs. Naphthalene can also enter your body through your skin when you handle mothballs, particularly if you have used an oil-based skin lotion. You can also breathe in naphthalene vapors from clothes that have been stored in mothballs.

Once naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene enter your body, small amounts will dissolve in your blood. Your blood carries them to your liver and other organs. These organs change them so that they pass through your body, mainly into your urine. Some naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene, and their breakdown products can be present in your stool. Naphthalene also has been found in some samples of fatty tissue and breast milk taken from the general U.S. population, but the concentrations of naphthalene were low. Most naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene that enters your body is expected to leave quickly within 1–3 days.

See Chapter 3 for more information on how naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene enter and leave your body.

1.5 HOW CAN NAPHTHALENE, 1-METHYLNAPHTHALENE, AND 2-METHYLNAPHTHALENE AFFECT MY HEALTH?

Scientists use many tests to protect the public from harmful effects of toxic chemicals and to find ways for treating persons who have been harmed.

One way to learn whether a chemical will harm people is to determine how the body absorbs, uses, and releases the chemical. For some chemicals, animal testing may be necessary. Animal testing may also help identify health effects such as cancer or birth defects. Without laboratory animals, scientists would lose a basic method for getting information needed to make wise decisions that protect public health. Scientists have the responsibility to treat research animals with care and compassion. Scientists must comply with strict animal care guidelines because laws today protect the welfare of research animals.

Exposure to a large amount of naphthalene may damage or destroy some of your red blood cells. This could cause you to have too few red blood cells until your body replaces the destroyed cells. This problem is called hemolytic anemia. People, particularly children, have developed this problem after eating naphthalene-containing mothballs or deodorant blocks. Anemia has also occurred in infants wearing diapers that have been stored in mothballs. If your ancestors were from Africa or Mediterranean countries, naphthalene may be more dangerous to you than to people of other origins. These populations have a higher incidence of problems with an enzyme that usually protects red blood cells from damage created by oxygen in the air.

Some of the symptoms that occur with hemolytic anemia are fatigue, lack of appetite, restlessness, and a pale appearance to your skin. Exposure to a large amount of naphthalene, such as by eating mothballs, may cause nausea, vomiting, diarrhea, blood in the urine, and a yellow color to the skin. If you have these symptoms, you should see a doctor quickly.

Anemia is a common condition in pregnancy that can be due to causes other than naphthalene exposure. However, if you are a pregnant woman and are anemic due to naphthalene exposure, then it is possible that your unborn child may be anemic as well. Naphthalene can move from your blood to your baby's blood. Once your baby is born, naphthalene may also be carried from your body to your baby's body through your milk. It is not completely clear if naphthalene causes reproductive effects in animals; most evidence says that it does not.

Laboratory rabbits, guinea pigs, mice, and rats sometimes develop cataracts (cloudiness) in their eyes after swallowing naphthalene at high dose levels. It is not certain whether cataracts also develop in humans exposed to naphthalene, but the possibility exists.

When mice or rats breathed in naphthalene vapors daily throughout their lives (2 years), cells in the lining of their noses or lungs were damaged. Some exposed female mice also developed lung tumors. Some exposed male and female rats developed nose tumors. When mice or rats were fed naphthalene in their food for 13 weeks, no tumors or other tissue changes were found. The only effect found was decreased body weight in rats that were fed naphthalene.

Based on these results from animal studies, the U.S. Department of Health and Human Services concluded that naphthalene is reasonably anticipated to be a human carcinogen. The International Agency for Research on Cancer (IARC) concluded that naphthalene is possibly carcinogenic to humans, because there is enough evidence that naphthalene causes cancer in animals, but not enough evidence about such an effect in humans. Under the EPA 1986 cancer guidelines, naphthalene was assigned to Group C – possible human carcinogen.

When mice were fed food containing 1-methylnaphthalene or 2-methylnaphthalene for most of their lives (81 weeks), the gas-exchange part of the lungs of some mice became filled with an abnormal material. This type of lung injury is called pulmonary alveolar proteinosis. A few mice also had lung tumors, but the numbers of mice with lung tumors were not enough to conclude that 1-methylnaphthalene or 2-methylnaphthalene caused the tumors. Pulmonary alveolar proteinosis has been seen in some people, but the cause of this uncommon lung disease in humans is unknown.

See Chapter 3 for more information on the effects of naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene on your health.

1.6 HOW CAN NAPHTHALENE, 1-METHYLNAPHTHALENE, AND 2-METHYLNAPHTHALENE AFFECT CHILDREN?

This section discusses potential health effects in humans from exposures during the period from conception to maturity at 18 years of age.

Hospitals have reported many cases of hemolytic anemia in children, including newborns and infants, who either ate naphthalene mothballs or deodorant cakes or who were in close contact with clothing or blankets stored in naphthalene mothballs. Newborns or infants are thought to be especially susceptible to this effect on the blood, because their bodies are less able to get rid of naphthalene than adults.

Newborn mice appear to be more susceptible to lung injury than adult mice, when they are injected with naphthalene. These results suggest that children may be more susceptible to lung injury from naphthalene than adults. Scientists do not know if lung injury from breathing in naphthalene in childhood may lead to lung disease later in life.

There are no reports that prenatal or postnatal exposure to naphthalene has caused developmental problems in human offspring. When pregnant mice, rats, or rabbits were fed naphthalene during their pregnancy, the development of their offspring was normal. Normal offspring development occurred even when the amounts of naphthalene given were large enough to prevent the pregnant animals from gaining their normal amount of weight.

There are no studies in humans or animals indicating whether or not children are more susceptible to health effects from 1-methylnaphthalene or 2-methylnaphthalene.

1.7 HOW CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO NAPHTHALENE, 1-METHYLNAPHTHALENE, AND 2-METHYLNAPHTHALENE?

If your doctor finds that you have been exposed to substantial amounts of naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene, ask whether your children might also have been exposed. Your doctor might need to ask your state health department to investigate.

The most important way that families can reduce the risk of exposure to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene is to avoid smoking tobacco, generating smoke during cooking, or using fireplaces or heating appliances in their homes. If families use naphthalene-containing moth repellants, the material should be enclosed in containers that prevent vapors from escaping. The containers should not be accessible to young children. Blankets and clothing stored with naphthalene moth repellents should be aired outdoors to remove naphthalene odors and washed before they are used. To further minimize the risk of exposure to naphthalene, families should inform themselves of the contents of air deodorizers that are used in their homes, and refrain from using deodorizers with naphthalene.

1.8 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO NAPHTHALENE, 1-METHYLNAPHTHALENE, AND 2-METHYLNAPHTHALENE?

Several tests determine whether you have been exposed to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene. These tests include measuring naphthalene, 1-methylnaphthalene, 2-methylnaphthalene, or their breakdown products in samples of urine, stool, blood, maternal milk, or body fat. These tests require special equipment, which is not routinely available in a doctor's office. Body fluids, urine, stool samples, or tissue samples can be sent to a special laboratory for the tests. These tests cannot determine exactly how much naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene you were exposed to or predict whether harmful effects will occur. If the samples are collected within a day or two of exposure, then the tests can show if you were exposed to a large or small amount of naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene.

See Chapters 3 and 7 for more information on tests for exposure to naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene.

1.9 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

The federal government develops regulations and recommendations to protect public health. Regulations *can* be enforced by law. The EPA, the Occupational Safety and Health Administration (OSHA), and the Food and Drug Administration (FDA) are some federal agencies that develop regulations for toxic substances. Recommendations provide valuable guidelines to protect public health, but *cannot* be enforced by law. The Agency for Toxic Substances and Disease Registry (ATSDR) and the National Institute for Occupational Safety and Health (NIOSH) are two federal organizations that develop recommendations for toxic substances.

Regulations and recommendations can be expressed as "not-to-exceed" levels, that is, levels of a toxic substance in air, water, soil, or food that do not exceed a critical value that is usually based on levels that affect animals; they are then adjusted to levels that will help protect humans. Sometimes these not-to-exceed levels differ among federal organizations because they used different exposure times (an 8-hour workday or a 24-hour day), different animal studies, or other factors.

Recommendations and regulations are also updated periodically as more information becomes available. For the most current information, check with the federal agency or organization that provides it. Some regulations and recommendations for naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene include the following:

The federal government has developed regulations and advisories to protect individuals from the possible health effects of naphthalene in the environment. OSHA set a limit of 10 parts per million (ppm) for the level of naphthalene in workplace air over an 8-hour workday. NIOSH set a limit of 500 ppm for the level of naphthalene in workplace air expected to be immediately

dangerous to life or health. Exposure to workplace air concentrations above this limit for more than 30 minutes would be expected to impair a worker's ability to escape the contaminated workplace.

EPA recommends that children not drink water with over 0.5 ppm naphthalene for more than 10 days or over 0.4 ppm for any longer than 7 years. Adults should not drink water with more than 1 ppm for more than 7 years. For water consumed over a lifetime (70 years), EPA suggests that it contain no more than 0.1 ppm naphthalene.

Industrial releases of naphthalene into the environment of more than 100 pounds must be reported to EPA.

There are no regulations or advisories for 1-methylnaphthalene or 2-methylnaphthalene.

See Chapter 8 for more information on government regulations for naphthalene.

1.10 WHERE CAN I GET MORE INFORMATION?

If you have any more questions or concerns, please contact your community or state health or environmental quality department, or contact ATSDR at the address and phone number below.

ATSDR can also tell you the location of occupational and environmental health clinics. These clinics specialize in recognizing, evaluating, and treating illnesses that result from exposure to hazardous substances.

Toxicological profiles are also available on-line at www.atsdr.cdc.gov and on CD-ROM. You may request a copy of the ATSDR ToxProfiles™ CD-ROM by calling the toll-free information and technical assistance number at 1-888-42ATSDR (1-888-422-8737), by e-mail at atsdric@cdc.gov, or by writing to:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road NE
Mailstop F-32
Atlanta, GA 30333
Fax: 1-770-488-4178

Organizations for-profit may request copies of final Toxicological Profiles from the following:

National Technical Information Service (NTIS)
5285 Port Royal Road
Springfield, VA 22161
Phone: 1-800-553-6847 or 1-703-605-6000
Web site: http://www.ntis.gov/

2. RELEVANCE TO PUBLIC HEALTH

2.1 BACKGROUND AND ENVIRONMENTAL EXPOSURES TO NAPHTHALENE, 1-METHYLNAPHTHALENE, AND 2-METHYLNAPHTHALENE IN THE UNITED STATES

Naphthalene and methylnaphthalenes occur naturally in fossil fuels such as petroleum and coal, and are produced when organic materials (e.g., fossil fuels, wood, tobacco) are burned. Naphthalene is also produced commercially from either coal tar or petroleum. In 2000, estimates of commercial production of naphthalene in Japan, Western Europe, and the United States were 179, 205, and 107 thousand tonnes. Commercially-produced naphthalene is predominately used in the production of phthalic anhydride, which is used as an intermediate for polyvinyl chloride plasticizers such as di(2-ethylhexyl) phthalate. In 1999, this use of naphthalene accounted for 73 and 60% of commercial demand for naphthalene in Japan and the United States, respectively. Other uses of naphthalene include production of naphthalene sulfonates (used in concrete additives and synthetic tanning agents), pesticides (e.g., carbaryl insecticides and moth repellents), and dye intermediates.

Naphthalene is frequently present in industrial and automobile emissions and effluents and in various media in the general environment due to its natural occurrence in coal and petroleum products and emissions, its use as an intermediate in the production of plasticizers, resins, and insecticides, and its use in a variety of consumer products such as moth repellants. In 2002, environmental releases of naphthalene reported under the EPA Toxics Release Inventory (TRI) program were about 2.07 million pounds in air emissions, 0.03 million pounds in surface water discharges, 0.23 million pounds in underground injection discharges, and 0.37 million pounds in releases to land. These figures reflect estimates that most naphthalene entering the environment is discharged to the air, with the largest releases associated with the combustion of plant material and fossil fuels and volatilization from naphthalene-containing consumer products.

Monitoring studies of outdoor ambient air levels of naphthalene have reported concentrations in the range of about 0.4–170 $\mu g/m^3$, with a median naphthalene concentration of 0.94 $\mu g/m^3$ (0.0002 ppm) reported for urban/suburban air samples collected from 11 U.S. cities. The highest outdoor air concentrations have been found in the immediate vicinity of certain industrial sources and hazardous waste sites. For example, average concentrations of naphthalene in ambient air at five hazardous waste sites and one landfill in New Jersey ranged from 0.42 to 4.6 $\mu g/m^3$ (0.00008–0.0009 ppm). In indoor air, emissions

from cooking, tobacco smoking, or moth repellants are expected to be the predominant sources of naphthalene. Indoor air concentrations of naphthalene in homes with smoking residents and homes without smoking residents were reported to be 2.2 μg/m^3 (0.0004 ppm) and 1.0 μg/m^3 (0.0002 ppm), respectively. A study of indoor and outdoor air in 24 low-income homes in North Carolina found naphthalene levels ranging from 0.33–9.7 μg/m^3 and 0.57–1.82 μg/m^3 respectively. Methylnaphthalenes have also been detected in ambient outdoor and indoor air. For example, average concentrations of 1-methylnaphthalene and 2-methylnaphthalene in ambient outdoor air samples were reported to be 0.51 and 0.065 μg/m^3, respectively, whereas 2-methylnaphthalene in indoor air samples showed an average concentration of 1.5 μg/m^3 (0.0003 ppm). Based on a median concentration of 0.95 μg/m^3 (0.0002 ppm) naphthalene in urban and suburban air samples and an inhalation rate of 20 m^3/day, the average daily intake of naphthalene from ambient air is estimated at 19 μg/day, or 0.3 μg/kg/day assuming 70-kg body weight.

Levels of naphthalene (and methylnaphthalenes), when detected in water, sediments, and soil tend to be low: usually <10 μg/L in surface water or groundwater, <500 μg/kg in sediments, and 0–3 μg/kg in untreated agricultural soils. However, in the immediate vicinity of point sources of release, such as chemical waste sites, concentrations can be higher. For example, concentrations of 6.1 and 2.9 mg/kg were reported for naphthalene and methylnaphthalene, respectively, in soil samples contaminated with coal tar.

2.2 SUMMARY OF HEALTH EFFECTS

Reports that establish associations between naphthalene exposure and health effects in humans are restricted to numerous reports of hemolytic anemia or cataracts following acute exposure or occupational exposure to naphthalene, either by ingestion or by inhalation of naphthalene vapors, but these reports have not identified exposure levels associated with these effects. A relationship appears to exist between an inherited deficiency in the enzyme, glucose 6-phosphate dehydrogenase (G6PD), and susceptibility to naphthalene-induced hemolysis. Newborn infants also appear to be susceptible to naphthalene-induced hemolysis presumably due to a decreased ability to conjugate and excrete naphthalene metabolites. The only studies of cancer in humans exposed to naphthalene are two case series reports of cancer; one report of four laryngeal cancer cases (all of whom were smokers) among workers in a naphthalene purification plant in East Germany, and another report of 23 cases of colorectal carcinoma admitted to a hospital in Nigeria. NTP, EPA, and IARC concur that these studies provide inadequate evidence of naphthalene

carcinogenicity in humans. No cohort mortality or morbidity studies or case-control studies examining possible associations between naphthalene exposure and increased risk of cancer (or other health effects) are available.

Epidemiology studies, case reports, or controlled-exposure studies examining the potential health effects of human exposure to 1-methylnaphthalene or 2-methylnaphthalene by any route of exposure are not available.

Results from animal studies exposed to naphthalene by oral administration, by inhalation exposure, or by parenteral administration identify several health effects of potential concern for humans, including maternal toxicity during pregnancy with acute oral exposure, decreased body weight (without lesions developing in any tissues or organs) with intermediate oral exposure, and increased incidence of nonneoplastic and neoplastic lesions in the nose (in rats and mice) and the lung (in mice only) with chronic inhalation exposure.

Hemolytic and Ocular Effects of Naphthalene in Animals. Rats and mice do not appear to be susceptible to the hemolytic effects of naphthalene as hematological end points have not been affected in acute or intermediate duration oral studies or in acute 14-day inhalation studies. There is one report of hemolytic anemia in a few dogs orally exposed to naphthalene, but the data are inadequate to describe dose-response relationships that can be reliably extrapolated to human exposure scenarios. Naphthalene-induced cataracts or lens opacities are well studied in rats and rabbits and appear to occur at acute- or intermediate-duration oral exposure levels >500 mg/kg/day. Naphthalene-induced cataracts were not found with intermediate-duration (i.e., 13 weeks) oral exposure at lower dose levels up to 200 mg/kg/day in mice or 400 mg/kg/day in rats.

Maternal and Developmental Toxicity of Naphthalene in Animals. Acute oral exposure of pregnant rats to naphthalene doses of 150 or 450 mg/kg/day (but not 50 mg/kg/day) during gestation has produced maternal toxicity including clinical signs (lethargy and prone position) and severe decreases in body weight gain, but clear effects on the developing fetus have not been found at maternal oral doses as high as 450 mg/kg/day in rats, 300 mg/kg/day in mice, or 120 or 400 mg/kg/day in rabbits. Reduced numbers of mouse pups per litter were observed when naphthalene (300 mg/kg/day) in corn oil was orally administered to pregnant mice; however, no fetotoxic effects were seen when pregnant rabbits were orally administered naphthalene at even higher doses (400 mg/kg/day) but delivered in methylcellulose rather than in an oil vehicle. It is unclear if these differences are due to species differences in sensitivity or to

the vehicle used to deliver naphthalene. The finding of maternal toxicity in orally exposed pregnant rats serves as the basis of the acute oral MRL for naphthalene (see Section 2.3). Dermal or inhalation developmental toxicity studies in animals are not available.

Body Weight Effects of Naphthalene in Animals. Comprehensive intermediate-duration (13 weeks) oral toxicity studies found no evidence for naphthalene-induced lesions in any tissue or organs in male or female Fischer 344 rats exposed to doses as high as 400 mg/kg/day or in male or female B6C3F1 mice exposed to doses as high as 200 mg/kg/day. The only biologically significant effects found in these studies were decreases in rat terminal body weights compared with controls at dose levels of 200 mg/kg/day (12% decrease in male rats) and 400 mg/kg/day (28 and 23% decreases in male and female rats, respectively). No effect on food consumption was observed in exposed rats. Exposed male mice had higher body weights than controls, and exposed female mice had lower body weights than controls, but mean body weights were not decreased by more than 5%. In another intermediate-duration oral study with CD-1 mice that focused on a battery of immunologic tests (but did not include comprehensive histopathologic examination of tissues), no biologically significant effects were found except for decreases in weights of several organs (brain, liver, and spleen) in mice exposed to 133 mg/kg/day, but not to 53 or 5.3 mg/kg/day. The lack of naphthalene-induced lesions in these organs in the NTP studies suggests that the brain, liver, and spleen are not sensitive targets of naphthalene following intermediate oral exposure. Body weight changes in rats were the most sensitive, biologically relevant effects observed in the available toxicity studies in animals orally exposed for intermediate durations. These effects were considered in deriving the intermediate-duration oral MRL for naphthalene (see Section 2.3). Chronic-duration oral toxicity studies with naphthalene in animals are not available.

Cancer and Respiratory Effects of Naphthalene in Animals. Chronic inhalation studies found increased incidences of nonneoplastic and neoplastic lesions in the nose of rats, nonneoplastic lesions in the nose of mice, and neoplastic and nonneoplastic lesions in the lungs of mice. In mice of both sexes, chronic inhalation of 10 or 30 ppm naphthalene induced inflammation of the nose and lung, metaplasia of the olfactory epithelium, and hyperplasia of the nasal respiratory epithelium. In female mice (but not male mice), exposure to 30 ppm (but not 10 ppm) increased the incidence of benign lung tumors (alveolar/bronchiolar adenomas) compared with controls. One other female mouse exposed to 30 ppm showed a malignant lung tumor (alveolar/bronchiolar carcinoma). In rats of both sexes, inhalation of 10, 30, or 60 ppm naphthalene induced nonneoplastic and neoplastic lesions only in the nasal cavity. Nonneoplastic nasal lesions included (1) hyperplasia, atrophy, chronic inflammation, and hyaline degeneration of the olfactory epithelium and (2) hyperplasia, metaplasia or degeneration of the respiratory epithelium or

glands. Neoplastic lesions associated with naphthalene exposure in rats were olfactory epithelial neuroblastoma (a rare malignant tumor) and respiratory epithelial adenoma. The chronic inhalation MRL for naphthalene is based on the LOAEL of 10 ppm for nonneoplastic lesions in the olfactory epithelium and respiratory epithelium of the nose of rats (see Section 2.3).

The mechanisms by which naphthalene causes nonneoplastic or neoplastic lesions in the respiratory tract of rodents are incompletely understood, but are thought to involve reactive metabolites of naphthalene, including 1,2-naphthalene oxide, 1,2-naphthoquinone, 1,4-naphthoquinone, and possibly 1,2-dihydroxy-3,4-epoxy-1,2,3,4-tetrahydronaphthalene(see Sections 3.4.3. and 3.5).

Comparison of species susceptibility to naphthalene-induced nonneoplastic lung damage suggests that mice are much more sensitive than rats (e.g., nonneoplastic or neoplastic lung lesions were not found in chronically exposed rats in the NTP study) and that differences in rates and stereoselectivity of naphthalene metabolism to epoxide intermediates may be involved in this species difference. Acute (4-hour) inhalation exposure of mice to naphthalene concentrations as low as 2–10 ppm induced lung injury, whereas rats exposed to naphthalene concentrations as high as 110 ppm showed no signs of lung injury. Some evidence has been reported that rates and stereoselectivity of naphthalene metabolism in primate lung tissue may be more like rats than mice. In *in vitro* studies with microsomes from lymphoblastoid cells, which expressed recombinant human CYP2F1, metabolism of naphthalene to epoxide intermediates was demonstrated, but the predominant enantiomeric form produced (1*S*,2*R*-oxide) was different from the form (1*R*,2*S*-oxide) produced by mouse CYP2F2. Although these observations on epoxide formation may suggest that mice may be more sensitive than humans to acute naphthalene lung toxicity from epoxide intermediates, the possible role of other potentially reactive metabolites of naphthalene (e.g., the naphthoquinone metabolites) is unknown with chronic exposure scenarios. To date, mechanistic understanding of species differences in naphthalene bioactivation in the lung is too incomplete to definitively rule out the possible human relevance of naphthalene-induced lung lesions in mice (see Section 3.5).

In contrast, the olfactory epithelium and respiratory epithelium of the nose of rats and mice do not appear to differ in sensitivity to naphthalene nonneoplastic toxicity from chronic inhalation exposure. Nonneoplastic nasal lesions were found in nearly all exposed animals of both species at the lowest exposure level, 10 ppm, in both chronic studies. CYP monooxygenases, which might be involved in naphthalene metabolism and bioactivation, have been demonstrated to exist in nasal respiratory epithelial and olfactory epithelial tissue from rodents and humans. Studies designed to specifically characterize

metabolism of naphthalene in nasal tissue, however, have not been conducted, with the exception of a single study, which examined *in vitro* rates of metabolism of naphthalene to naphthalene oxides in postmitochondrial supernatants from mouse, rat, and hamster olfactory tissue. Metabolic rates (units of nmol/min/mg protein) showed the following order: mouse (87.1) > rat (43.5) > hamster (3.9). This order did not correspond with species differences in sensitivity to single intraperitoneal injections of naphthalene in a companion study. The lowest dose levels producing substantial necrosis and exfoliation in olfactory epithelium were 200 mg/kg in rats and 400 mg/kg in mice and hamsters. To date, mechanistic understanding of species differences in naphthalene bioactivation in the respiratory tissues is too incomplete to definitively rule out the possible human relevance of naphthalene-induced nasal lesions in rodents (nonneoplastic lesions in rats and mice and neoplastic lesions in rats; see Section 3.5).

It is unknown whether the naphthalene-induced neoplastic lesions found in mice (lung adenomas) and rats (nose respiratory epithelial adenomas and olfactory epithelial neuroblastomas) are produced via a genotoxic mode of action or a nongenotoxic mode requiring tissue damage and regenerative responses as precursor events. Results from genotoxicity tests for naphthalene have been predominately (but not completely) negative (see Section 3.3), and the general sites of neoplastic lesions, the nose in rats and the lungs in mice, show some correspondence (but not complete) with the general sites of nonneoplastic lesions. However, mechanistic understanding of naphthalene's carcinogenic mode of action is too incomplete to rule out the possibility of a genotoxic mode of action. Key issues that remain unexplained or unstudied include:

(1) the possible significance of the few positive genotoxicity results that have been obtained, including: reverse mutations in *Salmonella typhimurium* by 1,2-naphthoquinone; *in vitro* formation of N-7 guanine adducts of DNA by 1,2-naphtoquinone; reverse mutations for luminescence in the marine bacteria, *Vibrio fischeri*, by naphthalene; induction of sister chromatid exchanges in Chinese hamster ovary cells by naphthalene and in human mononuclear leukocytes by 1,2- or 1,4-naphthoquinone; induction of chromosomal aberrations in Chinese hamster ovaries and preimplantation mouse embryos by naphthalene; induction of somatic mutations and recombination in *Drosophila melanogaster* by naphthalene; and weak (about 2-fold) induction of micronuclei in red blood cells from *Pleurodeles waltl* larvae by naphthalene.

(2) the lack of a mechanistic explanation of why nearly all rats and mice develop nasal nonneoplastic lesions following chronic exposure to naphthalene at concentrations ≥10 ppm, but only some rats develop nasal tumors;

(3) the lack of a mechanistic explanation of why both male and female mice exposed to naphthalene show similar incidences of chronic lung inflammation following chronic exposure to 10 or 30 ppm, but only female mice showed statistically significant increased incidence of lung tumors;

(4) the lack of *in vivo* genotoxicity assays involving target tissues of naphthalene carcinogenicity (nose and lung); and

(5) the lack of information on the possible threshold exposure levels for nonneoplastic nasal lesions in rats and mice at air concentrations <10 ppm.

The National Toxicology Program *11th Report on Carcinogens* includes naphthalene in its list of chemicals *reasonably anticipated to be human carcinogen.*

International Agency for Research on Cancer concluded that naphthalene is *possibly carcinogenic to humans* (Group 2B) based on specific evaluations that there is inadequate evidence in humans and sufficient evidence in animals for the carcinogenicity of naphthalene. IARC considered the findings for nasal tumors in male and female rats and lung tumors in female mice in the NTP bioassays as sufficient evidence, noting that both nasal tumor types (olfactory epithelial neuroblastomas and respiratory epithelial adenomas) are rare in untreated rats.

EPA last assessed the carcinogenicity of naphthalene before the availability of the results from the chronic rat bioassay. In the EPA (1998c) *Toxicological Review on Naphthalene,* it was concluded that there was inadequate evidence in humans and limited evidence in animals of naphthalene carcinogenicity (increased incidence of lung tumors in female mice). Under the EPA 1986e cancer guidelines, naphthalene was assigned to Group C—*possible human carcinogen.* Under the EPA 1996a proposed cancer guidelines, it was judged that the human carcinogenic potential of naphthalene via the oral or inhalation routes "cannot be determined", but it was noted that there was suggestive evidence of potential human carcinogenicity based on increased lung tumors in female mice. Currently, the EPA Integrated Risk Information System (IRIS) Office is reassessing the inhalation carcinogenicity of naphthalene.

Cancer and Respiratory Effects of 1- and 2-Methylaphthalene in Animals. Increased incidences of pulmonary alveolar proteinosis have been observed in mice of both sexes exposed to 1-methyl-

naphthalene in the diet for 81 weeks at approximate dose levels of 72–75 and 140–144 mg/kg/day and 2-methylnaphthalene in the diet at doses of 50–54 and 108–114 mg/kg/day. Histologic examination of major tissues and organs in these studies showed no other exposure-related nonneoplastic or neoplastic lesions at other sites (including the bronchiolar regions of the lung). Mice dermally exposed to 30 or 119 mg/kg of methylnaphthalene (a mixture of 1- and 2-methylnaphthalene) for 30–61 weeks also showed increased incidence of pulmonary alveolar proteinosis. The chronic studies with mice exposed to 1- or 2-methylnaphthalene in the diet provide the basis for the chronic oral minimal risk levels (MRLs) for these substances (see Section 2.3).

Pulmonary alveolar proteinosis is characterized by an accumulation in the alveolar lumen of foamy cells, cholesterol crystals, and proteinaceous materials rich in lipids. The condition is rare in humans and has not been associated with human exposure to 2-methylnaphthalene or 1-methylnaphthalene. Human subjects with this condition can display pulmonary function deficits. The absence of pulmonary alveolar proteinosis in a 13-week range-finding study that exposed B6C3F1 mice to dietary doses as high as 2,500 mg/kg/day suggests that the development of this lesion requires chronic-duration exposure.

The mechanisms by which 1- or 2-methylnaphthalene may cause pulmonary alveolar proteinosis are poorly understood, but light and electron microscopic observations of lung tissues from mice repeatedly exposed to dermal doses of methylnaphthalene indicate that type II pneumocytes are a specific cellular target. It has been hypothesized that, in response to 1- or 2-methylnaphthalene, type II pneumocytes produce increased amounts of lamellar bodies due to hyperplasia and hypertrophy, and eventually transform into balloon cells. The rupture of balloon cells is hypothesized to lead to the accumulation of proteinaceous materials rich in lipids in the alveolar lumen. It is unknown whether the methyl-naphthalenes themselves or their metabolites are responsible for the development of pulmonary alveolar proteinosis.

The chronic dietary studies with 1- or 2-methylnaphthalene provide limited evidence for the carcinogenicity of these chemicals. In the 1-methylnaphthalene study, respective incidences of mice with lung adenomas or carcinomas were 5/50, 2/50, and 5/50 for control through high-dose females, and 2/49, 13/50, and 15/50 for males. With 2-methylnaphthalene, incidences for lung adenomas or carcinomas were 5/50, 4/49, and 6/48 for females and 2/49, 10/49, and 6/49 for males. The tumorigenic response was predominantly benign and was only consistently seen in male mice exposed to 1-methylnaphthalene. The available data on the methylnaphthalenes appear inadequate to determine their carcinogenicity potential in

humans, given the lack of any human studies on the potential carcinogenicity of the methylnaphthalenes and the limited evidence of carcinogenicity in animals.

The NTP *11th Report on Carcinogens* does not include 1-methylnaphthalene or 2-methylnaphthalene on its list of chemicals *known to be human carcinogens* or *reasonably anticipated to be human carcinogens.* IARC has not assessed the carcinogenicity potential of the methylnaphthalenes. The EPA concluded that the available data for 2-methylnaphthalene are *inadequate to assess human carcinogenic potential*, noting that there are no human data and the available evidence of 2-methylnaphthalene in animals is limited and insufficient to determine that 2-methylnaphthalene is carcinogenic to humans.

2.3 MINIMAL RISK LEVELS (MRLs)

Estimates of exposure levels posing minimal risk to humans (MRLs) have been made for naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene. An MRL is defined as an estimate of daily human exposure to a substance that is likely to be without an appreciable risk of adverse effects (noncarcinogenic) over a specified duration of exposure. MRLs are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive health effect(s) for a specific duration within a given route of exposure. MRLs are based on noncancerous health effects only and do not consider carcinogenic effects. MRLs can be derived for acute, intermediate, and chronic duration exposures for inhalation and oral routes. Appropriate methodology does not exist to develop MRLs for dermal exposure.

Although methods have been established to derive these levels (Barnes and Dourson 1988; EPA 1990), uncertainties are associated with these techniques. Furthermore, ATSDR acknowledges additional uncertainties inherent in the application of the procedures to derive less than lifetime MRLs. As an example, acute inhalation MRLs may not be protective for health effects that are delayed in development or are acquired following repeated acute insults, such as hypersensitivity reactions, asthma, or chronic bronchitis. As these kinds of health effects data become available and methods to assess levels of significant human exposure improve, these MRLs will be revised.

Inhalation MRLs

- An MRL of 0.0007 ppm was derived for chronic inhalation exposure to naphthalene.

The MRL was derived from two chronic inhalation toxicity and carcinogenicity studies with mice (NTP 1992a) and rats (Abdo et al. 2001; NTP 2000). In one study, groups of 75 B6C3F1 mice of each sex were exposed by inhalation at concentrations of 0, 10, or 30 ppm, 6 hours/day, 5 days/week for 104 weeks. In the other study, groups of 49 male and 49 female F344/N rats were exposed to naphthalene at concentrations of 0, 10, 30, or 60 ppm, 6 hours/day, 5 days/week for 105 weeks. The lowest exposure level in both studies, 10 ppm, was a lowest-observed-adverse-effect level (LOAEL) in both sexes of both species for nonneoplastic lesions in nasal olfactory epithelium (metaplasia in mice, and hyperplasia, atrophy, and chronic inflammation in rats) and respiratory epithelium (hyperplasia in mice, and hyperplasia, metaplasia, hyaline degeneration, or gland hyperplasia in rats). At 10 ppm, nearly all of the animals showed nasal lesions. Exposed rats also showed increased incidences of nasal tumors (respiratory epithelial adenomas and olfactory epithelial neuroblastomas), but mice did not develop nose tumors. Exposed mice also showed an increased incidence of chronic lung inflammation at both exposure levels and an increased incidence of lung tumors in females exposed to 30 ppm. Lung lesions did not occur in exposed rats.

Following EPA (1994b) *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry,* equations for a category 1 gas producing nasal effects were used to derive human equivalent concentrations of 0.2 ppm based on the rat data and 0.3 ppm based on the mouse data (see Appendix B). Using public health protection reasoning, the $LOAEL_{HEC}$ based on the rat data, 0.2 ppm, was selected as the point of departure for the chronic inhalation MRL, which was divided by a total uncertainty factor of 300 (10 for the use of a LOAEL, 3 for extrapolation from animals to humans using dosimetric adjustment, and 10 for human variability) to derive the MRL of 0.0007 ppm ($3x10^{-3}$ mg/m^3).

No appropriate data were located on effects of acute- and intermediate-duration inhalation exposure in humans or animals that could be used to derive acute and intermediate MRLs for inhalation exposure to naphthalene.

No appropriate data were located for deriving inhalation MRLs for 1-methylnaphthalene or 2-methylnaphthalene.

Oral MRLs

- An MRL of 0.6 mg/kg/day was derived for acute oral exposure to naphthalene.

A rat developmental toxicity study involving exposure of Sprague-Dawley rats to gavage doses of 50, 150, or 450 mg/kg/day naphthalene on gestation days 6-15 was selected as the basis of the acute oral MRL (NTP 1991a). The only maternal or fetal effects observed at the lowest dose level were slow respiration, lethargy, or prone body posture in most dams following dose administration on the first and second day of dosing. These effects did not occur on subsequent days of dosing at this dose level. Because of the transient nature of these observations and the lack of any other effect, 50 mg/kg/day was judged to be a minimal lowest-observed-adverse-effect level (LOAEL) for clinical signs of toxicity. At 150 and 450 mg/kg/day, clinical signs of toxicity were more persistent and were accompanied with severe decreases in body weight gain during the exposure period (31 and 53%, respectively, compared with controls). No exposure-related fetal effects were found in any of the exposure groups compared with the controls in this study.

The MRL was calculated from the minimal LOAEL of 50 mg/kg/day using an uncertainty factor of 90 (3 for the use of a minimal LOAEL, 10 for extrapolation from animals to humans, and 3 for human variability) to derive the MRL of 0.6 mg/kg/day (see Appendix A). An uncertainty factor of 3 was used for human variability because the critical effect is based on effects in a sensitive animal subpopulation. Pregnant rats appear to be more sensitive for the effects observed (clinical signs of toxicity in response to gavage exposure and decreased body weight gain) than nonpregnant rats. In 13-week gavage studies with nonpregnant rats (NTP 1980b), similar persistent clinical signs were not observed following administration of doses as high as 200 mg/kg/day, but were observed at 400 mg/kg/day. In nonpregnant rats exposed for 13 weeks, significant body weight decreases occurred at 200 mg/kg/day throughout exposure, but not at 100 mg/kg/day (NTP 1980b) or in nonpregnant mice exposed for 13 weeks to 133 mg/kg/day (Shopp et al. 1984) or 200 mg/kg/day (NTP 1980a). Mice in the NTP (1980a) study showed transient signs of toxicity (lethargy, rough hair coats, and decreased food consumption), but these only occurred between weeks 3 and 5 in the 200-mg/kg/day group.

- The acute-duration oral MRL of 0.6 mg/kg/day is adopted as the intermediate-duration oral MRL for naphthalene.

There are three intermediate-duration oral toxicity studies in laboratory animals that were considered for deriving the intermediate-duration oral MRL for naphthalene. A 13-week comprehensive oral toxicity study in Fischer 344 rats found no adverse exposure-related effects other than decreased body weight (NTP 1980b). This study identified 100 mg/kg/day as a no-observed-adverse-effect level (NOAEL) and 200 mg/kg/day as a LOAEL for decreased body weight in male and female rats. Another 13-week

comprehensive oral toxicity study in B6C3F1 mice found no adverse effects in mice exposed to doses as high as 200 mg/kg/day (NTP 1980a). Another 90-day gavage study in CD-1 mice focused on immune system variables and other toxicity variables (e.g., body weight, organ weight, haematological parameters) and identified 133 mg/kg/day as a LOAEL and 53 mg/kg/day as a NOAEL for weight decreases in several organs (brain, liver, and spleen), but found no biologically significant exposure-related changes in other end points evaluated (Shopp et al. 1984). This study, however, did not include histopathological examination of tissues.

The findings from the three intermediate-duration oral toxicity studies do not collectively identify a clear, biologically significant target of toxicity other than body weight changes in rats (see Appendix A for comprehensive descriptions of the design and results of these studies). Consideration was given to basing the MRL on the NOAEL of 53 mg/kg/day and LOAEL of 133 mg/kg/day for decreases in absolute weight of brain, liver, and spleen, and in relative weight of spleen, in female mice (Shopp et al. 1984). However, the biological significance of these effects is uncertain because (1) the effects were only observed in females, and (2) histological effects in the affected organs were not observed in the other 13-week oral studies with rats and mice.

As discussed in Appendix A, a potential intermediate-duration MRL of 0.7 mg/kg/day was derived based on the duration-adjusted NOAEL of 71 mg/kg/day for decreased body weight in male and female rats exposed by gavage to naphthalene 5 days/week for 13 weeks (NTP 1980b) and a total uncertainty factor of 100 (10 for extrapolating from rats to humans and 10 for human variability). Because the value of 0.7 mg/kg/day is slightly larger than the acute-duration oral MRL of 0.6 mg/kg/day, the acute MRL is expected to be protective for intermediate-duration exposure scenarios and was adopted as the intermediate-duration oral MRL.

No appropriate studies were located for deriving an MRL for chronic oral exposure to naphthalene. One chronic study was located that examined the toxicity of naphthalene in rats (Schmahl 1955). No treatment-related effects were reported at a dose level of 41 mg/kg/day for 700 days. The study was not suitable as the basis for deriving a chronic MRL because only one dose level was evaluated, histopathological examination was limited, and dosing was not precisely controlled.

- An MRL of 0.07 mg/kg/day was derived for chronic oral exposure to 1-methylnaphthalene.

The MRL for 1-methylnaphthalene was derived from an 81-week study in groups of 50 male and 50 female mice using diets containing 0, 71.6 (males), 75.1 (females), 140.2 (males), or 143.7 (females) mg/kg/day (Murata et al. 1993). Food intake, clinical signs, and body weight were determined throughout the study. At the end of 81 weeks, peripheral blood samples were collected and the animals were sacrificed. Organ weights were determined and the tissues examined histologically; tumors were identified and characterized. Hematological parameters and biochemical indices were evaluated in the blood samples.

Male and female mice in both exposure groups showed increased incidences of pulmonary alveolar proteinosis. In males, there was also a significant increase in pulmonary adenomas. The alveolar nodules were filled with an amorphous acidophilic material, cholesterol crystals, and foamy cells. They were not accompanied by inflammation, edema, or fibrosis. The LOAEL of 71.6 mg/kg/day for pulmonary alveolar proteinosis in female mice was used for the derivation of the MRL (see Appendix A), employing an uncertainty factor of 1,000 (10 for using a LOAEL, 10 for extrapolating from animals to humans, and 10 for human variability).

- An MRL of 0.04 mg/kg/day was derived for chronic oral exposure to 2-methylnaphthalene.

The chronic MRL is based on a study in which groups of 50 male and 50 female B6C3F1 mice were exposed to dietary levels of 0, 0.075, or 0.15% 2-methylnaphthalene (Murata et al. 1997). Average intakes were reported as 0, 54.3, or 113.8 mg/kg/day for males and 0, 50.3, or 107.6 mg/kg/day for females. Survival and food consumption were not affected by exposure. Mean final body weights were decreased by 7.5 and 4.5% in high-dose males and females, respectively; these changes are not considered to be biologically significant. Histopathology only found exposure-related changes in the lung. Tissues examined were brain, heart, kidney, liver, lung, pancreas, salivary glands, spleen, testis, adrenals, bone, eye, Harderian glands, mammary gland, ovary, seminal vesicle, skeletal muscle, skin, small and large intestine, spinal cord, stomach, trachea, uterus, and vagina. No evidence of bronchiolar Clara cell necrosis or sloughing was found. Females showed statistically significantly decreased differential counts of stab and segmented form neutrophils and increased lymphocytes compared to controls, but the biological significance of these changes is not clear due to a lack of reporting of the data (i.e., the report did not specify the response magnitudes or the dose levels at which they occurred). Incidences for mice with pulmonary alveolar proteinosis were (control through high-dose groups): 5/50, 27/49, and 22/49 for females, and 4/49, 21/49, and 23/49 for males. Incidences for mice with lung adenomas were: 4/50, 4/49, and 5/48 in females, and 2/49, 9/49, and 5/49 in males. Only the lung adenoma incidence in the male

54.3-mg/kg/day groups was significantly different from the control incidence. Combined incidences for lung adenomas or adenocarcinomas were: 5/50, 4/49, and 6/48 for females, and 2/49, 10/49, and 6/49 for males.

Support for pulmonary alveolar proteinosis as the critical effect for the chronic oral MRL for 2-methylnaphthalene comes from chronic duration studies with the isomer, 1-methylnaphthalene, and methylnaphthalene (a mixture of 1- and 2-methylnaphthalene). Increased incidence of pulmonary alveolar proteinosis was reported in B6C3F1 mice exposed to 1-methylnaphthalene in the diet for 81 weeks at dose levels as low as 71.6 mg/kg/day (Murata et al. 1993), and in mice dermally exposed to 30 or 119 mg/kg of methylnaphthalene for 30–61 weeks (a mixture of 1- and 2-methylnaphthalene) (Emi and Konishi 1985; Murata et al. 1992).

The lower 95% confidence limit on a benchmark dose associated with 5% extra risk for pulmonary alveolar proteinosis in male mice (4 mg/kg/day) was selected as the point of departure for deriving the chronic-duration oral MRL for 2-methylnaphthalene (see Appendix A). A benchmark response of 5% extra risk was selected over a default value of 10% extra risk in order to provide protection for children who may develop pulmonary alveolar proteinosis. This selection is supported by reports that children with pulmonary alveolar proteinosis (albeit of unknown etiology) experience more severe symptoms of respiratory dysfunction than do adults (EPA 2003r; Mazzone et al. 2001). The point of departure was divided by an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability) to derive the chronic oral MRL of 0.04 mg/kg/day for 2-methylnaphthalene.

No appropriate studies were located for deriving acute or intermediate-duration oral MRLs for 1-methylnaphthalene or 2-methylnaphthalene.

3. HEALTH EFFECTS

3.1 INTRODUCTION

The primary purpose of this chapter is to provide public health officials, physicians, toxicologists, and other interested individuals and groups with an overall perspective on the toxicology of naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene. It contains descriptions and evaluations of toxicological studies and epidemiological investigations and provides conclusions, where possible, on the relevance of toxicity and toxicokinetic data to public health.

A glossary and list of acronyms, abbreviations, and symbols can be found at the end of this profile.

3.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

To help public health professionals and others address the needs of persons living or working near hazardous waste sites, the information in this section is organized first by route of exposure (inhalation, oral, and dermal) and then by health effect (death, systemic, immunological, neurological, reproductive, developmental, genotoxic, and carcinogenic effects). These data are discussed in terms of three exposure periods: acute (14 days or less), intermediate (15–364 days), and chronic (365 days or more).

Levels of significant exposure for each route and duration are presented in tables and illustrated in figures. The points in the figures showing no-observed-adverse-effect levels (NOAELs) or lowest-observed-adverse-effect levels (LOAELs) reflect the actual doses (levels of exposure) used in the studies. LOAELs have been classified into "less serious" or "serious" effects. "Serious" effects are those that evoke failure in a biological system and can lead to morbidity or mortality (e.g., acute respiratory distress or death). "Less serious" effects are those that are not expected to cause significant dysfunction or death, or those whose significance to the organism is not entirely clear. ATSDR acknowledges that a considerable amount of judgment may be required in establishing whether an end point should be classified as a NOAEL, "less serious" LOAEL, or "serious" LOAEL, and that in some cases, there will be insufficient data to decide whether the effect is indicative of significant dysfunction. However, the Agency has established guidelines and policies that are used to classify these end points. ATSDR believes that there is sufficient merit in this approach to warrant an attempt at distinguishing between

"less serious" and "serious" effects. The distinction between "less serious" effects and "serious" effects is considered to be important because it helps the users of the profiles to identify levels of exposure at which major health effects start to appear. LOAELs or NOAELs should also help in determining whether or not the effects vary with dose and/or duration, and place into perspective the possible significance of these effects to human health.

The significance of the exposure levels shown in the Levels of Significant Exposure (LSE) tables and figures may differ depending on the user's perspective. Public health officials and others concerned with appropriate actions to take at hazardous waste sites may want information on levels of exposure associated with more subtle effects in humans or animals (LOAELs) or exposure levels below which no adverse effects (NOAELs) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels or MRLs) may be of interest to health professionals and citizens alike.

Levels of exposure associated with carcinogenic effects (Cancer Effect Levels, CELs) of naphthalene, are indicated in Tables 3-1 and 3-2 and Figures 3-1 and 3-2.

A User's Guide has been provided at the end of this profile (see Appendix B). This guide should aid in the interpretation of the tables and figures for Levels of Significant Exposure and the MRLs.

3.2.1 Inhalation Exposure

3.2.1.1 Death

Two Greek infants died as a consequence of acute hemolysis that resulted from exposure to naphthalene-treated materials (clothing, diapers, blankets, rugs, etc.). Both infants exhibited a severe form of jaundice (kernicterus), which often causes brain damage (Valaes et al. 1963). Exposure levels experienced by these children are unknown. One infant suffered from a glucose-6-phosphate dehydrogenase (G6PD) deficiency. The other infant was apparently heterozygous for this trait. Individuals with a G6PD genetic defect are prone to hemolysis after exposure to a variety of chemical oxidizing agents including nitrates, nitrites, aniline, phenols (Dean et al. 1992), and naphthalene.

No studies were located that documented lethal effects in humans after inhalation exposure to 1-methylnaphthalene or 2-methylnaphthalene.

Exposure to 78 ppm naphthalene for 4 hours did not cause any deaths in rats. In addition, no definitive adverse clinical signs were observed during the 14 days after exposure, and no gross pathologic lesions were observed at necropsy (Fait and Nachreiner 1985). A high background mortality in the male control group precluded drawing conclusions regarding the effects of lifetime exposures to 10 and 30 ppm naphthalene (6 hours/day, 5 days/week) on lifetime mortality; no apparent effects on mortality occurred in the females (NTP 1992a). Similarly, exposure of male and female rats to 10, 30, or 60 ppm naphthalene (6 hours/day, 5 days/week) for 2 years did not affect survival, compared to controls (Abdo et al. 2001; NTP 2000).

No studies were located that documented lethal effects in animals after inhalation exposure to 1-methylnaphthalene or 2-methylnaphthalene.

3.2.1.2 Systemic Effects

No studies were located that documented dermal effects in humans or animals after inhalation exposure to naphthalene. Most of the human data come from occupational and domestic settings where mothballs were the source of the naphthalene vapors. The highest NOAEL values and all LOAEL values from each reliable study for systemic effects in each species and duration category are recorded in Table 3-1 and plotted in Figure 3-1. No studies were located that documented systemic effects in humans after inhalation exposure to 1-methylnaphthalene or 2-methylnaphthalene. In animals, one study evaluated hematological end points in dogs following acute inhalation exposure to undetermined air concentrations of 1-methylnaphthalene or 2-methylnaphthalene (Lorber 1972). This study, however, did not identify reliable NOAEL or LOAEL values, and the results are not included in Table 3-1 or Figure 3-1.

Respiratory Effects. No studies were located that documented respiratory effects in humans after inhalation exposure to naphthalene.

The nose is the most sensitive toxicity target in rats and mice following chronic inhalation exposure to naphthalene. Chronic inhalation exposure resulted in increased incidences of nonneoplastic and neoplastic lesions in the nose of rats (Abdo et al. 2001; Long et al. 2003; NTP 2000), nonneoplastic lesions in the nose of mice (NTP 1992a), and neoplastic and nonneoplastic lesions in the lungs of mice (NTP 1992a). No exposure-related lesions were found in other tissues or organs in these studies, which included comprehensive histopathological examinations of major tissues and organs. Nearly all mice of

Table 3-1 Levels of Significant Exposure to Naphthalene (Nap) Or Methylnaphthalene (1-Mn Or 2-Mn) - Inhalation

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (ppm)	LOAEL Less Serious (ppm)	LOAEL Serious (ppm)	Reference Chemical Form
	ACUTE EXPOSURE						
	Systemic						
1	Rat (Sprague-Dawley)	4 h	Resp	100			West et al. 2001 NAP
2	Mouse B6C3F1	14 d 5 d/wk 6 hr/d	Hemato	30			NTP 1992a NAP

Table 3-1 Levels of Significant Exposure to Naphthalene (Nap) Or Methylnaphthalene (1-Mn Or 2-Mn) - Inhalation (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (ppm)	LOAEL Less Serious (ppm)		LOAEL Serious (ppm)		Reference Chemical Form
3	Mouse (Swiss-Webster)	4 h	Resp	2	10	(Clara cell necrosis and decreased Clara cell mass [volume/surface area] in proximal airways)	75	(Proximal and terminal epithelium devoid of Clara cells)	West et al. 2001 NAP
	Neurological								
4	Rat (Wistar)	4 h		26	44	(increased latency of paw lick response to being placed on a hot surface [decreased pain sensitivity]; no change in rotarod performance)			Korsak et al. 1998 1-MN
5	Rat (Wistar)	4 h		39	61	(increased latency of paw lick response to being placed on a hot surface [decreased pain sensitivity]; no change in rotarod performance)			Korsak et al. 1998 2-MN

Table 3-1 Levels of Significant Exposure to Naphthalene (Nap) Or Methylnaphthalene (1-Mn Or 2-Mn) - Inhalation (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (ppm)	LOAEL Less Serious (ppm)	LOAEL Serious (ppm)	Reference Chemical Form
	CHRONIC EXPOSURE						
	Systemic						
6	Rat (Fischer- 344)	105 wk 5 d/wk 6 hr/d vapor	Resp		10[b] (inflammation of the nose; olfactory epithelium: atypical hyperplasia, atrophy, degeneration; nasal respiratory epithelium: hyperplasia, squamous metaplasia, degeneration; Bowman's glands: hyperplasia)		NTP 2000 (Abdo et al. 2001) NAP
			Cardio	10			
			Gastro	10			
			Musc/skel	10			
			Hepatic	10			
			Renal	10			
			Endocr	10			
			Ocular	10			
			Bd Wt	10			

Table 3-1 Levels of Significant Exposure to Naphthalene (Nap) Or Methylnaphthalene (1-Mn Or 2-Mn) - Inhalation (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (ppm)	LOAEL Less Serious (ppm)	LOAEL Serious (ppm)	Reference Chemical Form
7	Mouse B6C3F1	104 wk 5 d/wk 6 hr/d	*Resp*		10 (inflammation of the nose and lung, metaplasia of the olfactory epithelium, and hyperplasia of the respiratory epithelium)		NTP 1992a NAP

Table 3-1 Levels of Significant Exposure to Naphthalene (Nap) Or Methylnaphthalene (1-Mn Or 2-Mn) - Inhalation (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (ppm)	LOAEL Less Serious (ppm)	LOAEL Serious (ppm)	Reference Chemical Form
8	Mouse B6C3F1	104 wk 5 d/wk 6 hr/d	Cardio	30			NTP 1992a NAP
			Gastro	30			
			Hepatic	30			
			Renal	30			
			Dermal	30			
	Neurological						
9	Rat (Fischer- 344)	105 wk 5 d/wk 6 hr/d vapor		60			NTP 2000 (Abdo et al. 2001) NAP

Table 3-1 Levels of Significant Exposure to Naphthalene (Nap) Or Methylnaphthalene (1-Mn Or 2-Mn) - Inhalation (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (ppm)	LOAEL Less Serious (ppm)	LOAEL Serious (ppm)	Reference Chemical Form
10	Mouse B6C3F1	104 wk 5 d/wk 6 hr/d		30			NTP 1992a NAP
	Reproductive						
11	Rat (Fischer- 344)	105 wk 5 d/wk 6 hr/d vapor		60			NTP 2000 (Abdo et al. 2001) NAP

Table 3-1 Levels of Significant Exposure to Naphthalene (Nap) Or Methylnaphthalene (1-Mn Or 2-Mn) - Inhalation (continued)

Key to figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (ppm)	LOAEL Less Serious (ppm)	LOAEL Serious (ppm)		Reference Chemical Form
12	Mouse B6C3F1	104 wk 5d/wk 6 hr/d		30				NTP 1992a NAP
	Cancer							
13	Rat (Fischer- 344)	105 wk 5d/wk 6hr/d vapor				10	(CEL: nasal respiratory epithelial adenomas in males & in females at higher concentrations; olfactory epithelial neuroblastomas in both sexes at higher concentrations)	NTP 2000 (Abdo et al. 2001) NAP
14	Mouse B6C3F1	104 wk 5 d/wk 6 hr/d				30	(CEL: pulmonary alveolar adenomas in females)	NTP 1992a NAP

a The number corresponds to the entries in Figure 3-1.

b Used to derive a chronic-duration Minimal Risk Level (MRL) of 0.0007 ppm; based on a human equivalent concentration LOAEL of 0.2 ppm which was divided by an uncertainty factor of 300 (10 for the use of LOAEL, 3 for extrapolating from rodents to humans with interspecies dosimetric adjustment, and 10 for human variability).

Cardio = cardiovascular; d = day(s); Gastro = gastrointestinal; Hemato = hematological; hr = hour(s); LOAEL = lowest-observed-adverse-effect level; NOAEL = no-observed-adverse-effect level; Resp = respiratory; wk = week(s)

Figure 3-1. Levels of Significant Exposure to Naphthalene (NAP) Or Methylnaphthalene (1-MN Or 2-MN)- Inhalation

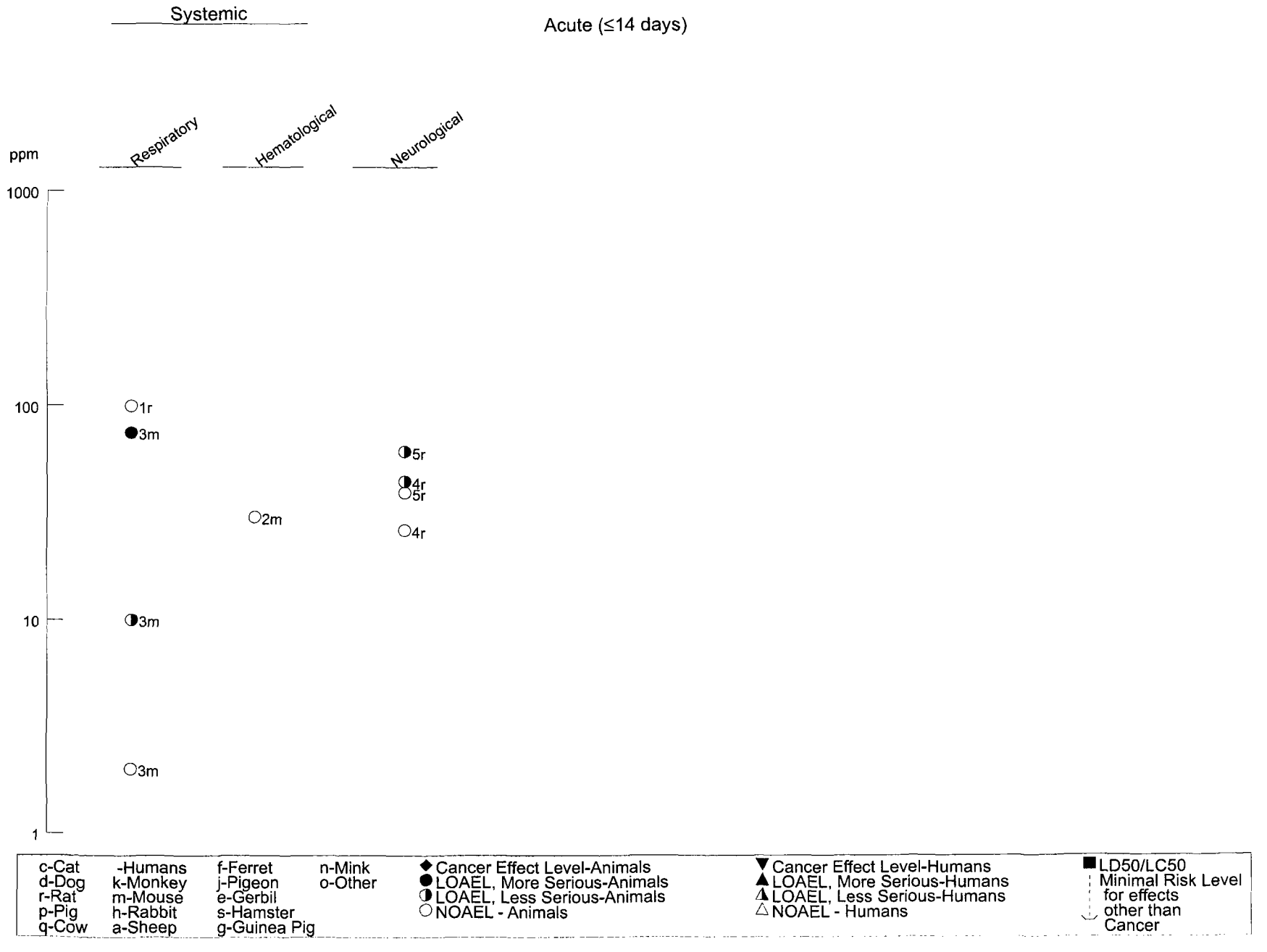
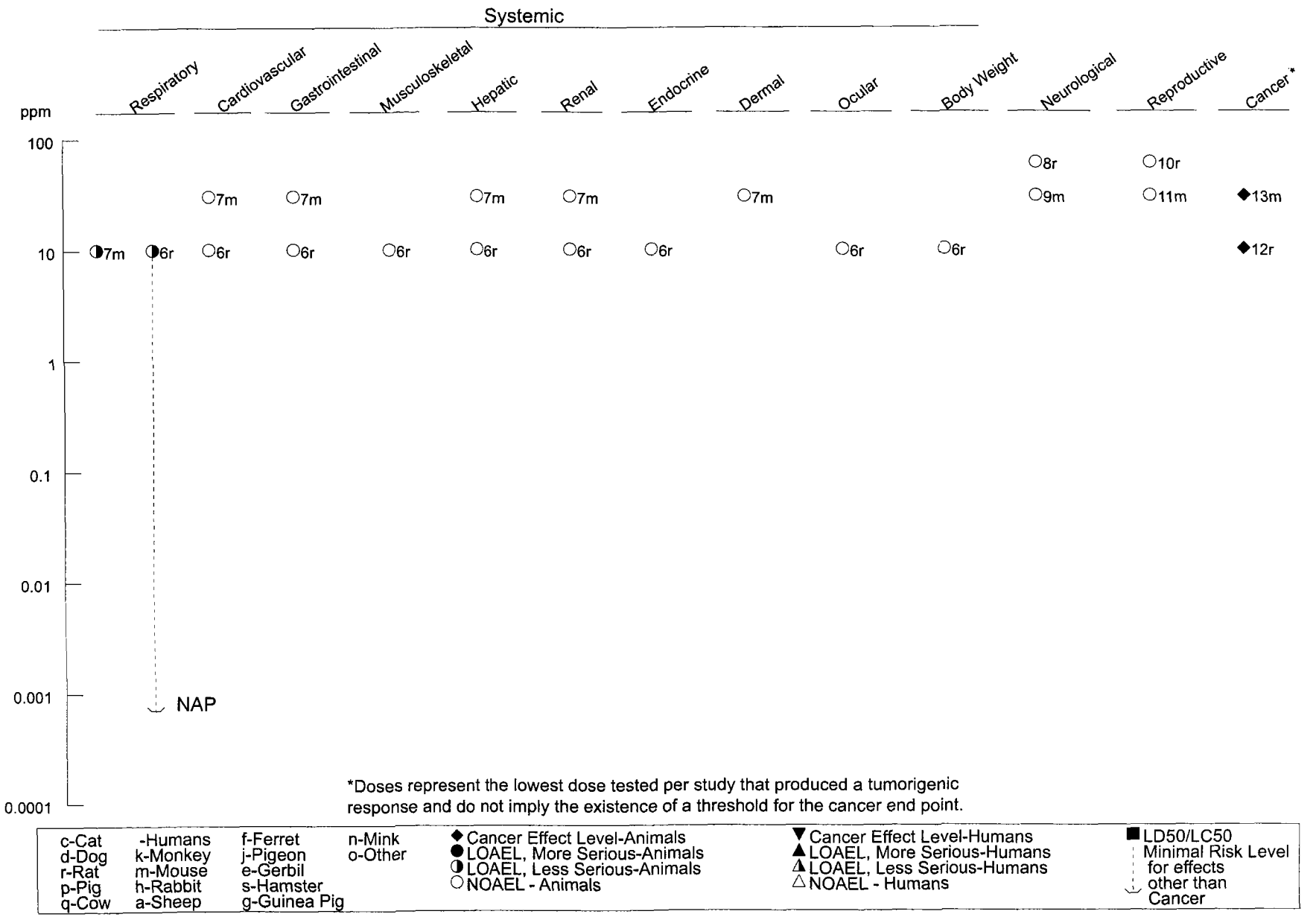


Figure 3-1. Levels of Significant Exposure to Naphthalene (NAP) Or Methylnaphthalene (1-MN Or 2-MN) - Inhalation (*Continued*)

Chronic (≥365 days)



both sexes (>95%) exposed to naphthalene vapors for 2 years (10 or 30 ppm) showed chronic inflammation and metaplasia of the olfactory epithelium and hyperplasia of the nasal respiratory epithelium (NTP 1992a). Chronic lung inflammation was also observed in exposed mice, but at lower incidences than incidences for nasal lesions. Incidences for chronic lung inflammation were 0/70, 21/69, and 56/135 for male mice and 3/69, 13/65, and 52/135 for female mice exposed to 0, 10, or 30 ppm. In addition, exposure to 30 ppm (but not 10 ppm) increased the incidence of benign lung tumors (alveolar/bronchiolar adenomas) in female mice, compared with controls. One other female mouse exposed to 30 ppm showed a malignant lung tumor (alveolar/bronchiolar carcinoma). In rats of both sexes, inhalation of 10, 30, or 60 ppm naphthalene induced nonneoplastic and neoplastic lesions only in the nasal cavity (Abdo et al. 2001; NTP 2000). Nearly all rats in each exposure group (>95%) showed nonneoplastic nasal lesions. Nonneoplastic nasal lesions in exposed rats included (1) hyperplasia, atrophy, chronic inflammation, and hyaline degeneration of the olfactory epithelium and (2) hyperplasia, metaplasia, or degeneration of the respiratory epithelium or glands. Neoplastic lesions associated with naphthalene exposure in rats were olfactory epithelial neuroblastoma (a rare malignant tumor) and respiratory epithelial adenoma.

The chronic inhalation MRL for naphthalene is based on the LOAEL of 10 ppm for nonneoplastic lesions in the olfactory epithelium and respiratory epithelium of the nose of rats (NTP 2000; see Table 3-1, Figure 3-1, Appendix A, and Section 2.3). To derive the chronic MRL, the rat LOAEL was converted to a human equivalent concentration of 0.2 ppm for continuous exposure using EPA (1994b) equations for a category 1 gas producing nasal effects and divided by an uncertainty factor of 300 (10 for the use of a LOAEL, 3 for extrapolation from animals to humans using dosimetric adjustment, and 10 for human variability). Naphthalene-induced damage to the nasal tissue is thought to be due to reactive metabolites formed in the nasal tissues (Buckpitt et al. 2002). Sections 3.4.3 and 3.5 discuss current mechanistic hypotheses in more detail.

Acute (4-hour) inhalation exposure to naphthalene induced necrosis of Clara cells in the epithelium of the proximal airways of the lungs of mice at exposure levels as low as 10 ppm, but did not affect lung tissue in rats at concentrations as high as 100 ppm (West et al. 2001). These results, and those from the chronic inhalation studies, show that mice are more susceptible than rats to lung damage from inhaled naphthalene. However, there are no studies that have examined nasal tissues for the development of lesions following acute inhalation exposure. No acute inhalation MRL was derived for naphthalene, due to the lack of such data and the results of the chronic studies indicating that nasal tissues are the critical toxicity targets of inhaled naphthalene in both rats and mice.

A change to mouth breathing occurred in rats during exposure to 78 ppm naphthalene, but no other effects on respiration were noted (Fait and Nachreiner 1985).

Cardiovascular Effects. No studies were located that documented cardiovascular effects in humans after inhalation exposure to naphthalene.

No histological changes were seen in the hearts of mice (30 ppm) or rats (60 ppm) that were exposed to naphthalene for 2 years (Abdo et al. 2001; NTP 1992a, 2000).

Gastrointestinal Effects. Nausea, vomiting, and abdominal pain were reported in eight adults and one child exposed to naphthalene vapors from large numbers of mothballs (300–500) scattered throughout their homes for odor and pest control (Linick 1983). Air samples collected in one home contained naphthalene at 20 ppb; concentrations could have been higher when the mothballs were fresh. Gastrointestinal symptoms disappeared after the mothballs were removed. Few location-specific background data to support this air concentration were reported.

There were no histopathological changes in the stomach or intestines of mice (30 ppm) or rats (60 ppm) exposed to naphthalene for 2 years (Abdo et al. 2001; NTP 1992a, 2000).

Hematological Effects. Hemolytic anemia is the most frequently reported manifestation of naphthalene exposure in humans. Acute hemolytic anemia was observed in 21 infants exposed to naphthalene via mothball-treated blankets, woolen clothes, or materials in the infants' rooms (Valaes et al. 1963). Ten of these children had a G6PD genetic defect that increased their sensitivity to hemolysis from a variety of chemicals, including naphthalene. Clinical observations included high serum bilirubin values, methemoglobin, Heinz bodies, and fragmented red blood cells. Inhalation appeared to be the primary route of exposure because in all children but two, the naphthalene-treated material was not worn next to the skin. One of the exceptions was an infant who wore diapers that had been stored in naphthalene.

Anemia was reported in nine individuals exposed to large numbers of mothballs distributed throughout their homes (Linick 1983). The nature of the anemia and specific levels of naphthalene exposure were not identified. In one home, the naphthalene concentration was determined to be 20 ppb at the time of testing, but could have been higher when the mothballs were first distributed.

In another study, a woman who was exposed to reportedly high (but unmeasured) concentrations of a combination of naphthalene and paradichlorobenzene for several weeks in a hot, poorly ventilated work area developed aplastic anemia (Harden and Baetjer 1978). It is difficult to determine the contribution of naphthalene to the aplastic anemia since there was simultaneous exposure to paradichlorobenzene.

In animals, no treatment-related effects on hematologic parameters (hematocrit, hemoglobin concentration, erythrocyte counts, mean cell volume, reticulocytes, and leucocytes) were observed among mice exposed to 10 and 30 ppm naphthalene for 14 days (NTP 1992a). Due to high mortality in the control males, hematology measurements were not continued beyond 14 days.

The effects of 1-methylnaphthalene (pure and practical grade) and 2-methylnaphthalene (pure and practical grade) on the hematocrit values, total and differential white blood cell counts, and reticulocyte counts were determined in intact and splenectomized dogs. Each compound was dispersed in the atmosphere in a refined kerosene base using a fogger. Exposures occurred on four consecutive mornings (Lorber 1972). Based on the information presented, it was not possible to determine the exposure concentration.

Pure 1-methylnaphthalene increased the reticulocyte counts in the splenectomized dogs but not the intact dogs. Reticulocyte values remained elevated for 10 days after the fogging ceased. Practical grade 1-methylnaphthalene increased leukocyte counts in intact and splenectomized dogs and neutrophil counts in intact dogs, but pure 1-methylnaphthalene had no effect on these parameters. 2-Methylnaphthalene had no effect on any of the parameters monitored (Lorber 1972).

Neither 1-methylnaphthalene nor 2-methylnaphthalene had an effect on hematocrit values, suggesting that these compounds do not cause hemolysis under the conditions of the study. Since the increased reticulocyte counts were seen only in splenectomized dogs, it is difficult to interpret whether or not this change signifies increased hematopoiesis in response to 1-methylnaphthalene exposure (Lorber 1972).

Musculoskeletal Effects. No studies were located that documented musculoskeletal effects in humans after inhalation exposure to naphthalene.

Histological examination of the femur did not reveal compound-related effects in mice (NTP 1992a) or rats (Abdo et al. 2001; NTP 2000) exposed for 2 years to naphthalene concentrations as high as 30 or 60 ppm, respectively.

Hepatic Effects. Jaundice has been reported in infants and adults after exposure to naphthalene (Linick 1983; Valaes et al. 1963). However, the jaundice is a consequence of hemolysis rather than a direct effect of naphthalene on the liver. Infant exposures lasted 1–7 days (Valaes et al. 1963); adult exposure durations were not provided (Linick 1983). Dose was not determined in either instance, although a concentration of 20 ppb was measured in the home of one affected individual (Linick 1983).

In animals, no treatment-related gross or histopathological lesions of the liver were reported in mice (NTP 1992a) or rats (Abdo et al. 2001; NTP 2000) exposed for 2 years to naphthalene concentrations as high as 30 or 60 ppm, respectively.

Renal Effects. Renal disease was reported in nine individuals (details not specified) exposed to large numbers of mothballs in their homes, but symptoms were not described and dose could not be determined (Linick 1983).

In animals, no treatment-related gross or histopathological lesions of the kidneys were observed in mice (NTP 1992a) or rats (Abdo et al. 2001; NTP 2000) exposed for 2 years to naphthalene concentrations as high as 30 or 60 ppm, respectively.

Ocular Effects. Twenty-one workers exposed to naphthalene for up to 5 years in a plant that manufactured dye intermediates were examined for eye problems (Ghetti and Mariani 1956). During the period of exposure, plant conditions were primitive, involving heating of naphthalene in open vats and considerable worker contact with the naphthalene. Eight of the 21 workers developed multiple pin-point lens opacities that had no correlation with the age of the workers. These effects were not overtly noticeable and apparently had no effect on vision. They were judged to be a consequence of naphthalene exposure on the basis of their location in the crystalline lens and the fact that occurrence did not correlate with age. Exposure involved long-term inhalation of vapors and direct contact of vapors with the eyes and skin.

Retinal bleeding and the beginnings of a cataract were identified in a worker from a naphthalene storage area who was most likely exposed to naphthalene through inhalation and dermal/ocular contact (van der Hoeve 1906). The duration of exposure prior to seeking medical attention for eye irritation and problems with vision was not identified.

In animals, no treatment-related gross or histopathological lesions of the eyes were observed in mice (NTP 1992a) or rats (Abdo et al. 2001; NTP 2000) exposed for 2 years to naphthalene concentrations as high as 30 or 60 ppm, respectively. However, during a 4-hour exposure of rats to a concentration of 78 ppm, irritation to the eyes was evidenced through lacrimation (Fait and Nachreiner 1985).

3.2.1.3 Immunological and Lymphoreticular Effects

No studies were located that examined immunological or lymphoreticular end points in humans or animals after inhalation exposure to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene.

3.2.1.4 Neurological Effects

Infants are prone to permanent neurological damage (kernicterus) as a consequence of the jaundice that results from naphthalene-induced hemolysis. Bilirubin is absorbed by vulnerable brain cells and this leads to convulsions and sometimes death. Survivors often suffer from motor disturbances and mental retardation (McMurray 1977). Kernicterus was diagnosed in 8 of 21 Greek infants that experienced hemolysis as a result of naphthalene exposure (Valaes et al. 1963). Two of the eight died. One of the infants that died had no G6PD enzyme activity and the other had intermediate activity. Two of the infants were normal with regard to the G6PD trait. Of the remaining infants, three had no G6PD activity and the fourth had intermediate activity. Brain damage seldom occurs in adults as a consequence of jaundice (McMurray 1977).

Nausea, headache, malaise, and confusion were reported in several individuals (children and adults) exposed to large numbers of mothballs in their homes (Linick 1983). Actual levels and duration of exposure were unknown, although a concentration of 20 ppb was measured in one of the affected residences.

In animals, no treatment-related gross or histopathological lesions of the brain were observed in mice (NTP 1992a) or rats (Abdo et al. 2001; NTP 2000) exposed for 2 years to naphthalene concentrations as high as 30 or 60 ppm, respectively. Clinical observations (made twice daily in these studies) revealed no gross behavioral changes except that exposed mice tended to huddle together in cage corners during exposure periods.

No studies were located that documented neurological effects in humans after inhalation exposure to 1-methylnaphthalene or 2-methylnaphthalene.

In male Wistar rats, decreased sensitivity to pain occurred after 4-hour inhalation exposures to 253 or 407 mg/m^3 1-methylnaphthalene (44 or 70 ppm), or 352 or 525 mg/m^3 2-methylnaphthalene (61 or 90 ppm), but not after exposure to 152 mg/m^3 (26 ppm) 1-methylnaphthalene or 229 mg/m^3 (39 ppm) 2-methylnaphthalene (Korsak et al. 1998). Decreased sensitivity to pain was measured as a decreased time to begin licking of the paws after being placed on a hot plate at 54.5 °C. The ability of exposed rats to balance on a rotating rod (rotarod performance), however, was not affected by any of these exposure conditions (Korsak et al. 1998). NOAEL and LOAEL values for decreased pain sensitivity from this study are included in Table 3-1 and Figure 3-1.

3.2.1.5 Reproductive Effects

No studies were located that documented reproductive effects in humans after inhalation exposure to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene.

In animals, histological examination did not reveal damage to male or female reproductive organs in mice (NTP 1992a) or rats (Abdo et al. 2001; NTP 2000) exposed for 2 years to 30 or 60 ppm, respectively.

No studies were located that documented reproductive effects in animals after inhalation exposure to 1-methylnaphthalene or 2-methylnaphthalene.

3.2.1.6 Developmental Effects

No studies were located that examined developmental end points in humans or animals after inhalation exposure to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene.

3.2.1.7 Cancer

No studies were located that documented carcinogenic effects in humans after inhalation exposure to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene.

In animals, inhalation exposure to naphthalene (6 hours/day) has been associated with: (1) increased incidences of F344/N rats of both sexes with nasal tumors following 2 years of exposure (Abdo et al. 2001; NTP 2000); (2) increased incidences of female B6C3F1 mice, but not male mice, with lung tumors following 2 years of exposure (NTP 1992a); and (3) increased number of tumors per tumor-bearing A/J strain mice following 6 months of exposure (Adkins et al. 1986).

In F344/N rats, incidences of nasal respiratory epithelial adenomas were statistically significantly elevated, compared with controls, in males exposed to 0, 10, 30, or 60 ppm naphthalene (0/49, 6/49, 8/48, or 15/48), but not in females (0/49, 0/49, 4/49, 2/49) (Abdo et al. 2001; NTP 2000). Incidences for olfactory epithelial neuroblastoma were 0/49, 0/49, 4/48, and 3/48 in male rats, and 0/49, 2/49, 4/48, and 12/49 in female rats. Both tumor types are rare in NTP control F344/N rats (NTP 2000). For example, neither tumor type was observed in 299 control male rats given NTP-2000 feed or 1,048 control male rats given NIH-07 feed. NTP (2000) concluded that there was clear evidence of carcinogenic activity of naphthalene in male and female F344/N rats based on increased incidences of respiratory epithelial adenoma and olfactory epithelial neuroblastoma of the nose. Nearly all rats in all exposure groups showed nonneoplastic nasal lesions in both olfactory and respiratory epithelia, including atypical hyperplasia in olfactory epithelium, hyaline degeneration in olfactory and respiratory epithelia, and Bowman's gland hyperplasia.

In B6C3F1 mice, statistically significant increased incidence of alveolar/bronchiolar adenomas and carcinoma was found in 30-ppm females, but not in 10-ppm females or in males (females: 5/69, 2/65, 29/135; males: 7/70, 17/69, and 31/135) (NTP 1992a). Although Fisher Exact tests indicated that incidences in both exposed male groups and the high-dose female group were significantly increased compared with control groups, logistic regression analysis, which modeled tumor incidence as a function of dose and exposure time, indicated that only the incidence in the 30-ppm female group was elevated compared with controls. The response was predominantly benign; only one female mouse in the 30-ppm group developed a carcinoma. Exposed mice of both sexes also showed increased incidences of chronic lung inflammation (males: 0/70, 21/69, 56/135; females: 3/69, 13/65, 52/135). Nonneoplastic nasal lesions were found in nearly all exposed mice, but no nasal tumors developed. On the basis of this analysis, NTP (1992a) determined that there was some evidence of naphthalene carcinogenicity in female mice, but no evidence of carcinogenicity in male mice in this study.

In a 6-month study, there was a statistically significant increase in the number of tumors per tumor-bearing mouse, but not in the number of mice with pulmonary adenomas after exposure to 10 or 30 ppm

naphthalene vapors (Adkins et al. 1986). However, the incidence of adenomas in the control group for this experiment was significantly lower than the pooled incidence observed in the control groups of eight concurrently conducted 6-month studies, and the difference in tumor incidence was not significantly greater than that of the historic controls.

No studies were located that documented carcinogenic effects in animals after inhalation exposure to 1-methylnaphthalene or 2-methylnaphthalene.

3.2.2 Oral Exposure

3.2.2.1 Death

Death has been documented in humans who intentionally ingested naphthalene. A 17-year-old male died 5 days after the ingestion of an unknown quantity of naphthalene mothballs. Death was preceded by vomiting, evidence of gastrointestinal bleeding, blood-tinged urine, and coma (Gupta et al. 1979). A 30-year-old female died following similar sequelae 5 days after reportedly swallowing 40 mothballs (25 were recovered intact from the stomach upon autopsy) (Kurz 1987). No studies were located that documented lethal effects in humans after oral exposure to 1-methylnaphthalene or 2-methylnaphthalene.

Several animal studies have been conducted to estimate lethal doses of naphthalene. Mice appear to be more sensitive than rats or rabbits. The LD_{50} values in male and female mice were 533 and 710 mg/kg, respectively (Shopp et al. 1984). An LD_{50} of 354 mg/kg was estimated in female mice treated with naphthalene once daily by gavage for 8 consecutive days (Plasterer et al. 1985). The dose response curve appeared to be very steep because no deaths occurred at 250 mg/kg/day, but all animals died with a dose of 500 mg/kg/day. At the 300 mg/kg/day dose, mortality was approximately 15%. In a different study with a 14-day dosing period, 10% of the males and 5% of the females died at a dose of 267 mg/kg/day, but none were affected by doses of 27 and 53 mg/kg/day (Shopp et al. 1984).

The oral LD_{50} values in male and female rats were 2,200 and 2,400 mg/kg, respectively, in one study (Gaines 1969), and 2,600 in a second study that did not differentiate by sex (Papciak and Mallory 1990). Male rats tolerated daily doses of 1,000 mg/kg without lethality, even after 18 days of administration (Yamauchi et al. 1986). In an increasing dose study, Germansky and Jamall (1988) treated male rats with naphthalene at doses beginning at 100 mg/kg/day and raised the dose weekly to a final level of 750 mg/kg/day over 6 weeks. Doses were then kept constant for an additional 3 weeks. The animals

tolerated 750 mg/kg/day with no mortalities. No increase in mortality was observed in rats administered naphthalene at 41 mg/kg/day in a 2-year feeding study (Schmahl 1955).

Although few data are available, rabbits appear to tolerate naphthalene in doses similar to those administered to rats. Two different rabbit strains were administered 1,000 mg/kg twice per week for 12 weeks without lethality (Rossa and Pau 1988).

Male and female mice survived oral exposure to doses of 71.6–143.7 mg/kg/day 1-methylnaphthalene for 81 weeks (Murata et al. 1993). No studies were located that documented lethal effects in animals after ingestion of 1-methylnaphthalene.

All LOAEL values for lethality in each species after acute exposure to naphthalene are recorded in Table 3-2 and plotted in Figure 3-2.

3.2.2.2 Systemic Effects

No studies were located that documented musculoskeletal or dermal effects in humans or animals after oral exposure to naphthalene; data were available for all other systems. The highest NOAEL values and all LOAEL values from each reliable study for systemic effects in each species and duration category are recorded in Table 3-2 and plotted in Figure 3-2.

No studies were located that documented systemic effects in humans after oral exposure to 1-methyl-naphthalene or 2-methylnaphthalene. In animals, data are restricted to two studies with B6C3F1 mice exposed to 1-methylnaphthalene (Murata et al. 1993) or 2-methylnaphthalene (Murata et al. 1997) in the diet for 81 weeks. The highest chronic NOAEL values and the lowest LOAEL value for systemic effects in mice are recorded in Table 3-2 and plotted in Figure 3-2.

Respiratory Effects. No reports have been located to indicate that there are direct effects of oral exposure to naphthalene on the respiratory system in humans. In situations where respiratory effects such as hypoxia or pulmonary edema were noted, the respiratory effects appear to be secondary to hemolysis and the events leading to general multiple organ failure (Gupta et al. 1979; Kurz 1987). On hospital admission, one male infant was described as experiencing labored breathing after presumably chewing a

Table 3-2 Levels of Significant Exposure to Naphthalene (nap) Or Methylnaphthalene (1-mn Or 2-mn) - Oral

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
ACUTE EXPOSURE							
Death							
1	Rat Sherman	once (GO)				2200 (LD50 - male) 2400 (LD50 - female)	Gaines 1969 NAP
2	Rat Sprague-Dawley	once (GO)				2600 LD50	Papciak and Mallory 1990 NAP
3	Mouse CD-1	8 d 1x/d (GO)				300 (5/33 died)	Plasterer et al. 1985 NAP
4	Mouse CD-1	once (GO)				710 (LD50) 533 (LD50)	Shopp et al. 1984 NAP
5	Mouse CD-1	14 d 1x/d (GO)				267 (10/96 male, 3/60 female)	Shopp et al. 1984 NAP
Systemic							
6	Human	once	Gastro		109 (adbominal pain)		Gidron and Leurer 1956 NAP
			Hemato			109 (hemolytic anemia)	
			Other			109 (106 degree F fever)	
7	Rat Sprague-Dawley	9 d Gd 6-15 (GO)	Bd Wt	50		150 (31% decrease in maternal body weight gain)	NTP 1991a NAP

Table 3-2 Levels of Significant Exposure to Naphthalene (nap) Or Methylnaphthalene (1-mn Or 2-mn) - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg)	LOAEL Less Serious (mg/kg)	LOAEL Serious (mg/kg)	Reference Chemical Form
8	Rat Sprague-Dawley	once (GO)	Resp		1000 lung lesions		Papciak and Mallory 1990 NAP
9	Rat Sprague-Dawley	once (GO)	Gastro		1000 stomach lesions		Papciak and Mallory 1990 NAP
10	Rat NS	10 d 1x/d (G)	Hepatic		1000 (39% increase in liver weight; increased lipid peroxidation, aniline hydroxylase activity)		Rao and Pandya 1981 NAP
			Renal	1000			
			Ocular	1000			
11	Mouse CD-1	14 d 1x/d (GO)	Resp	267 M 53 F	267 F (increase in lung weight)		Shopp et al. 1984 NAP
			Hemato	267			
			Hepatic	267			
			Renal	267			
			Bd Wt	53	267 (6% (female) or 13% (male) decreased final body weight)		
12	Dog NS	once (F)	Hemato			1525 (hemolysis)	Zuelzer and Apt 1949 NAP

Table 3-2 Levels of Significant Exposure to Naphthalene (nap) Or Methylnaphthalene (1-mn Or 2-mn) - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
13	Rabbit NS	5 d (F)	Hepatic	2000			Srivastava and Nath 1969 NAP
			Ocular			2000 (cataracts)	
14	Rabbit NS	10 d 1x/d (GO)	Ocular			1000 (lens opacities, decreased ascorbic acid in aqueous humor)	van Heyningen and Pirie 1967 NAP
Immuno/ Lymphoret							
15	Mouse CD-1	14 d 1x/d (GO)		53	267 (30% decrease in thymus weight in males; 18% decrease in spleen weight in females)		Shopp et al. 1984 NAP
Neurological							
16	Rat Sprague-Dawley	9d Gd 6-15 (GO)			50[b] (transient clinical signs of toxicity in dams; at higher exposure levels, signs were more persistent and accompanied by decreases in body weight gain)		NTP 1991a NAP
17	Mouse CD-1	14 d (GO)		267			Shopp et al. 1984 NAP
Reproductive							
18	Rat Sprague-Dawley	9 d Gd 6-19 (GO)		450			NTP 1991a NAP

Table 3-2 Levels of Significant Exposure to Naphthalene (nap) Or Methylnaphthalene (1-mn Or 2-mn) - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
19	Mouse CD-1	8d Gd 7-14 (GO)				300 (>10% maternal mortality)	Plasterer et al. 1985 NAP
20	Rabbit New Zealand white	14 d Gd 6-19 (GO)		120			NTP 1992b NAP
Developmental							
21	Rat Sprague-Dawley	9 d Gd 6-15 (GO)				150 (decreased maternal weight gain >20%; no fetotoxic or teratogenic effects at 150 or 450 mg/kg/day)	NTP 1991a NAP
				50			
22	Mouse CD-1	8d Gd 7-14 (GO)		300			Plasterer et al. 1985 NAP
23	Rabbit New Zealand white	14 d Gd 6-19 (GO)		120			NTP 1992b NAP
24	Rabbit New Zealand white	13 d 1x/d Gd 6-18 (G)		40	200 (maternal dyspnea, cyanosis, body drop, hypoactivity with no pathological aberrations)		PRI 1985, 1986 NAP

Table 3-2 Levels of Significant Exposure to Naphthalene (nap) Or Methylnaphthalene (1-mn Or 2-mn) - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
INTERMEDIATE EXPOSURE							
Systemic							
25	Rat blue spruce	9 wk 3.5d/wk (GO)	Resp	169			Germansky and Jamall 1988 NAP
			Hepatic		169 (elevated lipid peroxides)		
			Bd Wt			169 (20% decreased body weight gain)	
26	Rat Brown-Norway	4 wk 3.5d/wk (GO)	Ocular			500 (lens opacity)	Kojima 1992 NAP
27	Rat Sprague-Dawley Brown-Norway	6 wk	Ocular			500 (cataract formation)	Murano et al. 1993 NAP

Table 3-2 Levels of Significant Exposure to Naphthalene (nap) Or Methylnaphthalene (1-mn Or 2-mn) - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)		LOAEL Serious (mg/kg/day)		Reference Chemical Form
28	Rat Fischer 344	13 wk 5x/wk (GO)	Resp	400					NTP 1980b NAP
			Cardio	400					
			Gastro		400	(intermittent diarrhea)			
			Hemato	400					
			Hepatic	400					
			Renal	*200 M* 400 F	*400 M*	*(10% had cortical tubular* degeneration)			
			Ocular	400					
			Bd Wt	100	200	(decreased terminal body weight: 12% male & 6% female)	400		
29	Rat black-hooded	79 d (GO)	Ocular				5000	(lens opacity)	Rathbun et al. 1990 NAP
30	Rat Brown-Norway	102 d NS (GO)	Ocular				700	(lens opacity)	Tao et al. 1991 NAP
31	Rat 5 strains	4-6 wk (GO)	Ocular				1000	(lens opacity)	Xu et al. 1992b NAP

Table 3-2 Levels of Significant Exposure to Naphthalene (nap) Or Methylnaphthalene (1-mn Or 2-mn) - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
32	Rat Wistar	18 d 1x/d (G)	Hepatic		1000 (elevated lipid peroxides)		Yamauchi et al. 1986 NAP
			Ocular			1000 (cataracts)	
33	Mouse B6C3F1	13 wk 5x/wk 1x/d (GO)	Resp	200			NTP 1980a NAP
			Cardio	200			
			Gastro	200			
			Hemato	200			
			Hepatic	200			
			Renal	200			
			Ocular	200			
			Bd Wt	200			

Table 3-2 Levels of Significant Exposure to Naphthalene (nap) Or Methylnaphthalene (1-mn Or 2-mn) - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)		LOAEL Serious (mg/kg/day)		Reference Chemical Form
34	Mouse CD-1	90 d 7d/wk 1x/d (GO)	Resp	133					Shopp et al. 1984 NAP
			Hemato	133					
			Hepatic	133					
			Renal	133					
			Bd Wt	133					
			Other	53	133	(decreases in absolute weights of brain (9%), liver (18%), and spleen (28%) and relative weight of spleen (24%) in females only)			
35	Rabbit NS	5 wk	Ocular				500	(destruction of retinal photoreceptors and vascularization of the retinal area)	Orzalesi et al. 1994 NAP
36	Rabbit Chinchilla Bastard New Zealand white	12 wk 2d/wk 1x/d (GO)	Ocular				1000	(cataracts)	Rossa and Pau 1988 NAP
37	Rabbit NS	4 wk 1x/d (GO)	Ocular		1000	(increased ascorbic acid in lens)			van Heyningen 1970 NAP

Table 3-2 Levels of Significant Exposure to Naphthalene (nap) Or Methylnaphthalene (1-mn Or 2-mn) - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
38	Rabbit NS	4 wk 1x/d (GO)	Ocular			1000 (lens opacities, retinal damage)	van Heyningen and Pirie 1967 NAP
Immuno/ Lymphoret							
39	Rat Fischer 344	13 wk 5d/wk 1x/d (GO)			400 (lymphoid depletion of thymus in 2/10 females)		NTP 1980b NAP
				200			
40	Mouse CD-1	90 d (GO)		133			Shopp et al. 1984 NAP
Neurological							
41	Rat Fischer 344	13 wk 5x/wk (GO)			400 (hunched posture and lethargy)		NTP 1980b NAP
42	Mouse B6C3F1	13 wk 5d/wk 1x/d (GO)		200			NTP 1980a NAP
43	Mouse CD-1	90 d (GO)		133			Shopp et al. 1984 NAP
Reproductive							
44	Rat Fischer 344	13 wk 5x/wk (GO)		400			NTP 1980b NAP

Table 3-2 Levels of Significant Exposure to Naphthalene (nap) Or Methylnaphthalene (1-mn Or 2-mn) - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
45	Mouse B6C3F1	13 wk 5d/wk 1x/d (GO)		200			NTP 1980a NAP
CHRONIC EXPOSURE							
Systemic							
46	Mouse B6C3F1	81 wk (F)	Resp		71.6[c] (increased incidence of pulmonary alveolar proteinosis in males and females)		Murata et al. 1993 1-MN
			Cardio	143.7			
			Gastro	143.7			
			Hemato	143.7			
			Hepatic	143.7			
			Renal	143.7			
			Endocr	143.7			
			Bd Wt	143.7			

Table 3-2 Levels of Significant Exposure to Naphthalene (nap) Or Methylnaphthalene (1-mn Or 2-mn) - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
47	Mouse (B6C3F1)	81 wk (F)	Resp		50.3[d] (increased incidence of pulmonary alveolar proteinosis in males and females)		Murata et al. 1997 2-MN
			Cardio	113.8			
			Gastro	113.8			
			Hemato	113.8			
			Musc/skel	113.8			
			Hepatic	113.8			
			Renal	113.8			
			Dermal	113.8			
			Ocular	113.8			
			Bd Wt	113.8			
Immuno/ Lymphoret							
48	Mouse B6C3F1	81 wk 1x/d		143.7			Murata et al. 1993 1-MN
		(F)					
49	Mouse (B6C3F1)	81 wk (F)		113.8			Murata et al. 1997 2-MN

Table 3-2 Levels of Significant Exposure to Naphthalene (nap) *Or Methylnaphthalene (1-mn Or 2-mn)* - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form
Neurological							
50	Mouse B6C3F1	81 wk 1x/d (F)		143.7			Murata et al. 1993 1-MN
51	Mouse (B6C3F1)	81 wk (F)		113.8			Murata et al. 1997 2-MN
Reproductive							
52	Mouse B6C3F1	81 wk 1x/d (F)		143.7 F			Murata et al. 1993 1-MN
53	Mouse (B6C3F1)	81 wk (F)		113.8			Murata et al. 1997 2-MN

Table 3-2 Levels of Significant Exposure to Naphthalene (nap) Or Methylnaphthalene (1-mn Or 2-mn) - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)		Reference Chemical Form
Cancer								
54	Mouse B6C3F1	81 wk 1x/d (F)				71.6	(CEL: increased incidence of lung adenomas in males only)	Murata et al. 1993 1-MN
55	Mouse (B6C3F1)	81 wk (F)				54.3	(CEL: increased incidence of lung adenomas in males only; not at higher exposure level in males or in females at either exposure level)	Murata et al. 1997 2-MN

a The number corresponds to the entries in Figure 3-2

b Used to derive an acute-duration Minimal Risk Level (MRL) of 0.6mg/kg/day; based on a minimal LOAEL of 50 mg/kg/day for transient clinical signs of toxicity in pregnant rats, which was divided by an uncertainty factor of 90 (3 for the use of a minimal LOAEL, 10 for extrapolation from animals to humans, and 3 for human variability). Based on an analysis of results from the three available intermediate-duration oral toxicity studies in animals (NTP 1980a,b; Shopp et al. 1984), the acute-duration MRL is expected to be applicable to and protective for intermediate-duration exposure scenarios (see Section 2.3 and Appendix A).

c Used to derive a chronic-duration Minimal Risk Level (MRL) of 0.07 mg/kg/day for 1-MN; based on a LOAEL of 71.6 mg/kg/day which was divided by an uncertainty factor of 1000 (10 for use the use of a LOAEL, 10 for extrapolation from animals to humans; and 10 for human variability)

d Used to derive a chronic-duration Minimal Risk Level (MRL) of 0.04 mg/kg/day for 2-MN; based on a BMDL (LED05) of 4 mg/kg/day which was divided by an uncertainty factor of 100 (10 for extrapolation from animals to humans, and 10 for human variability).

Bd Wt = body weight; BMDL (LED05) = lower 95% confidence limit on a dose associated with 5% extra risk; BUN = blood urea nitrogen; Cardio = cardiovascular; d = day(s); Endocr = endocrine; F = females; (F) = feed; (G) = gavage; Gastro = gastrointestinal; Gd = gestation day(s); (G) = gavage in oil; Hemato = hematological; hr = hour(s); Immuno = immunological; LD50 = lethal dose, 50% kill; LOAEL = lowest-observed-adverse-effect level; M = males; NOAEL = no-observed-adverse-effect level; NS = not specified; Resp = respiratory; wk = week(s); x = time(s); 1-Mn = 1-methylnaphthalene; 2-Mn = 2-methylnaphthalene.

Figure 3-2. Levels of Significant Exposure to Naphthalene (NAP) or Methylnaphthalene (1-MN or 2-MN) - Oral

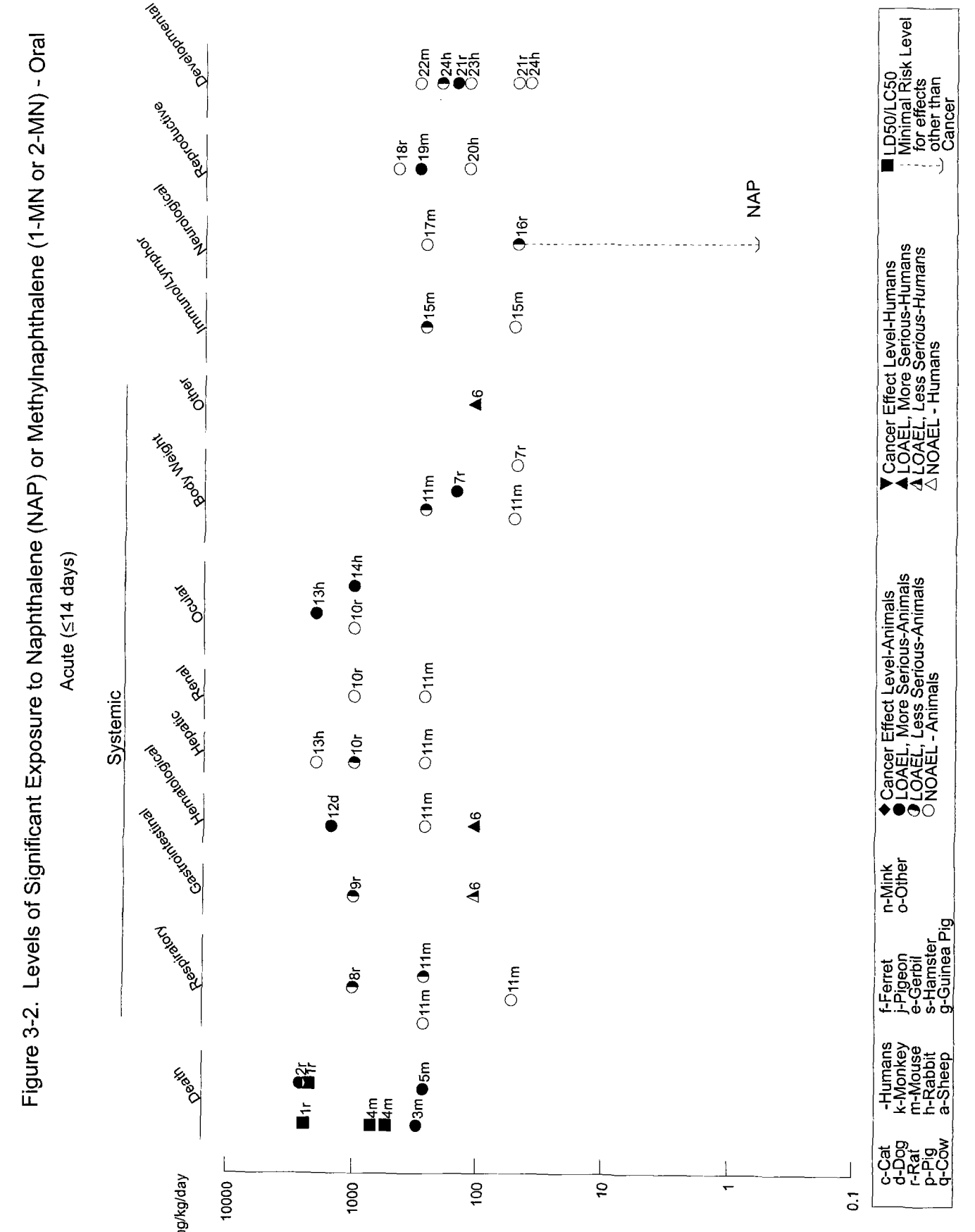


Figure 3-2. Levels of Significant Exposure to Naphthalene (NAP) or Methylnaphthalene (1-MN or 2-MN) - Oral (*Continued*)

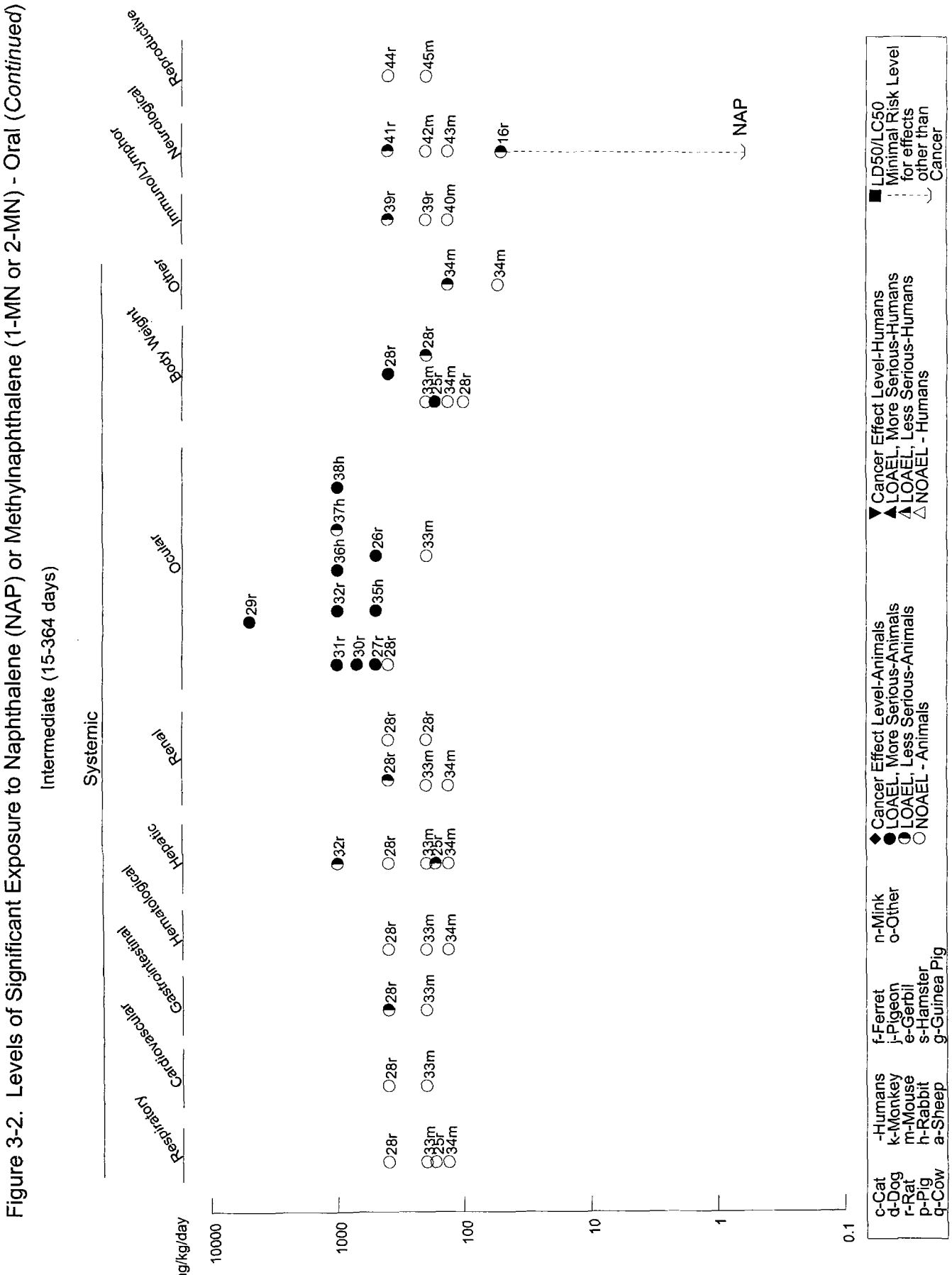
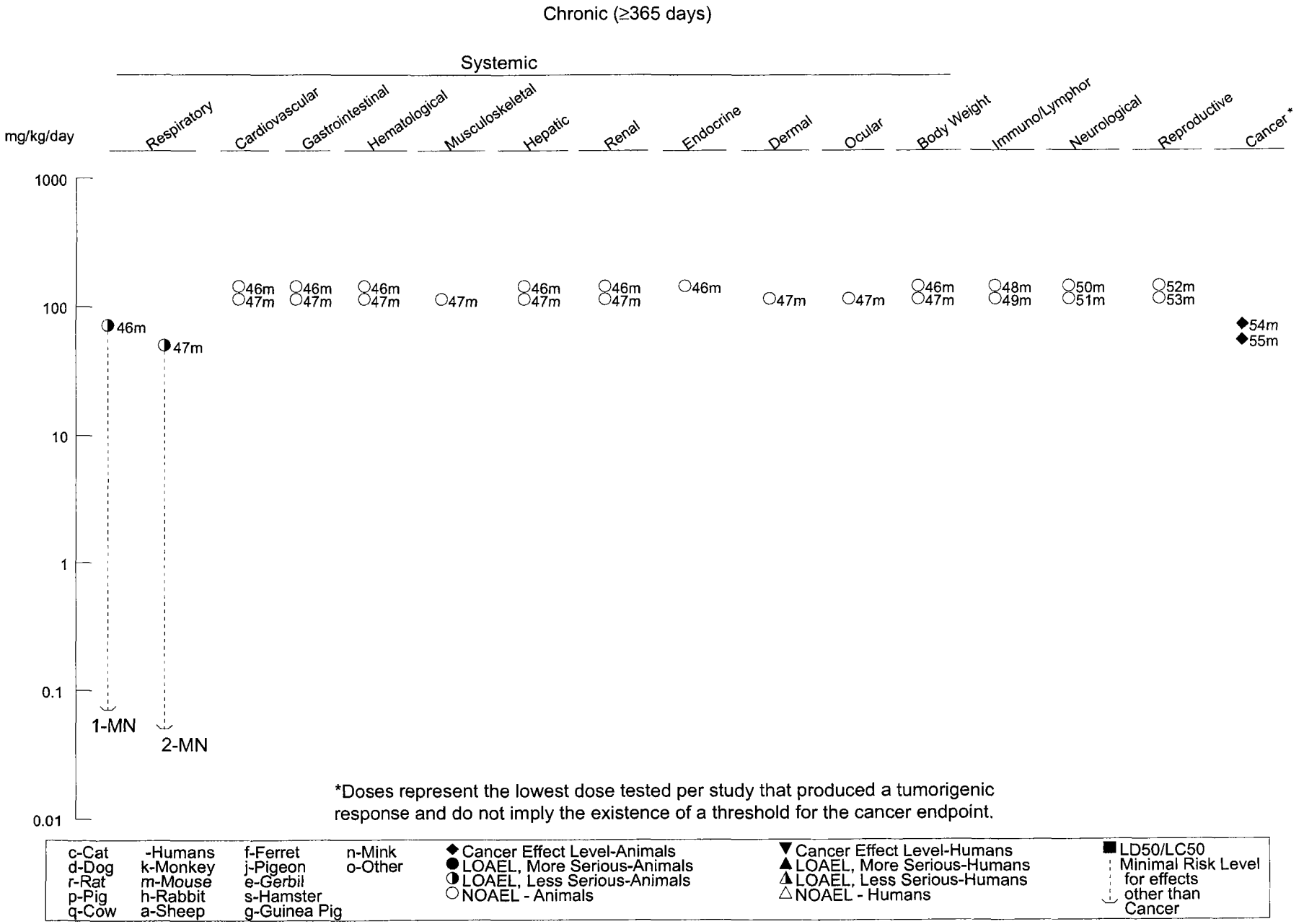


Figure 3-2. Levels of Significant Exposure to Naphthalene (NAP) or Methylnaphthalene (1-MN or 2-MN) - Oral (*Continued*)



naphthalene-containing diaper pail deodorant block (Haggerty 1956). This may have been a reflection of the reduced oxygen carrying capacity of the blood due to hemolysis.

Lesions of the lungs were seen in rats that died after being given a single large dose of naphthalene (1,000–4,000 mg/kg) during an LD_{50} study (Papciak and Mallory 1990). On the other hand, no significant respiratory toxicity was seen in rats following oral administration of naphthalene at time-weighted average doses of 169 mg/kg/day for 9 weeks (Germansky and Jamall 1988). Dosages were increased from 100 to 750 mg/kg/day over a 6-week period and held constant at 750 mg/kg/day for the last 3 weeks of the 9-week exposure period.

Lung weights were increased in female mice administered naphthalene at 267 mg/kg/day for 14 days; however, these effects were not seen in either sex at 133 mg/kg/day for 90 days (Shopp et al. 1984). No gross or histopathological lesions of the lungs were noted in mice at doses up to 200 mg/kg/day (NTP 1980a) or in rats at doses of 400 mg/kg/day (NTP 1980b) after 13 weeks of exposure.

There was a significantly increased incidence of pulmonary alveolar proteinosis in male and female B6C3F1 mice fed diets containing 1-methylnaphthalene for 81 weeks (Murata et al. 1993). The lesions contained acidophilic amorphous material, foam cells, and cholesterol crystals. There was no apparent inflammation, edema, or fibrosis of the tissues. Average administered doses were 0, 71.6, or 140.2 mg/kg/day for males and 0, 75.1, or 143.7 mg/kg/day for females. Respective incidences for pulmonary alveolar proteinosis in the control, low-, and high-dose groups were 4/49, 23/50, and 19/49 for males and 5/50, 23/50, and 17/49 for females. Histopathological examination of major organs and tissues only found exposure-related lesions in the lung. This effect was used as the basis of the chronic-duration oral MRL for 1-methylnaphthalene.

Pulmonary alveolar proteinosis is characterized by the accumulation of surfactant material in the alveolar lumen, and has been hypothesized to be caused by either excessive secretion of surfactant by type II pneumocytes, or disruption of surfactant clearance by macrophages (Lee et al. 1997; Mazzone et al. 2001; Wang et al. 1997). Electron microscopic examination of lungs of mice exposed dermally to a mixture of 1-methylnaphthalene and 2-methylnaphthalene showed that alveolar spaces were filled with numerous myelinoid structures resembling lamellar bodies of type II pneumocytes (Murata et al. 1992).

In a companion study, pulmonary alveolar proteinosis was the only exposure-related lesion found in B6C3F1 mice of both sexes exposed to 2-methylnaphthalene in the diet at doses as low as 50.3 mg/kg/day

(Murata et al. 1997). Average administered doses were 0, 54.3, or 113.8 mg/kg/day for males and 0, 50.3, or 107.6 mg/kg/day for females. Respective incidences for pulmonary alveolar proteinosis in the control, low-, and high-dose groups were 4/49, 21/49, and 23/49 for males and 5/50, 27/49, and 22/49 for females. This effect was used as the basis of the chronic-duration oral MRL for 2-methylnaphthalene.

Cardiovascular Effects. No studies were located that demonstrate any direct effects of naphthalene ingestion on the cardiovascular system. In those reports where cardiovascular effects such as increased heart rate and decreased blood pressure were noted in humans, the cardiovascular effects appeared to be secondary to the hemolytic effects and the events leading to general multiple organ failure (Gupta et al. 1979; Kurz 1987).

No gross or histopathological lesions of the heart were noted in mice at doses up to 200 mg/kg/day (NTP 1980a) or in rats at doses of 400 mg/kg/day (NTP 1980b) after 13 weeks of exposure.

Heart weights were significantly decreased (6–7%) in male and female mice that were fed 1-methylnaphthalene for 81 weeks in their diet. However, the changes in heart weight were not dose-related and there were no accompanying tissue abnormalities (Murata et al. 1993). Histopathological examination revealed no lesions in the hearts of mice fed 1-methylnaphthalene at doses as high as 143.7 mg/kg/day (Murata et al. 1993) or 2-methylnaphthalene at doses as high as 113.8 mg/kg/day (Murata et al. 1997).

Gastrointestinal Effects. Gastrointestinal disorders are common following naphthalene ingestion by humans. These effects have been attributed to the irritant properties of naphthalene (Kurz 1987). Nausea, vomiting, abdominal pain, and diarrhea (occasionally containing blood) have been reported (Bregman 1954; Gidron and Leurer 1956; Gupta et al. 1979; Haggerty 1956; Kurz 1987; MacGregor 1954; Ojwang et al. 1985). While the presence of blood in the stool is indicative of intestinal bleeding, only a few areas of mucosal hemorrhage were noted in postmortem examination of the intestines (Kurz 1987). These areas were restricted to the small bowel and colon. No frank erosions or perforations were noted anywhere in the gastrointestinal tract.

A single dose of 1,000–4,000 mg/kg was associated with stomach lesions and discoloration of the intestines in rats that died during an LD_{50} study. The survivors were not affected (Papciak and Mallory 1990). No gross or histopathological lesions of the stomach, small intestine, and colon were noted in mice at doses of up to 200 mg/kg/day (NTP 1980a) or in rats at doses of up to 400 mg/kg/day after

13 weeks of exposure (NTP 1980b). There was some intermittent diarrhea in the rats, but this may not have been treatment related.

No histopathological lesions were seen in the stomach or intestines of mice fed 71.6–143.7 mg/kg/day 1-methylnaphthalene for 81 weeks (Murata et al. 1993) or 50.3–113.8 mg/kg/day 2-methylnaphthalene for 81 weeks (Murata et al. 1997).

Hematological Effects. The most commonly reported hematologic effect in humans following the ingestion of naphthalene is hemolytic anemia (Dawson et al. 1958; Gidron and Leurer 1956; Gupta et al. 1979; Haggerty 1956; Kurz 1987; MacGregor 1954; Mackell et al. 1951; Melzer-Lange and Walsh-Kelly 1989; Ojwang et al. 1985; Shannon and Buchanan 1982). Changes observed in hematology and blood chemistry are consistent with this effect: hemolysis, decreased hemoglobin and hematocrit values, increased reticulocyte counts, serum bilirubin levels, and Heinz bodies. This was caused by hemolysis. Most of the reported case studies provide no information on dose. However, in one case report, a 16-year-old girl swallowed 6 g of naphthalene before exhibiting hemolytic anemia (Gidron and Leurer 1956). This is a dose of 109 mg/kg (assuming a 55-kg body weight). The hematological condition of this individual, who was an immigrant from Kurdistan, was not provided.

As mentioned previously, there is an association between G6PD deficiency and the hemolytic effects of naphthalene (Dawson et al. 1958; Melzer-Lange and Walsh-Kelly 1989; Shannon and Buchanan 1982). Individuals with a genetic defect for this enzyme show an increased susceptibility to hemolysis from naphthalene exposure.

Few hematologic changes have been reported in animals. Standard laboratory animals do not appear to be sensitive to the hemolytic effects of naphthalene. In CD-1 mice, naphthalene at doses up to 267 mg/kg/day for 14 days or up to 133 mg/kg/day for 90 days did not result in hemolytic anemia (Shopp et al. 1984). However there was an increase in eosinophils in the 14- and 90-day studies. There was an increase in prothrombin time at 14 days. The clinical significance of these observations is not clear; the effects are not considered to be adverse.

There were no pronounced changes in red cell related hematological parameters in mice following 13-week exposures to doses of up to 200 mg/kg/day (NTP 1980a) and up to 400 mg/kg/day in rats (NTP 1980b). In male mice exposed to 200 mg/kg/day for 13 weeks, there was a decrease in segmented neutrophils and an increase in lymphocytes, but in male rats given 400 mg/kg/day, there were increased

neutrophils and decreased lymphocytes. These effects are not considered to be biologically significant or adverse.

Hemolytic anemia was reported by Zuelzer and Apt (1949) in a dog receiving a single 1,525 mg/kg dose of naphthalene in food and in another dog receiving approximately 263 mg/kg/day for 7 days in food. Dogs are more susceptible to chemically induced hemolysis than are rats and mice.

Exposure to 75.1 or 143.7 mg/kg/day 1-methylnaphthalene for 81 weeks was associated with a slight but statistically significant increase in the hemoglobin concentration, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration in female mice (Murata et al. 1993). Corresponding changes were not observed in male mice given comparable doses of 1-methylnaphthalene, or in male or female mice exposed to 2-methylnaphthalene doses as high as 113.8 mg/kg/day (Murata et al. 1997). Consistent exposure-related changes were not found in differential white blood cell counts or several serum biochemical parameters in male and female mice exposed to 1-methylnaphthalene or 2-methyl-naphthalene in these studies. The results from these studies do not provide consistent evidence that hematological parameters are consistent toxicity targets of chronic oral exposure to 1-methylnaphthalene or 2-methylnaphthalene.

Hepatic Effects. Evidence of hepatotoxicity following oral exposure to naphthalene has been reported in humans, based on elevated plasma levels of hepatic enzymes (such as aspartate aminotransferase and lactic acid dehydrogenase) (Kurz 1987; Ojwang et al. 1985) and liver enlargement (Gupta et al. 1979; MacGregor 1954). The relationship between liver enlargement and potential naphthalene-induced hemolysis is unknown.

There is limited evidence of hepatic effects in laboratory animals, but the liver does not appear to be a critical toxicity target of orally administered naphthalene. A 39% increase in liver weight, a modest elevation in activity of aniline hydroxylase, and evidence of lipid peroxidation were observed in male rats treated with naphthalene at 1,000 mg/kg/day for 10 days (Rao and Pandya 1981). Male rats demonstrated an elevation in hepatic lipid peroxides at naphthalene doses of 1,000 mg/kg/day for 18 days (Yamauchi et al. 1986). In rats administered increasing doses of naphthalene up to 750 mg/kg/day (time-weighted average of 169 mg/kg/day), hepatic lipid peroxides were doubled at the end of 9 weeks of treatment (Germansky and Jamall 1988).

No effects on liver weight were observed in male or female mice receiving naphthalene at doses up to 267 mg/kg/day for 14 days or male mice receiving 133 mg/kg/day for 90 days (Shopp et al. 1984). Absolute liver weight was statistically significantly decreased, compared with the control value (by about 18%), in female mice receiving 133 mg/kg/day naphthalene for 90 days, but the biological significance of this change is unclear. Relative liver weight in exposed females was not changed to a statistically significant degree, and several serum biochemical end points indicative of liver damage (e.g., lactate dehydrogenase, SGPT, SGOT, and alkaline phosphatase) were unaffected in male and female mice exposed to doses up to 133 mg/kg/day for 90 days (Shopp et al. 1984). No other consistent biologically relevant exposure-related changes in serum chemistry end points were found. Activities of two hepatic microsomal mixed function oxidases (aniline hydroxylase, aminopyrine N-demethylase) were unchanged in exposed mice, although hepatic activities of benzo[a]pyrene hydroxylase were statistically significantly decreased in exposed mice (Shopp et al. 1984). The biological significance of this change is unclear. Supporting the concept that the liver is not a critical toxicity target of oral exposure to naphthalene, no gross or histopathological lesions of the liver were noted in mice at doses of up to 200 mg/kg/day (NTP 1980a) or in rats at doses of up to 400 mg/kg/day after 13 weeks of exposure (NTP 1980b).

There were no changes in liver weights or tissue histopathology in male or female mice that consumed 71.6–143.7 mg/kg/day 1-methylnaphthalene in the diet for 81 weeks (Murata et al. 1993) or 50.3–113.8 mg/kg/day 2-methylnaphthalene in the diet for 81 weeks (Murata et al. 1997).

Renal Effects. Renal toxicity has been reported in case studies of humans who ingested naphthalene. Frequent findings include the elevation of creatinine and blood urea nitrogen and the presence of proteinuria and hemoglobinuria (Gupta et al. 1979; Haggerty 1956; Kurz 1987; MacGregor 1954; Ojwang et al. 1985; Zuelzer and Apt 1949). The presence of blood in the urine and increased concentrations of urobilinogen are a consequence of acute hemolysis and do not reflect any direct action of naphthalene on the kidney. Oliguria (Kurz 1987) and anuria (Gupta et al. 1979) were noted in two case reports, although urine output was normal in a third (Ojwang et al. 1985). Painful urination with swelling of the urethral orifice was also associated with medicinal naphthalene ingestion (Lezenius 1902). Proximal tubule damage and general tubular necrosis were found in postmortem examinations of two individuals who died following naphthalene ingestion (Gupta et al. 1979; Kurz 1987).

Renal effects were not consistently observed in animals exposed orally to naphthalene. Following 10 days of exposure of rats to naphthalene at 1,000 mg/kg/day, no changes were noted in kidney weight, lipid peroxidation, or in the activity of alkaline phosphatase and aniline hydroxylase (Rao and Pandya

1981). No changes were observed in the kidney weights of mice administered naphthalene at doses up to 267 mg/kg/day for 14 days or 133 mg/kg/day for 90 days (Shopp et al. 1984). No gross or histopathological lesions of the kidney were noted in mice at doses of up to 200 mg/kg/day (NTP 1980a) or in rats at doses of up to 200 mg/kg/day after 13 weeks of exposure (NTP 1980b). In the male rats, 10% showed cortical tubular degeneration that may have been compound-related at a dose of 400 mg/kg/day (NTP 1980b).

Relative kidney weights were increased slightly in male mice fed diets containing 71.6 or 140.2 mg/kg/day 1-methylnaphthalene for 81 weeks (Murata et al. 1993). The females were not affected, and there were no histopathological lesions in the males or females. There were no changes in kidney weights or tissue histopathology in male or female mice consuming 50.3–113.8 mg/kg/day 2-methylnaphthalene in the diet for 81 weeks (Murata et al. 1997).

Ocular Effects. In an early report of naphthalene toxicity, a 36-year-old pharmacist who ingested an unspecified amount of unpurified naphthalene in a castor oil emulsion over a 13-hour period as treatment of an intestinal disorder became nearly blind 8 or 9 hours later (Lezenius 1902). A medical examination the following month revealed constricted visual fields associated with optic atrophy and bilateral zonular cataracts. At 1.5 meters, the patient's vision was limited to finger counting.

Several animal studies have demonstrated ocular changes following oral naphthalene exposure. Within 1 week following exposure to naphthalene (500 or 1,000 mg/kg/day), lens densities were increased in rats and cataracts developed within 4 weeks (Kojima 1992; Murano et al. 1993; Yamauchi et al. 1986). Eight rabbits (strain not identified) developed cataracts during oral administration of naphthalene at 2,000 mg/kg/day for 5 days (Srivastava and Nath 1969). Cataracts began to develop by the first day after a single 1,000 mg/kg naphthalene dose in three Chinchilla Bastard rabbits (Rossa and Pau 1988). In the solitary New Zealand white rabbit tested, cataracts began to develop after administration of four 1,000 mg/kg doses (dosing 2 times/week) and maximized after 12 weeks (Rossa and Pau 1988).

When naphthalene was administered orally at 1,000 mg/kg/day for up to 28 days, cataracts developed in 10 of 16 Dutch (pigmented) rabbits and in 11 of 12 albino rabbits (Van Heyningen and Pirie 1976). Lens changes were seen as early as day 2 of exposure. The authors noted that albino strains were more likely to develop cataracts over a 4-week course of treatment at 1,000 mg/kg/day than pigmented strains such as the Dutch rabbit.

In contrast, administration of a time-weighted-average 500-mg/kg/day dose of naphthalene in corn oil by gavage for 6 weeks resulted in more rapid development of cataracts in pigmented Brown-Norway rats than in nonpigmented Sprague-Dawley rats (Murano et al. 1993). Cataracts developed in three distinct phases. In the first phase, water clefts formed in the anterior subcapsular region of the eye. The second stage was the development of a semicircular opaque area in the lens, and the last stage was the appearance of a wedge-shaped opacity that could be seen with retroillumination and a wide, zonular-ring opacity that was seen with slit imaging. Each stage occurred about 1 week earlier in the Brown-Norway rats than in the Sprague Dawley rats. The first stage began 1 week after treatment was initiated in the Brown-Norway rats, and stage three cataracts were seen in all animals by the end of the 6 weeks. Progressive development of lens opacities was also reported in rats that were exposed to 700 or 5,000 mg/kg/day naphthalene by gavage for 79–102 days (Rathburn et al. 1990; Tao et al. 1991).

Damage to the eyes with continued exposure to naphthalene is not limited to lens opacification (Orzalesi et al. 1994). Retinal damage was noted in pigmented rabbits given time-weighted-average doses of 500 mg/kg/day naphthalene in corn oil by gavage for 5 weeks. The first changes to the retina occurred at about 3 weeks with degeneration of the photoreceptors. There was a subsequent increase in the retinal pigment epithelium as these cells phagocytized the debris from the photoreceptors. By the end of 6 weeks, the photoreceptor layer had almost entirely disappeared and was replaced with fibroglial tissue. As damage progressed, there was dense subretinal neovascularization of the area.

A number of biochemical changes were seen in the eyes after acute- and intermediate-duration naphthalene exposures. After 1 week of treatment with 1,000 mg/kg/day, glutathione levels in the lens were decreased in rats (Xu et al. 1992b; Yamauchi et al. 1986). After 30 days of treatment with doses of 5,000 mg/kg/day, total glutathione levels were reduced by 20% (Rathbun et al. 1990), and there was a 22% reduction at 60 days with a dose of 700 mg/kg/day (Tao et al. 1991). At 60 days, glutathione peroxidase activity in the lens was decreased by up to 45% and there was a 20–30% decrease in glutathione reductase activity (Rathbun et al. 1990). Comparable decreases in the activities of both enzymes were seen at 102 days with lower naphthalene doses (Tao et al. 1991). No changes were observed in the activity of glutathione synthetase or gamma-glutamyl cysteine synthetase (Rathbun et al. 1990). After 4 weeks of compound treatment (500 mg/kg/day), the activities of aldose reductase, sorbitol dehydrogenase, lactic dehydrogenase, and glutathione reductase were lower than in controls (Kojima 1992). No changes in ocular lipid peroxides were reported when male Blue Spruce pigmented rats were administered incremental doses of naphthalene that peaked at 750 mg/kg/day for 9 weeks (Germansky

and Jamall 1988). Lens and capsule LDH activities were greatly reduced in rabbits while o-diphenyl oxidase activity was elevated with a dose of 2,000 mg/kg/day for 5 days (Srivastava and Nath 1969).

In 13-week studies, histopathologic examination revealed no ocular lesions in F344/N rats or B6C3F1 mice exposed to doses as high as 400 or 200 mg/kg/day, respectively (NTP 1980a, 1980b). In a 2-year rat feeding study, no eye damage was seen at a naphthalene dosage of 41 mg/kg/day (Schmahl 1955). The details of the eye examination were not provided.

There were no changes in eye tissue histopathology in male or female mice that consumed 71.6–143.7 mg/kg/day 1-methylnaphthalene in the diet for 81 weeks (Murata et al. 1993) or 50.3–113.8 mg/kg/day 2-methylnaphthalene in the diet for 81 weeks (Murata et al. 1997).

Body Weight Effects. No studies were located that documented effects on body weight in humans after oral exposure to naphthalene.

In pregnant Sprague-Dawley rats exposed to 50, 150, or 450 mg/kg/day on gestation days 6–15, body weight gains were depressed by 31 and 53% at 150 and 450 mg/kg/day, respectively, but were unaffected at 50 mg/kg/day. The decreased body weight gains were accompanied by persistent clinical signs of toxicity (slow respiration, lethargy, or prone position) at the 150 and 450 mg/kg/day dose levels, but these signs were only apparent at the 50-mg/kg/day level during the first 2 days of dosing. The minimal LOAEL of 50 mg/kg/day for transient clinical signs and the LOAEL of 150 mg/kg/day for clinical signs associated with decreased body weight gains in pregnant rats are the basis of the acute oral MRL for naphthalene (see Section 2.3 and Appendix A).

In animals, body weight effects appear to be the critical effect associated with intermediate-duration oral exposure to naphthalene. After 13 weeks of exposure to naphthalene, mean terminal body weights in F344/N rats exposed to gavage doses ≥200 mg/kg/day were decreased by more than 10% relative to control values (NTP 1980b). Body weights were decreased by 12 and 28% in 200- and 400-mg/kg/day male rats, and by 23% in 400-mg/kg/day female rats. Food consumption was not affected by exposure. In B6C3F1 mice exposed to naphthalene doses up to 200 mg/kg/day for 13 weeks, exposed males gained more weight than controls during exposure, whereas exposed females gained less weight than controls (NTP 1980a). However, terminal body weights in exposed female mice were within 95% of control values, indicating that the naphthalene-induced changes were not biologically significant. In male and female CD-1 mice exposed to doses as high as 133 mg/kg/day for 90 days, average terminal body weight

in exposed groups were within 90% of control values (Shopp et al. 1984). Mice exposed to 267 mg/kg/day naphthalene for 14 days showed a decreased body weight gain; terminal body weights were decreased by 6% in females and 13% in males compared with control values (Shopp et al. 1984).

As discussed in Section 2.3 and Appendix A, the NOAEL of 100 mg/kg/day and the LOAEL of 200 mg/kg/day for decreased body weights in rats exposed by gavage to naphthalene 5 days/week for 13 weeks (NTP 1980b) provide the best available basis for MRL derivation among the findings from the studies in animals orally exposed to naphthalene for intermediate-durations. However, because an intermediate-duration oral MRL based on these data is slightly larger than the acute-duration oral MRL for naphthalene, the acute MRL was adopted as the intermediate-duration oral MRL for naphthalene (as indicated in Figure 3-2 and discussed in Section 2.3).

There was no significant difference between body weights of mice that were given up to 143.7 mg/kg/day 1-methylnaphthalene in their diets and those of the control animals throughout an 81-week exposure period (Murata et al. 1993). In mice exposed to 2-methylnaphthalene doses as high as 113.8 mg/kg/day in the diet for up to 81 weeks, average body weights were within 10% of control values (Murata et al. 1997).

Other Systemic Effects. Several humans who consumed naphthalene experienced elevated body temperatures which may have been related to their hemolytic crisis (Chusid and Fried 1955; Gidron and Leurer 1956; Haggerty 1956; Kurz 1987; MacGregor 1954; Ojwang et al. 1985). However, in some situations, bacterial infections rather than hemolysis may have been the cause of the fever (Kurz 1987; Melzer-Lange and Walsh-Kelly 1989; Ojwang et al. 1985; Zuelzer and Apt 1949).

No studies were located that documented other systemic effects in animals after oral exposure to naphthalene.

3.2.2.3 Immunological and Lymphoreticular Effects

No studies were located that documented immunological or lymphoreticular effects in humans after oral exposure to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene. However, an enlarged spleen is a frequent consequence of hemolysis and was noted in the postmortem examination of one human subject who died after ingesting a large quantity of naphthalene (Kurz 1987).

Mice treated with naphthalene at oral doses as high as 267 mg/kg/day for 14 days showed no effects on humoral immune responses, delayed hypersensitivity responses, bone marrow stem cell number, or bone marrow DNA synthesis (Shopp et al. 1984). Mitogenic responses to concanavalin A (but not to lipopolysaccharide) were reduced in high dose females only. None of these effects were noted at doses of 27 or 53 mg/kg/day. At naphthalene doses of 133 mg/kg/day for 13 weeks, naphthalene had no effect on immune function (Shopp et al. 1984). After 14 days, thymus weights were reduced approximately 30% in male mice, but no differences were seen with a dose of 133 mg/kg/day at 13 weeks (Shopp et al. 1984). There was lymphoid depletion of the thymus in 2 of 10 female rats exposed to 400 mg/kg/day naphthalene for 13 weeks (NTP 1980b).

Spleen weights were reduced approximately 20% in female mice exposed to 267 mg/kg/day naphthalene for 14 days and 25% in females exposed to 133 mg/kg/day for 13 weeks (Shopp et al. 1984).

Monocyte concentrations were significantly elevated in male and female mice exposed to 71.6–143.7 mg/kg/day 1-methylnaphthalene for 81 weeks (Murata et al. 1993). The increase in monocyte counts appeared to be dose related. The authors hypothesized that these changes may have been a physiological response to the pulmonary alveolar proteinosis seen in the exposed animals. There were no changes in spleen or thymus weights and the histopathology of these tissues was normal. With 81 weeks of exposure of male and female B6C3F1 mice to 2-methylnaphthalene, neutrophils were reported to be decreased, and lymphocytes increased, compared with control values, but neither the magnitude of these changes, or the dose groups in which they occurred, were specified in the study report (Murata et al. 1997). As with 1-methylnaphthalene, histologic examination revealed no exposure-related lesions in the spleen or thymus.

The highest NOAEL values and all LOAEL values from each reliable naphthalene study for immunological/lymphoreticular effects in each species and duration category are recorded in Table 3-2 and plotted in Figure 3-2. The highest NOAEL values from the 1-methylnaphthalene and 2-methyl-naphthalene studies for immunological/lymphoreticular effects are also recorded in Table 3-2 and plotted in Figure 3-2.

3.2.2.4 Neurological Effects

The neurologic symptoms of naphthalene ingestion reported in human case studies include confusion (Ojwang et al. 1985), altered sensorium (Gupta et al. 1979), listlessness and lethargy (Bregman 1954; Chusid and Fried 1955; Kurz 1987; MacGregor 1954; Zuelzer and Apt 1949), and vertigo (Gidron and Leurer 1956). Muscle twitching, convulsions (Kurz 1987; Zuelzer and Apt 1949), decreased responses to painful stimuli, and coma occurred prior to death in individuals who ingested naphthalene (Gupta et al. 1979; Kurz 1987). At autopsy, the brain has appeared edematous (Gupta et al. 1979; Kurz 1987), with separation of neural fibers and swelling of myelin sheaths being noted histologically (Gupta et al. 1979). The neurologic symptomatology could result from the cerebral edema, which was probably secondary to acute hemolysis.

No studies were located that documented neurological effects in humans after oral exposure to 1-methylnaphthalene or 2-methylnaphthalene.

Dose-related clinical signs of toxicity were apparent in female Sprague-Dawley rats exposed to doses of 50, 150, or 450 mg/kg/day naphthalene for 10 days during organogenesis. Slow respiration and lethargy were observed in a large percentage of the exposed animals. Some rats were dazed, had periods of apnea, or were unable to move after exposure. In the lowest dose group, 73% of the animals were affected on the first day of dosing. In the two higher dose groups, over 90% of the rats were affected (NTP 1991a).

The animals in the 50-mg/kg/day group acclimatized quickly. Symptoms were only apparent during the first 2 days of dosing. Clinical signs of toxicity persisted for longer periods in the higher dose groups, and were accompanied by decreased body weight gains (31 and 53% decreased at 150 and 450 mg/kg/day, respectively compared with control). It is not known if the observed clinical signs were due to treatment-related effects on the nervous system or were the indirect consequence of severe systemic toxicity, as indicated by the dramatic decreases in body weight gain. Comparable effects were not observed in F344/N rats exposed to doses of up to 400 mg/kg/day for 13 weeks or in B6C3F1 mice at doses of up to 200 mg/kg/day (NTP 1980a, 1980b). These results suggest that pregnant animals may be more susceptible to the effects of naphthalene than non-pregnant animals. The minimal LOAEL of 50 mg/kg/day for transient clinical signs of toxicity and the LOAEL of 150 mg/kg/day for more persistent signs of toxicity accompanied with depressed weight gain in pregnant rats exposed on gestation days 6–15 are the basis of the acute oral MRL for naphthalene (see Section 2.3 and Appendix A).

There were no changes in the brain weights in mice exposed to naphthalene at doses up to 267 mg/kg/day for 14 days or 133 mg/kg/day for 90 days (Shopp et al. 1984). No gross or histopathological lesions of the brain were noted in mice at doses of up to 200 mg/kg/day (NTP 1980a) or in rats at doses of up to 400 mg/kg/day after 13 weeks of exposure (NTP 1980b). Transient clinical signs of neurotoxicity were observed in rats following daily gavage administration of 400 mg/kg, but not 200 mg/kg, doses (NTP 1980b). In mice, transient lethargy was observed following dose administration only between weeks 3 and 5 in the highest dose group, 200 mg/kg/day (NTP 1980a).

Absolute brain weight was significantly increased in male mice fed diets containing 71.6 or 140.2 mg/kg/day 1-methylnaphthalene for 81 weeks (Murata et al. 1993), or 54.3 or 113.8 mg/kg/day 2-methylnaphthalene for 81 weeks (Murata et al. 1997). The increases in brain weights were not dose related and there were no histopathological abnormalities of the brain. There were no differences in brain weights or histopathology in the female mice given comparable doses (Murata et al. 1993, 1997).

No studies were located that documented neurological effects in animals after oral exposure to 2-methylnaphthalene.

The highest NOAEL values and all LOAEL values from each reliable study for neurological effects for naphthalene exposure in each species and duration category are recorded in Table 3-2 and plotted in Figure 3-2. The highest NOAEL values for neurological effects in the intermediate-duration 1-methylnaphthalene and 2-methylnaphthalene mouse studies are also recorded in Table 3-2 and plotted in Figure 3-2.

3.2.2.5 Reproductive Effects

No studies were located that documented reproductive effects in humans after oral exposure to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene.

Oral exposures of pregnant rabbits to naphthalene at dosages up to 400 mg/kg/day (gestational days 6–18), using methylcellulose as the vehicle, resulted in no apparent adverse reproductive effects (PRI 1986). When administered in corn oil to pregnant mice, however, a dosage of 300 mg/kg/day (gestational days 7–14) resulted in a decrease in the number of live pups per litter (Plasterer et al. 1985). It is not clear whether the observed differences in response are attributable to species differences or a possible increase

in the absorption of naphthalene when it is administered in corn oil compared with administration as a suspension in methyl cellulose.

Transient signs of toxicity were present in female rats exposed to doses of 50, 150, or 450 mg/kg/day on gestational days 6–15 (NTP 1991a). Effects on maternal weight gain were noted in the mid- and high-dose groups but not in the lowest dose group. The mid-dose group had a 31% decrease in weight gain while the high-dose group had a 53% weight gain decrease.

No treatment-related effects were reported on testicular weights of mice administered naphthalene at doses up to 267 mg/kg/day for 14 days or 133 mg/kg/day for 90 days (Shopp et al. 1984). No gross or histopathological lesions of the testes were noted in mice at doses of up to 200 mg/kg/day (NTP 1980a) or in rats at doses of up to 400 mg/kg/day after 13 weeks of exposure (NTP 1980b).

No gross or histopathological lesions of the testis, seminal vesicles, ovaries, uterus, or vagina were observed in mice exposed to 1-methylnaphthalene doses as high as 143.7 mg/kg/day (Murata et al. 1993) or 2-methylnaphthalene doses as high as 113.8 mg/kg/day (Murata et al. 1997).

The highest NOAEL values and all LOAEL values from each reliable study for reproductive effects in each species and duration category are recorded in Table 3-2 and plotted in Figure 3-2.

3.2.2.6 Developmental Effects

In humans, transplacental exposure of the fetus to naphthalene that had been ingested by the mother resulted in neonatal (and presumably fetal) hemolytic anemia (Anziulewicz et al. 1959; Zinkham and Childs 1957, 1958). No estimates of dose or duration were available, although in one case naphthalene consumption was described as being most pronounced during the last trimester (Zinkham and Childs 1958).

No studies were located that documented developmental effects in humans after oral exposure to 1-methylnaphthalene or 2-methylnaphthalene.

No congenital abnormalities were observed after oral administration of naphthalene at 300 mg/kg/day to pregnant mice on days 7–14 of gestation (Plasterer et al. 1985), or at doses up to 400 mg/kg/day to

pregnant rabbits on days 6–18 of gestation (PRI 1986). Similarly, naphthalene was not teratogenic in rats at doses up to 450 mg/kg/day during gestation days 6–15 (NTP 1991a). However, there was a slight, but dose-related, increase in fused sternebrae in female pups of rabbits administered doses of 20–120 mg/kg/day on days 6–19 of gestation (NTP 1992b). These effects were seen in 2 of 21 litters at 80 mg/kg/day and 3 of 20 litters at 120 mg/kg/day. No other developmental effects were noted in this study.

No studies were located that evaluated developmental end points in animals after oral exposure to 1-methylnaphthalene or 2-methylnaphthalene.

The highest NOAEL values and all LOAEL values from each reliable study for developmental effects in each species and duration category are recorded in Table 3-2 and plotted in Figure 3-2.

3.2.2.7 Cancer

No studies were located that documented carcinogenic effects in humans after oral exposure to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene.

In a 2-year feeding study of rats receiving naphthalene at about 41 mg/kg/day, no tumors were reported (Schmahl 1955). Specific details pertaining to the tissues examined were not provided.

The chronic dietary studies with 1-methylnaphthalene or 2-methylnaphthalene provide limited evidence for the carcinogenicity of these chemicals. Long-term exposure (81 weeks) of mice to 71.6 or 140.2 mg/kg/day 1-methylnaphthalene in the diet was associated with statistically significant increases in bronchiolar/alveolar adenomas in males, but not in females (Murata et al. 1993). Incidences for mice with lung adenomas were 2/49, 13/50, and 12/50 for control through high-dose male mice, and 4/50, 2/50, and 4/49 for female mice. Combined incidence for mice with lung adenomas or adenocarcinomas were 2/49, 13/50, and 15/50 for male mice, and 5/50, 2/50, and 5/50 for female mice. In mice exposed to 2-methylnaphthalene in the diet for 81 weeks, incidences for mice with lung adenomas were 2/49, 9/49, and 5/49 in males groups that received 0, 54.3, or 113.8 mg/kg/day, and 4/50, 4/49, and 5/48 in female groups that received comparable doses (Murata et al. 1997). Only the incidence in the 54.3-mg/kg/day group was elevated to a statistically significant degree.

3.2.3 Dermal Exposure

3.2.3.1 Death

Two cases of hemolytic anemia were observed in infants exposed to naphthalene-treated diapers (Schafer 1951; Valaes et al. 1963). One case was fatal. Jaundice, methemoglobinemia, hemolysis, and cyanosis were noted. In the fatal case the symptoms persisted, even after the naphthalene-containing diapers were no longer used (Schafer 1951). The author suggested that use of baby oil on the infant's skin might have facilitated the naphthalene absorption.

No treatment-related deaths occurred within the 14-day observation period when naphthalene was applied at 2,500 mg/kg to the skin of male and female rats or when doses of up to 1,000 mg/kg/day were applied to the skin for 6 hours/day, 5 days/week for 13 weeks (Frantz et al. 1986; Gaines 1969). There were also no deaths in New Zealand White rabbits after application of 2,000 mg/kg naphthalene to intact and abraded shaved areas of skin in an LD_{50} study (Papciak and Mallory 1990).

No studies were located that documented lethal effects in humans or animals after dermal exposure to 1-methylnaphthalene or 2-methylnaphthalene.

3.2.3.2 Systemic Effects

No studies were located that documented musculoskeletal effects in humans or animals after dermal exposure to naphthalene. The highest NOAEL and all LOAEL values for dermal exposure to naphthalene are recorded in Table 3-3. Data for systemic effects in humans or animals from dermal exposure to 1-methylnaphthalene or 2-methylnaphthlene are restricted to two studies that only examined the lung for lesions following repeated dermal exposure to methylnaphthalene, a mixture of 1-methylnaphthalene and 2-methylnaphthalene (Emi and Konishi 1985; Murata et al. 1992).

Respiratory Effects. No studies were located that documented respiratory effects in humans after dermal exposure to naphthalene.

No histological changes of the lungs were noted in rats dermally treated with doses of up to 1,000 mg/kg/day naphthalene (6 hours/day, 5 days/week) for 13 weeks (Frantz et al. 1986).

Table 3-3 Levels of Significant Exposure to Naphthalene (Nap) Or Methylnaphthalene (1-Mn Or 2-Mn) - Dermal

Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL	LOAEL		Reference Chemical Form
				Less Serious	Serious	
ACUTE EXPOSURE						
Systemic						
Rabbit New Zealand White	once 24hr contact	Dermal		2000 mg/kg	(skin irritation, edema, fissuring)	Papciak and Mallory 1990 NAP
Rabbit	once	Dermal		125 mg/kg	(reversible erythema)	PRI 1985a NAP
Immuno/ Lymphoret						
Gn Pig	3 wk 1x/wk		1000 mg/kg			PRI 1985c NAP

Table 3-3 Levels of Significant Exposure to Naphthalene (Nap) Or Methylnaphthalene (1-Mn Or 2-Mn) - Dermal (continued)

Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL	LOAEL			Reference Chemical Form
				Less Serious		Serious	
INTERMEDIATE EXPOSURE							
Systemic							
Rat	90 d 5d/wk 6 hr/d	Resp	1000 mg/kg/day				Frantz et al. 1986 NAP
		Cardio	1000 mg/kg/day				
		Gastro	1000 mg/kg/day				
		Hemato	1000 mg/kg/day				
		Hepatic	1000 mg/kg/day				
		Renal	1000 mg/kg/day				
		Dermal	300 mg/kg/day	1000 mg/kg/day	(increased incidence of excoriated skin and papules)		
Mouse (B6C3F1)	30 wk 2x/wk	Resp		119 mg/kg	(100% incidence of mice with pulmonary alveolar proteinosis)		Murata et al. 1992 1-MN+2-MN

Table 3-3 Levels of Significant Exposure to Naphthalene (Nap) Or Methylnaphthalene (1-Mn Or 2-Mn) - Dermal (continued)

Species (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL	LOAEL			Reference Chemical Form
				Less Serious	Serious		
CHRONIC EXPOSURE							
Systemic							
Mouse (B6C3F1)	61 wk 2x/wk	Resp	30 mg/kg		119 mg/kg	(31/32 mice had pulmonary alveolar proteinosis; an unspecified number died)	Emi and Konishi 1985 1-MN+2-MN

Cardio = cardiovascular; d = day(s); Gastro = gastrointestinal; Gn Pig = Guinea pig; Hemato = hematological; hr = hour(s); LOAEL = lowest-observed-adverse-effect level; NOAEL = no-observed-adverse-effect level; Resp = respiratory; wk = week(s); x = time(s). 1-Mn = 1-methylnaphthalene; 2-Mn = 2-methylnaphthalene.

Pulmonary alveolar proteinosis was noted in nearly all female B6C3F1 mice given dermal doses of methylnaphthalene (a mixture of 1-methylnaphthalene and 2-methylnaphthalene) twice a week at a dose level of 119 mg/kg for 30 weeks (Murata et al. 1992) or 61 weeks (Emi and Konishi 1985). Endogenous lipid pneumonia was the term used to describe this lesion in the earlier study. With the longer-duration exposure to 119 mg/kg methylnaphthalene, an unspecified number of mice died early. Pulmonary alveolar proteinosis developed in 3/11 female mice treated twice weekly with dermal doses of 30 mg/kg for 61 weeks, compared with 0/4 controls (Emi and Konishi 1985).

Cardiovascular Effects. No studies were located that documented cardiovascular effects in humans after dermal exposure to naphthalene.

No differences in organ weight or histological changes of the heart were noted in rats dermally treated with 1,000 mg/kg/day naphthalene (6 hours/day, 5 days/week) for 13 weeks (Frantz et al. 1986).

Gastrointestinal Effects. No studies were located that documented gastrointestinal effects in humans after dermal exposure to naphthalene.

No histological changes of the esophagus, stomach, or intestines were noted in rats dermally treated with 1,000 mg/kg/day naphthalene (6 hours/day, 5 days/week) for 13 weeks (Frantz et al. 1986).

Hematological Effects. Hemolytic anemia was reported in infants dermally exposed to diapers or other clothing treated with naphthalene mothballs (Dawson et al. 1958; Schafer 1951; Valaes et al. 1963). Jaundice, fragmentation of erythrocytes, Heinz bodies, methemoglobinemia, and reticulocytosis were observed. Several of the infants had G6PD deficiencies. Individuals with this genetic disorder are particularly susceptible to hemolysis from chemical agents. The application of oil to the skin may have aided absorption of naphthalene, as shown by the increasing severity of symptoms (jaundice and cyanosis) even after the use of the naphthalene-containing diapers ceased (Schafer 1951).

There were no changes in hemoglobin, hematocrit, red blood cell count, leukocyte count, or platelet count at 4 and 13 weeks in rats treated with doses of up to 1,000 mg/kg/day applied to the skin (6 hours/day, 5 days/week) for 13 weeks (Frantz et al. 1986).

Hepatic Effects. The liver was enlarged in two infants who experienced acute hemolysis after dermal exposure to naphthalene (Dawson et al. 1958; Schafer 1951). The relationship between liver enlargement and potential naphthalene-induced hemolysis is unknown.

There were no differences in liver weights or histological damage to the liver in rats dermally treated with doses of up to 1,000 mg/kg/day naphthalene (6 hours/day, 5 days/week) for 13 weeks (Frantz et al. 1986). In addition, the levels of aspartate amino transferase, alanine amino transferase, urea nitrogen, and bilirubin were not elevated in the exposed rats as compared to the controls.

Renal Effects. No studies were located that documented renal effects in humans after dermal exposure to naphthalene.

There were no differences in kidney weights or histological damage to the liver in rats dermally treated with doses of up to 1,000 mg/kg/day naphthalene (6 hours/day, 5 days/week) for 13 weeks (Frantz et al. 1986). In addition, the results of urinalysis conducted at 4 and 13 weeks on the treated rats were not different from the control results, indicating that there was no impairment of kidney function.

Dermal Effects. No studies were located that documented dermal effects in humans after dermal exposure to naphthalene.

A study in rabbits has shown that naphthalene is a mild dermal irritant, causing erythema and fissuring, when directly applied to the shaved, abraded, or nonabraded skin under a dressing; healing occurred within 6–7 days (Papciak and Mallory 1990; PRI 1985a). In rats that were dermally treated for 6 hours/day, 5 days/week, for 13 weeks with 1,000 mg/kg/day naphthalene, there was an increased incidence of excoriated skin lesions and papules (Frantz et al. 1986). However, similar lesions were seen in the controls and lower dose group animals. At the high dose, naphthalene appeared to exacerbate the severity of the lesions. Acute and chronic exposures of animal skin to naphthalene appear to cause dermal irritation.

Ocular Effects. Two case studies were reported in which humans experienced eye irritation and conjunctivitis as a result of naphthalene exposure (van der Hoeve 1906). In one case, a worker accidentally got naphthalene powder in his left eye. The exact amount was unknown, but was described by the worker as large. Despite immediate cleansing of the eye, the subject experienced conjunctivitis and pain shortly after exposure. Symptoms of irritation subsided, but then reappeared 6 weeks later. At

that time, the subject noticed decreased vision in his left eye. When examined by a doctor, the eye had retinal lesions (one fresh and others seemingly older); the entire retina appeared clouded. The subject's vision in the left eye was poorer than in the right. Five years earlier, vision was the same in both eyes.

In the second case study, an adult male who worked in a storage area where naphthalene was used as a pesticide complained of ocular pain, conjunctivitis, and impaired vision (van der Hoeve 1906). Neither the duration nor the mode of exposure was described. The subject most likely was exposed to naphthalene vapors. When examined by a doctor, the subject was found to have retinal bleeding and the beginning of a cataract.

Dermal and ocular contact with naphthalene vapors accompanied by inhalation may have contributed to the development of multiple lens opacities in 8 of 21 workers involved with a dye manufacturing process that used naphthalene as a raw material (Ghetti and Mariani 1956). Workers, who were employed at the plant for up to 5 years, melted naphthalene in open vats, resulting in high atmospheric vapor concentrations.

Mild ocular irritation was observed in the nonrinsed eyes of rabbits after instillation of naphthalene at 0.1 mg/eye (Papciak and Mallory 1990; PRI 1985b). Observed effects were reversible within 7 days after exposure. When the eyes were rinsed with water immediately after exposure, there were no signs of irritation (Papciak and Mallory 1990). Oral administration of naphthalene in rats resulted in cataract formation beginning at the posterior outer cortex, suggesting that this region is the most sensitive part of the lens (Kojima 1992). The lenses of pigmented Brown-Norway rats had changes, such as water cleft formation, during the first week that 10 mg/kg/day naphthalene was orally administered every other day (Murano et al. 1993). These rats were more sensitive to cataract formation than albino Sprague-Dawley rats, presumably because they more effectively metabolized naphthalene to the toxic compound naphthoquinone (Murano et al. 1993).

3.2.3.3 Immunological and Lymphoreticular Effects

No studies were located that documented immunological or lymphoreticular effects in humans after dermal exposure to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene. An enlarged spleen was noted in two human subjects dermally exposed to unspecified doses of naphthalene (Dawson et al. 1958;

Schafer 1951). However, spleen enlargement is a result of hemolysis rather than a direct effect of naphthalene on the spleen.

In animals, dermal application of pure naphthalene (1,000 mg/kg) 1 time/week for 3 weeks did not result in delayed hypersensitivity reactions in guinea pigs (Papciak and Mallory 1990; PRI 1985c).

No studies were located that documented immunological or lymphoreticular effects in animals after dermal exposure to 1-methylnaphthalene or 2-methylnaphthalene.

A NOAEL for immunological/lymphoreticular effects following dermal exposure to naphthalene is recorded in Table 3-3.

No studies were located that documented the following health effects in humans or animals after dermal exposure to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene:

3.2.3.4 Neurological Effects

3.2.3.5 Reproductive Effects

3.2.3.6 Developmental Effects

3.2.3.7 Cancer

3.3 GENOTOXICITY

No studies of genotoxic effects in humans exposed to naphthalene were located.

Table 3-4 summarizes results for naphthalene and its metabolites in bacterial mutation assays; *in vitro* eukaryotic gene mutation, cytogenetic, or DNA damage assays; and *in vivo* eukaryotic gene mutation, cytogenetic, or DNA damage assays.

Bacterial Gene Mutation Assays for Naphthalene. Naphthalene was not mutagenic in *Salmonella typhimurium* assays in the presence or absence of rat liver metabolic preparations (Bos et al. 1988; Connor et al. 1985; Florin et al. 1980; Gatehouse 1980; Godek et al. 1985; Kaden et al. 1979; McCann et al. 1975; Mortelmans et al. 1986; Nakamura et al. 1987; Narbonne et al. 1987; NTP 1992a; Sakai et al. 1985). The metabolites, 1-naphthol and 1,4-naphthoquine, were not mutagenic in several *S. typhimurium*

Table 3-4. Results of Genotoxicity Testing of Naphthalene or Metabolites[a]

Assay	Test system	Dose/ concentration	HID or LED	Result	Reference
Bacterial gene mutation assays					
Reverse mutation	*Salmonella typhimurium* TA1535, TA1537, TA98, TA100	100 µg/plate ±S9 activation	100	Negative	McCann et al. 1975
	S. typhimurium TA1535, TA1537, TA98, TA100	0.3–100 µg/plate ±S9 activation	100	Negative	Mortelmans et al. 1986
	S. typhimurium TA1535, TA1537, TA98, TA100	0.3–100 µg/plate ±S9 activation	100	Negative	NTP 1992a
	S. typhimurium TA1537, TA1538	10–200 µg/plate ±S9 activation	100	Negative, toxic above 100 µg/plate	Gatehouse 1980
	S. typhimurium TA98, TA100	10–50 µg/plate ±S9 activation	50	Negative	Bos et al. 1988
	S. typhimurium TA1535, TA1537, TA98, TA100	0.03–30 µmol/plate ±S9 activation	3	Negative, toxic above 3 µmol/plate	Florin et al. 1980
	S. typhimurium TA1535, TA1537, TA98, TA100	250 µg/plate ±S9 activation	250	Negative	Sakai et al. 1995
	S. typhimurium TA1535, TA1537, TA1538, TA98, TA100	3–300 µg/plate ±S9 activation	300	Negative, toxic above 300 µg/plate	Godek 1985
	S. typhimurium TM677	1–2 mM ±S9 activation	2	Negative	Kaden et al. 1979
	S. typhimurium TA98, TA1535	5–1,000 µg/plate ±S9 activation	1,000	Negative	Narbonne et al. 1987
	S. typhimurium UTH8413, UTH8414, TA98, TA100	100–2,000 µg/plate ±S9 activation	2,000	Negative	Conner et al. 1985
	S. typhimurium TA1535, TA1537, TA98, TA100	1,000 µg/plate ±S9 activation	1,000	Negative (1-naphthol)	McCann et al. 1975
	S. typhimurium TA98, TA1535	5–1,000 µg/plate ±S9 activation	1,000	Negative (1-naphthol)	Narbonne et al. 1987
	S. typhimurium TA1535, TA1537, TA98, TA100	250 µg/plate ±S9 activation	250	Negative (1,4-naphthoquinone)	Sakai et al. 1995

Table 3-4. Results of Genotoxicity Testing of Naphthalene or Metabolites[a]

Assay	Test system	Dose/ concentration	HID or LED	Result	Reference
Bacterial gene mutation assays (continued)					
	S. typhimurium TA97a, TA98, TA100, TA104	0–100 nmol/plate ±S9 activation	17.5	Positive (1,2-naphtho-quinone), 1.8- to 3.4-fold increase without S9; +S9 results similar to -S9 results	Flowers-Geary et al. 1996
SOS response	*S. typhimurium* TA1535/p5K1002 (uMuC-lacZ)	83 µg/mL ±S9 activation	83	Negative	Nakamura et al. 1987
	Escherichia coli K12 inductest (λ lysogen GY5027; uvrB-, envA-)	2,000 µg/plate ±S9 activation	2,000	Negative	Mamber et al. 1984
SOS chromotest	*E. coli* PQ37 (sfiA::lacZ fusion)	0.156–10.0 µg/assay ±S9 activation	10	Negative	Mersch-Sundermann et al. 1993
Pol A- or Rec assay	*E. coli* WP2/WP10 (uvrA-, recA-)	2,000 µg/mL ±S9 activation	2,000	Negative	Mamber et al. 1983
	E. coli WP2/WP67 (uvrA-, pol A-)	Dose not specified ±S9 activation	NS	Negative	Mamber et al. 1983
Pol A- or Rec assay	*E. coli* WP2/WP3478 (pol A-)	Dose not specified ±S9 activation	NS	Negative	Mamber et al. 1983
Mutatox (reversion to luminescence)	*Vibrio fischeri* M169	Up to 5,000 µg/tube ±S9 activation	0.203 0.625	Negative without S9 activation Positive with S9 activation	Arfsten et al. 1994
***In vitro* eukaryotic gene mutation, cytogenetic, or DNA damage assays**					
Mutation at hprt and tk loci	Human B-lymphoblastoid cell line MCL-5	40 µg/mL	40	Negative	Sasaki et al. 1997
	Human B-lymphoblastoid cell line MCL-5	40 µg/mL	40	Negative (1,4-naphthoquinone)	Sasaki et al. 1997
Chromosomal aberrations	Chinese hamster ovary cells	15–75 µg/mL ±S9 activation	30 75	Positive with S9 activation Negative without S9 activation	NTP 1992a
Chromosomal aberrations	Preimplantation whole mouse embryos	0.16 mM ±S9 activation	0.16	Positive, more pronounced with S9 activation	Gollahon et al. 1990 [abstract only]

Table 3-4. Results of Genotoxicity Testing of Naphthalene or Metabolites[a]

Assay	Test system	Dose/ concentration	HID or LED	Result	Reference
***In vitro* eukaryotic gene mutation, cytogenetic, or DNA damage assays (continued)**					
Sister chromatid exchange	Human mononuclear leukocytes	100 µM ± human liver microsomes	100	Negative	Tingle et al. 1993; Wilson et al. 1995
Sister chromatid exchange	Human mononuclear leukocytes	0–100 µM ± human liver microsomes	10	Positive (1,2- and 1,4-naphthoquinone) Negative (naphthalene 1,2-epoxide)	Wilson et al. 1996
Sister chromatid exchange	Chinese hamster ovary cells	9–90 µg/mL ±S9 activation	27	Positive with S9 in the second of two trials and without S9 in both trials	NTP 1992a
Alkaline elution (*in vitro*)	Rat hepatocytes	3 mM, 3-hour exposure	3 mM	Negative for increased incidence of DNA single-strand breaks	Sina et al. 1983
Unscheduled DNA synthesis (*in vitro*)	Rat primary hepatocytes	0.16–5,000 µg/mL	16	Negative, toxic above 16 µg/mL	Barfknecht et al. 1985
	Rat primary hepatocytes	0.5–1,000 nM/mL	1,000	Negative (1-naphthol, 2-naphthol)	Probst et al. 1981
Cell transformation	Fischer rat embryo cells (F1706P96)	0.1, 0.5 µg/mL	0.5	Negative	Freeman et al. 1973
	Syrian baby hamster kidney cells (BHK-21C13)	0.08–250 µg/mL +S9	250	Negative	Purchase et al. 1978
	Mouse (BALB/c) whole mammary gland cultures	0.001–1.0 µg/gland	0.1	Negative, cytotoxic above 0.1 µg/gland	Tonelli et al. 1979
	Mouse BALB/c 3T3 cell culture	15–150 µg/mL	150	Negative, toxic at highest dose	Rundell et al. 1983
	Human diploid fibroblasts (WI-38)	0.08–250 µg/mL +S9	250	Negative	Purchase et al. 1978
***In vivo* eukaryotic gene mutation, cytogenetic, or DNA damage assays**					
Somatic mutation, recombination	*Drosophila melanogaster*	1, 5, 10 mM (feeding larvae)	5	Positive, loss of heterozygosity of two recessive wing genes (about 2-fold increase in number of wing spots)	Delgado-Rodriguez et al. 1995
Micronuclei induction	Male ICR Swiss mice: bone marrow cells	50, 250, and 500 mg/kg gavage	500	Negative	Harper et al. 1984

Table 3-4. Results of Genotoxicity Testing of Naphthalene or Metabolites[a]

Assay	Test system	Dose/ concentration	HID or LED	Result	Reference
***In vivo* eukaryotic gene mutation, cytogenetic, or DNA damage assays (continued)**					
	Male and female CD-1 mice: bone marrow cells	250 mg/kg intraperitoneal	250	Negative	Sorg 1985
Micronuclei induction	Salamander larvae (*Pleurodeles waltl*): erythrocytes	0.125–0.5 ppm in the tank water	0.25	Positive at 0.5 ppm, weakly positive at 0.25 ppm	Djomo et al. 1995
Alkaline elution (*in vivo*)	DNA from hepatocytes of female rats given single oral doses	359 mg/kg oral	359	Negative for DNA single-strand breaks	Kitchin et al. 1992, 1994
Unscheduled DNA synthesis (*in vivo*)	Hepatocytes from rats given single oral doses	600, 1,000, and 1,600 mg/kg gavage	1,600	Negative	RTC 1999
DNA fragmentation	DNA fragmentation in liver or brain tissue from mice given single doses	0, 3, 32, and 158 mg/kg (0.01, 0.1, 0.5 of LD_{50}=316 mg/kg)	32	Positive (1.0- to 1.5-fold and 1.8- to 2.2-fold increase in DNA fragmentation at 32 and 158 mg/kg, respectively)	Bagchi et al. 2002
DNA fragmentation	DNA fragmentation in liver or brain tissue from rats given daily doses for up to 120 days	0, and 110 mg/kg in corn oil	110	Positive (1.9- to 2.5-fold maximal increases in DNA fragmentation in brain and liver tissue)	Bagchi et al. 1998a
DNA fragmentation	DNA fragmentation in liver or brain tissue from p53-deficient and standard mice given single oral doses	0, 3, 32, and 158 mg/kg (0.01, 0.1, and 0.5 of LD_{50}=316 mg/kg)	158 (std) 3 (-p53)	Positive (1.8- to 3.9-fold increases in DNA fragmentation in brain and liver tissue; p53-deficient (tumor suppressor gene) strain was more sensitive	Bagchi et al. 2000
Neoplastic transformation (*in vivo*)	F344 partially hepatectomized rats (sex not specified)	100 mg/kg gavage (in corn oil)	100	Negative for gamma-glutamyl trans-peptidase foci	Tsuda et al. 1980

[a]Metabolites are noted in result column.

DNA = dioxyribonucleic acid; HID = highest ineffective dose for negative tests; LED = lowest effective dose for positive tests; NS = not specified; SOS = an emergency system to repair single strand DNA breaks; std = standard deviation

strains in the presence or absence of metabolic activation (McCann et al. 1975; Narbonne et al. 1987; Sakai et al. 1985). Naphthalene was not mutagenic, with or without metabolic activation, in the Pol A- or Rec assays in several *Escherichia coli* strains (Mamber et al. 1983). Naphthalene did not damage DNA (as assayed by the induction of the SOS-repair system) in *E. coli* PQ37 (Mersch-Sundermann et al. 1993), in *E. coli* K12 (Mamber et al. 1984), or in *S. typhimurium* TA1535/p5K1002 (Nakamura et al. 1987).

1,2-Naphthoquinone induced reverse mutations in several *S. typhimurium* strains without a metabolic activation system (Flowers-Geary et al. 1996), and naphthalene, in the presence of rat liver metabolic activation, induced reverse mutations in the marine bacterium *Vibrio fischeri* (Arfsten et al. 1994).

In Vitro Eukaryotic Gene Mutation, Cytogenetic, or DNA Damage Assays for Naphthalene. *In vitro* eukaryotic gene mutation assays are restricted to a single report that naphthalene and 1,4-naphthoquinone (1,2-naphthoquinone was not tested) did not induce mutations at the hprt and tk loci in human lymphoblastoid cells (Sasaki et al. 1997). However, naphthalene (in the presence of rat liver metabolic activation) induced chromosomal aberrations in Chinese hamster ovary cells (NTP 1992a) and preimplantation whole mouse embryos (Gollahon et al. 1990). Naphthalene also induced sister chromatid exchanges (in the presence or absence of rat liver metabolic activation) in Chinese hamster ovary cells (NTP 1992a), but did not do so in human mononuclear leukocytes in the presence or absence of human liver microsomes (Tingle et al. 1993; Wilson et al. 1995). In contrast, 1,2-naphthoquinone and 1,4-naphthoquinone (but not 1,2-naphthalene oxide), in the absence of metabolic activation, induced sister chromatid exchanges in human leukocytes at concentrations (10 and about 50 μM) that depleted cellular glutathione levels and induced about 35-45% cell death (Wilson et al. 1996). Naphthalene did not induce cell transformations in several mammalian cell types (see Table 3-4) or DNA single-strand breaks (Sina et al. 1983) or unscheduled DNA synthesis (Barfknecht et al. 1985; Probst et al. 1981) in rat hepatocytes.

In cell-free test systems (not included in Table 3-4), 1,2-naphthoquinone formed N7 adducts with deoxyguanosine (McCoull et al. 1999) and caused DNA strand scission in the presence of NADPH and copper via reactive oxygen species from a Cu(II)/Cu(I) oxidation/reduction cycle (Flowers et al. 1997).

In Vivo Eukaryotic Gene Mutation, Cytogenetic, or DNA Damage Assays for Naphthalene. Naphthalene was mutagenic in *Drosophila melanogaster* (Delgado-Rodriquez et al. 1995), but no *in vivo* mutagenicity tests of naphthalene or its metabolites are available in mammalian systems (Table 3-4). Naphthalene induced micronuclei in erythrocytes of salamander (*Pleurodeles waltl*) larvae exposed to concentrations of 0.5 mM, but did not induce micronuclei in bone marrow of mice given single oral doses

(50, 250, or 500 mg/kg) or intraperitoneal doses (250 mg/kg) (Harper et al. 1984; Sorg 1985). Naphthalene did not cause increased single-stranded DNA breaks in hepatocytes of rats given single oral doses of 359 mg/kg (Kitchin et al. 1992, 1994), unscheduled DNA synthesis in hepatocytes from rats given single doses as high as 1,600 mg/kg (RTC 1999), or transformation foci (γ-glutamyl transpeptidase-positive) in livers of F344 partially hepatectomized rats given single 100 mg/kg doses, but did cause DNA fragmentation in brain and liver tissue from mice given single doses of 32 or 158 mg/kg (Bagchi et al. 2000, 2002) and rats exposed to 110 mg/kg/day for up to 120 days (Bagchi et al. 1998a). In the DNA fragmentation assays, the effect was accompanied by increased lipid peroxidation in the same tissues. It is unclear whether the apparent DNA damage in these assays was due to direct effects of naphthalene metabolites or reactive oxygen species or was secondary to cell death induced at an extranuclear site.

No studies were located that examined possible genotoxic effects of naphthalene or its metabolites in sensitive target tissues of naphthalene in rodents (lung and nasal epithelial tissue).

Genotoxicity Assays for 1-Methylnaphthalene and 2-Methylnaphthalene. No studies were located that documented genotoxic effects of 1-methylnaphthalene or 2-methylnaphthalene in humans or animals by any route of exposure. Data are limited to one *in vitro* study where 1-methylnaphthalene and 2-methylnaphthalene failed to induce chromosomal aberrations or sister chromatid exchanges in human peripheral lymphocytes (Kulka et al. 1988). In an *in vitro* microbial assay employing *S. typhimurium*, mutagenic activity was not detected with either compound, with either the presence or absence of microsomal activation (Florin et al. 1980). These studies are presented in Table 3-5.

3.4 TOXICOKINETICS

Little information is available that documented the toxicokinetics of naphthalene in humans by any route of exposure. No information on the toxicokinetics of 1-methylnaphthalene or 2-methylnaphthalene in humans was located. The available animal data pertaining to naphthalene are described in the following sections. The relevance of this information to the toxicokinetics of naphthalene in exposed humans, however, is not known.

No toxicokinetic data on 1-methylnaphthalene-exposed animals were located. Animal data pertaining to 2-methylnaphthalene were limited.

Table 3-5. Genotoxicity of 1-Methylnaphthalene and 2-Methylnaphthalene *In Vitro*

Species (test system)	End point	Results		Reference
		With activation	Without activation	
1-Methylnaphthalene				
Prokaryotic organisms:				
Salmonella typhimurium (TA98, TA100, TA1535, TA1537)	Gene mutation	–	–	Florin et al. 1980
Mammalian cells:				
Human lymphocytes	Chromosomal aberration, sister chromatid exchange	–	–	Kulka et al. 1988
2-Methylnaphthalene				
Prokaryotic organisms:				
S. typhimurium (TA98, TA100, TA1535, TA1537)	Gene mutation	–	–	Florin et al. 1980
Mammalian cells:				
Human lymphocytes	Chromosomal aberration, sister chromatid exchange	–	–	Kulka et al. 1988

– = negative result

3.4.1 Absorption

Based on the presence of adverse effects following exposure, humans and animals can absorb naphthalene by pulmonary, gastrointestinal, and cutaneous routes. However, the rate and extent of naphthalene absorption are unknown in many instances.

3.4.1.1 Inhalation Exposure

Clinical reports suggest that prolonged exposure to naphthalene vapors can cause adverse health effects in humans (Harden and Baetjer 1978; Linick 1983; Valaes et al. 1963). Unfortunately, the rate and extent of naphthalene absorption were not determined in these studies. Presumably naphthalene moves across the alveolar membrane by passive diffusion through the lipophilic matrix.

No animal data that documented the absorption of naphthalene after inhalation were located. The only data observed in animal studies involved localized effects in the lungs and nasal passages. Thus, it is not possible to conclude that they were the consequence of absorbed naphthalene. However, absorption can be presumed to occur based on the human data.

No information has been located that documented the absorption of 1-methylnaphthalene or 2-methylnaphthalene in humans or animals after inhalation exposure.

3.4.1.2 Oral Exposure

Several case reports indicate that naphthalene ingested by humans can be absorbed in quantities sufficient to elicit toxicity (Bregman 1954; Chusid and Fried 1955; Gidron and Leurer 1956; Gupta et al. 1979; Haggerty 1956; Kurz 1987; MacGregor 1954; Mackell et al. 1951; Ojwang et al. 1985; Santhanakrishnan et al. 1973; Shannon and Buchanan 1982; Zuelzer and Apt 1949). However, no studies have been located that report the rate or extent of absorption. Absorption of naphthalene presumably occurs by passive diffusion through the lipophilic matrix of the intestinal membrane.

In one patient who died as a result of naphthalene ingestion, 25 mothballs were found in the stomach 5 days after her death (Kurz 1987). A single naphthalene mothball reportedly weighs between 0.5 and 5 g

depending on its size (Ambre et al. 1986; Siegel and Wason 1986). The gastric contents of a person who mistakenly ingested naphthalene flakes still smelled strongly of naphthalene at least 2 days following ingestion (Ojwang et al. 1985). These findings suggest that dissolved naphthalene is transported slowly into the intestines. Uptake from the intestines is governed by the partition coefficient between the materials in the intestinal lumen and the membrane lipids. Ingestion of mothballs or other forms of particulate naphthalene will lead to continued absorption over a period of several days as the solid dissolves. Unfortunately, none of the human data permit a quantitative evaluation of absorption coefficients or rates.

No information that documented the absorption of naphthalene after oral administration to animals has been located. The occurrence of ocular effects in rats and rabbits indicates that gastrointestinal absorption does occur (Kojima 1992; Murano et al. 1993; Srivastava and Nath 1969).

No information was located that documented the absorption of 1-methylnaphthalene in humans or animals after oral administration. Systemic effects observed after the ingestion of 1-methylnaphthalene demonstrate that intestinal absorption does occur in rats (Murano et al. 1993).

No information has been located that documented absorption in humans after oral exposure to 2-methylnaphthalene. Small doses of 2-methylnaphthalene appear to be rapidly absorbed from the gastrointestinal tract in guinea pigs. At least 80% of a 10 mg/kg oral dose of 2-methylnaphthalene was absorbed within 24 hours based on recovery of the radiolabel in the urine (Teshima et al. 1983).

3.4.1.3 Dermal Exposure

Several cases of naphthalene toxicity in neonates have been reported in which the proposed route of exposure was dermal (Dawson et al. 1958; Schafer 1951). Each case involved the use of diapers which had been stored in contact with naphthalene (mothballs or naphthalene flakes). The authors proposed that the naphthalene was absorbed through the skin, causing hemolytic anemia. It was suggested that this absorption may have been enhanced by the presence of oils which had been applied to the babies' skin (Schafer 1951). Inhalation of vapors from the treated diapers probably contributed to the total exposure.

^{14}C-Naphthalene was rapidly absorbed when the neat material (43 µg) was applied for a 48-hour period under a sealed glass cap to shaved 13-cm^2 areas of rat skin. Half of the sample (3.3 µg/cm^3) was absorbed

in 2.1 hours (Turkall et al. 1994). When the naphthalene was mixed with either a sandy soil or a clay soil prior to contact with the skin, the presence of the soil slowed the absorption (Turkall et al. 1994). The absorption half-time from the clay and sandy soil samples were 2.8 and 4.6 hours, respectively. The rate of absorption did not influence the total amount of naphthalene absorbed in 48 hours since the areas under the plasma concentration curve did not differ significantly with any of the three exposure scenarios (0.42–0.63%/mL hour). The authors proposed that naphthalene was absorbed more slowly from the sandy soil than the clay soil because the sandy soil had a higher organic carbon content (Turkall et al. 1994). The sandy soil contained 4.4% organic matter and the clay soil 1.6% organic matter.

No studies were located that examined the absorption of 1-methylnaphthalene or 2-methylnaphthalene in humans or animals after dermal administration.

3.4.2 Distribution

There are limited data concerning the distribution of naphthalene in human tissues. Naphthalene was present in 40% of the adipose tissue samples that were analyzed as part of the National Human Adipose Tissue Survey (EPA 1986g). The maximum concentration observed was 63 ng/g. Naphthalene was also detected in human milk samples (concentration not reported) (Pellizzari et al. 1982). The sources of naphthalene in these milk and body fat samples are not known.

Information is available for the distribution of naphthalene in swine after oral exposure, the distribution of naphthalene in rats after dermal exposure, and the distribution of 2-methylnaphthalene in guinea pigs after oral exposure. No data were located for the inhalation exposure routes and no data were identified on the distribution of 1-methylnaphthalene by any route of exposure.

3.4.2.1 Inhalation Exposure

No studies were located that examined the distribution of naphthalene, 1-methylnaphthalene, or 2-methyl-naphthalene in humans or animals after inhalation exposure.

3.4.2.2 Oral Exposure

Naphthalene can cross the human placenta in concentrations high enough to cause red cell hemolysis and lead to anemia in newborn infants of mothers who consumed naphthalene during pregnancy (Anziulewicz et al. 1959; Zinkham and Childs 1957, 1958).

The distribution of naphthalene and its metabolites in young pigs given a single dose of 0.123 mg/kg (4.8 Ci/kg) ^{14}C-labeled naphthalene was monitored at 24 and 72 hours (Eisele 1985). At 24 hours, the highest percentage of the label (3.48±2.16% dose/mg tissue) was in the adipose tissue. The kidneys had the next highest concentration of label (0.96% dose/mg tissue), followed by the liver (0.26±0.06% dose/mg tissue) and lungs (0.16% dose/mg tissue). The heart contained 0.09±0.04% dose/mg tissue and the spleen contained 0.07±0.01% dose/mg tissue. At 72 hours, the amount of label in the fat had fallen to 2.18±1.16% dose/mg tissue, that in the liver to 0.34±0.24% dose/mg tissue, and the kidneys and lungs contained the same concentration (0.26% dose/mg tissue).

Pigs were also given oral doses of 0.006 mg/kg/day (0.22 Ci/kg/day) ^{14}C-labeled naphthalene for 31 days (Eisele 1985). With repeated administration of the radiolabel, the tissue distribution differed considerably from that observed with a single dose of the compound. The highest concentration of label was in the lungs (0.15% dose/mg tissue), followed by the liver and heart (0.11% dose/mg tissue). There was very little label in the fat tissue (0.03% dose/mg tissue). The spleen had 0.09±0.05% dose/mg tissue and the kidney had 0.09% dose/mg tissue.

In one dairy cow, naphthalene distributed to milk with both single and repeated doses of ^{14}C-labeled naphthalene. The label was distributed between the milk and the milk fat (Eisele 1985). When the cow was given naphthalene for a 31-day period, the amount of label found in the milk remained relatively constant throughout the exposure period. The amount in the milk fat was lower for the first 7 days than it was for the remainder of the exposure.

The tissue distribution of 2-methylnaphthalene was measured in guinea pigs 3, 6, 24, and 48 hours after oral administration of tritium-labeled 2-methylnaphthalene (10 mg/kg; 59 µCi/kg) (Teshima et al. 1983). The highest concentration of label was present in the gallbladder with 20.17 µg at 3 hours and 15.72 µg at 6 hours. (All concentrations are expressed in µg equivalents of ^{3}H/g wet tissue.) At 24 hours, the value fell to 0.43 µg and at 48 hours, to 0.04 µg. The presence of label in the gallbladder presumably reflects

the excretion of hepatic metabolites in the bile. The values for the kidney were 5.64 µg at 3 hours, 7.62 µg at 6 hours, 0.29 µg at 24 hours, and 0.09 µg at 48 hours.

Radiolabelled compound was detected in the liver immediately after exposure (Teshima et al. 1983). When converted to units of mass, hepatic concentrations were 1.71 µg at 3 hours and 2.66 µg at 6 hours, falling to 0.18 µg at 24 hours. Lung concentrations were similar to those for blood at all time points. The amount in blood at 3 hours was 0.75 µg and that for the lungs was 0.69 µg; at 6 hours, the blood had a concentration of 0.71 µg and the lung had 0.76 µg. The half-life of 2-methylnaphthalene in the blood was 10.4 hours. The decay of naphthalene in the other tissues examined was described as biphasic.

3.4.2.3 Dermal Exposure

No information was located that documented the distribution of naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene in humans after dermal exposure.

In rats, radiolabel from naphthalene distributed to the ileum, duodenum, and kidney (0.01–0.02% of initial dose) when tissues were analyzed 48 hours after naphthalene contact with the skin (Turkall et al. 1994). The largest concentration was found at the site of application (0.56% of initial dose). A total of 20 tissues were evaluated; the percentage of label in all other tissues was minimal.

No information that documented the distribution of 1-methylnaphthalene or 2-methylnaphthalene in dermally exposed animals was located.

3.4.2.4 Other Routes of Exposure

After intraperitoneal administration in mice, ^{14}C-labeled 2-methylnaphthalene distribution was measured in the fat, kidney, liver, and lung for 24 hours (Griffin et al. 1982). The amount of label in the fat peaked 3 hours after exposure and remained higher than the amount of label in other tissues at 8 hours. The liver, kidney, and lung followed the fat in order of decreasing concentration. The maximum concentration in the fat was 13 nmol equivalents/mg wet weight. The maximum value for the liver was 3.5 nmol equivalents/mg wet weight at 1 hour. Maximum values were about 1.75 nmol equivalents/mg wet weight for the kidneys at 2 hours and 0.8 nmol equivalents/mg wet weight for the lungs at 4 hours.

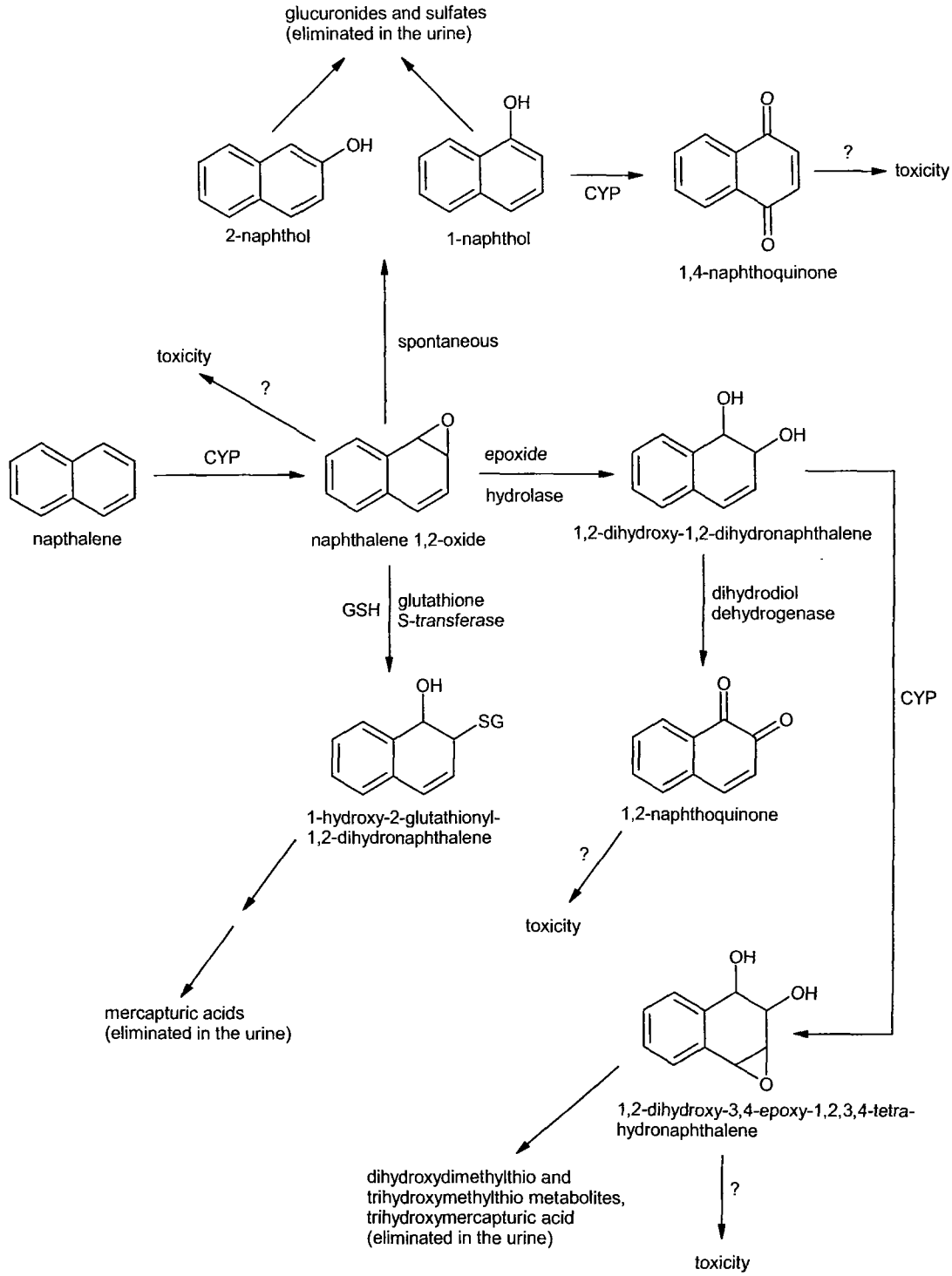
3.4.3 Metabolism

The metabolism of naphthalene in mammalian systems has been studied extensively and is depicted in Figure 3-3. The metabolic scheme in Figure 3-3 illustrates that there are multiple reactive metabolites formed from naphthalene: 1,2-naphthalene oxide, 1,2-naphthoquinone, 1,4-naphthoquinone, and 1,2-dihydroxy-3,4-epoxy-1,2,3,4-tetrahydronaphthalene. This section presents an overview of the metabolic scheme and the evidence for the involvement of the 1,2-epoxide and the naphthoquinones in naphthalene toxicity. The fourth metabolite listed above is expected to be reactive, but its potential role in naphthalene toxicity has not been investigated. A recent review of the metabolism and bioactivation of naphthalene has been published by Buckpitt et al. (2002).

The first step in naphthalene metabolism is catalyzed by cytochrome P-450 (CYP) oxygenases and produces a reactive electrophilic arene epoxide intermediate, 1,2-naphthalene oxide. In mammalian systems, several CYP isozymes have been demonstrated to metabolize naphthalene, including 1A1, 1A2, 1B1, 3A7, 3A5 (Juchau et al. 1998), 2E1 (Wilson et al. 1996), 2F2 (Buckpitt et al. 1995; Shultz et al. 1999), and 2B4 (Van Winkle et al. 1996). The epoxide can spontaneously rearrange to form naphthols (predominantly 1-naphthol) and subsequently conjugate with glucuronic acid or sulfate to form conjugates, which are excreted in urine.

Alternatively, the 1,2-epoxide can react with tissue macromolecules. This reaction is thought to be involved in several aspects of naphthalene toxicity, especially injury to Clara cells (ciliated cells in the epithelium of proximal and distal airways of the lung) from acute exposure to naphthalene (Buckpitt et al. 2002; Zheng et al. 1997). In pH 7.4 buffer, the epoxide has been shown to have a half-life of approximately 2–3 minutes, which is extended by the presence of albumins to about 11 minutes (Buckpitt et al. 2002; Kanekal et al. 1991). Mice are markedly more susceptible than rats to acute naphthalene-induced Clara cell injury (Buckpitt et al. 1992; West et al. 2001). The susceptibility difference apparently extends to chronic exposure scenarios. Mice exposed by inhalation to 10 or 30 ppm naphthalene for 2 years showed lung inflammation, but rats exposed to concentrations up to 60 ppm showed no lung inflammation (Abdo et al. 2001; NTP 1992a, 2000). The species difference in lung susceptibility has been correlated with higher rates of formation of a specific enantiomeric epoxide (1*R*,2*S*-naphthalene oxide) in lung microsomes and isolated dissected airways of mice compared with rats (Buckpitt et al. 1992, 1995). Rat, hamster, and monkey lung microsomes preferentially formed the 1*S*,2*R*-naphthalene oxide enantiomer and showed lower rates of formation of epoxides than mouse lung microsomes (Buckpitt et al. 1992). Microsomes from human lymphoblastoid cells expressing recombinant human

Figure 3-3. Scheme for Naphthalene Metabolism and Formation of Multiple Reactive Metabolites, That May Be Involved in Naphthalene Toxicity*



CYP = cytochrome P450 enzyme(s); GSH = reduced glutathione; SG = glutathione

*Adapted from Buckpitt et al. (2002) and Waidyanatha et al. (2002)

CYP2F1 also showed preferential formation of the 1*S*,2*R*-naphthalene oxide enantiomer, providing some evidence that human transformation of naphthalene to reactive epoxides in lung tissue may be more like rats than mice (Lanza et al. 1999).

In contrast to the lung, species differences in susceptibility at another sensitive target of naphthalene, the olfactory and respiratory epithelia of the nose, do not correlate with differences in rates of transformation to 1,2-epoxide derivatives in extracts of olfactory tissue (Buckpitt et al. 1992; Plopper et al. 1992a). Metabolic rates (units of nmol naphthalene converted to epoxide derivatives/minute/mg protein) in olfactory tissue extracts showed the following order: mouse (87.1) > rat (43.5) > hamster (3.9). However, rats were more susceptible to naphthalene-induced cell injury than mice or hamsters. The lowest single intraperitoneal doses producing necrosis and exfoliation in olfactory epithelium were 200 mg/kg in rats and 400 mg/kg in mice and hamsters. These observations suggest that the reasons for species differences in susceptibility to naphthalene toxicity are complex and do not solely involve the formation of the 1,2-epoxide metabolites. Although CYP monooxygenases, which might be involved in naphthalene metabolism and bioactivation, have been demonstrated to exist in nasal respiratory epithelial and olfactory epithelial tissue from rodents and humans (Thornton-Manning and Dahl 1997), studies designed to specifically characterize metabolism of naphthalene in nasal tissue are restricted to those by Buckpitt et al. (1992) and Plopper et al. (1992a).

In addition to being converted to the naphthols, the 1,2-epoxide can be conjugated with glutathione via glutathione-S-transferase catalysis. Figure 3-3 shows one such conjugate, 1-hydroxy-2-glutathionyl-1,2-dihydronaphthalene. The glutathionyl conjugates are converted in several steps to mercapturic acids, which are excreted in the urine. The conjugation of the epoxide is thought of as a detoxication mechanism, as evidenced by studies showing that glutathione depletion increased the degree of acute naphthalene-induced Clara cell injury in mice (Warren et al. 1982; West et al. 2000a). In addition, elevated activities of γ-glutamylcysteine synthetase, the enzyme catalyzing the rate limiting step in glutathione synthesis, were observed in dissected airways from mice that developed tolerance to acute naphthalene Clara cell cytotoxicity (West et al. 2000a).

The 1,2-epoxide can also be enzymatically hydrated by epoxide hydrolase to form 1,2-dihydroxy-1,2-dihydronaphthalene (Figure 3-3). This 1,2-dihydrodiol derivative was the major stable metabolite of naphthalene produced by human liver microsomes, whereas the major stable metabolite formed by mouse liver microsomes was 1-naphthol (Tingle et al. 1993). In the presence of an inhibitor of epoxide hydrolase (trichloropropene oxide), the major stable metabolite with human liver microsomes was

1-naphthol. How this species difference in liver metabolism may relate to the human relevance of toxicity of inhaled naphthalene in sensitive target tissues in the nose and lung of mice is unknown.

The 1,2-dihydrodiol can be catalytically transformed by dihydrodiol dehydrogenase to 1,2-naphthoquinone (also known as naphthalene-1,2-dione). 1,2-Naphthoquinone is both reactive itself and capable of producing reactive oxygen species through redox cycling (Flowers et al. 1997) and has been shown to be mutagenic in several strains of *S. typhimurium* (Flowers-Geary et al. 1996). In isolated Clara cells incubated with 0.5 mM naphthalene, 1,2-naphthoquinone was the major naphthalene derivative covalently bound to proteins, although covalent binding with the 1,2-epoxide was also observed (Zheng et al. 1997). The formation of the other naphthoquinone, 1,4-naphthoquinone, from 1-naphthol, presumably via a CYP monooxygenase, has been proposed based on the finding that, following incubations of liver microsomes with 1-naphthol, ethylene diamine, a compound that reacts readily with 1,2-naphthoquinone, did not trap reactive metabolites (D'Arcy Doherty et al. 1984). Cysteinyl adducts of both 1,2-naphthoquinone and 1,4-naphthoquinone (and of 1,2-naphthalene oxide) with hemoglobin and albumin have been detected in blood of rats given single oral doses of naphthalene ranging from 100 to 800 mg/kg (Troester et al. 2002; Waidyanatha et al. 2002). Levels of 1,2-naphthalene oxide adducts were greater than levels of 1,2-naphthoquinone adducts, which were greater than levels of 1,4-naphthoquinone adducts (Troester et al. 2002; Waidyanatha et al. 2002). In *in vitro* studies with whole human blood samples, 1,2- or 1,4-naphthoquinone induced increased frequencies of sister chromatid exchanges at concentrations $\geq$10 µM, whereas naphthalene 1,2-epoxide did not at concentrations up to 100 µM (Wilson et al. 1996). Similarly, incubation of human mononuclear leukocytes with 1,2-naphthoquinone or 1,4-naphthoquinone caused significant depletion of cellular glutathione levels and significant cytotoxicity at concentrations between 1 and 100 µM, whereas naphthalene 1,2-epoxide did not display these toxic actions in this concentration range (Wilson et al. 1996).

1,2-Naphthoquinone formed in lens tissue is thought to be involved in naphthalene-induced cataracts in rats and rabbits. The enzyme involved in the transformation of the 1,2-dihydrodiol to 1,2-naphthoquinone in lens tissue is thought to be aldose reductase (this enzyme is not specified in Figure 3-3). Support for this hypothesis includes findings that aldose reductase inhibitors prevent cataract formation in naphthalene-fed rats (Tao et al. 1991; Xu et al. 1992a), dihydrodiol dehydrogenase is apparently absent in rat lens (Greene et al. 2000), and aldose reductase appears to be the only enzyme in rat lens that can transform 1,2-dihydroxy-1,2-dihydronaphthalene to 1,2-naphthoquinone (Sugiyama et al. 1999).

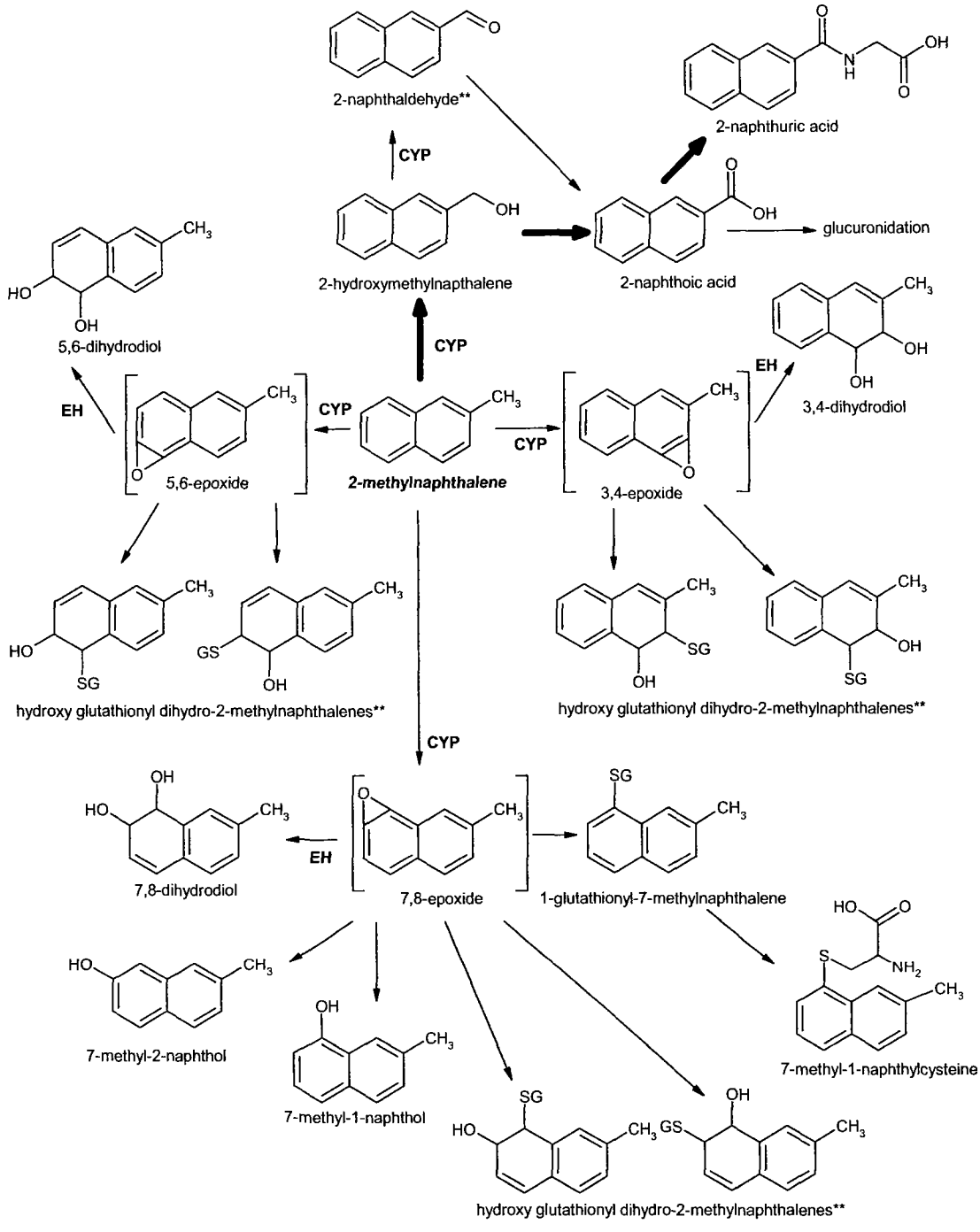
Support for the *in vivo* formation of another potentially reactive metabolite, 1,2-dihydroxy-3,4-epoxy-1,2,3,4-tetrahydronaphthalene, comes from the identification of several urinary metabolites, including a number of trihydroxytetrahydromethylthio derivatives (Horning et al. 1980) and a trihydroxytetrahydro-mercapturic acid (Pakenham et al. 2002). These urinary metabolites, however, are minor, and the importance of their common proposed precursor in naphthalene toxicity is unstudied to date. Figure 3-3 proposes an oxidative transformation of dihydrodiol derivative to the tetrahydrodiol epoxide derivative via CYP catalysis.

The methyl substituent of 1-methylnaphthalene and 2-methylnaphthalene presents the opportunity for side chain oxidation reactions in addition to the ring oxidation, which is the sole initial step in naphthalene metabolism. A proposed metabolic scheme for 2-methylnaphthalene is shown in Figure 3-4. Oxidation at the methyl group (the predominant path), or at several competitive positions on the rings, is catalyzed by CYP monooxygenases (Figure 3-4). No information was located that documented the metabolism of 1-methylnaphthalene. It may be similar to that for 2-methylnaphthalene with oxidation of the side chain and the ring.

In rats and mice, about 50–80% of 2-methylnaphthalene is oxidized at the 2-methyl group to produce 2-hydroxymethylnaphthalene (Breger et al. 1983; Teshima et al. 1983). This 2-hydroxymethyl-naphthalene metabolite is further oxidized to 2-naphthoic acid (Grimes and Young 1956; Melancon et al. 1982; Teshima et al. 1983), and this step proceeds either directly or through the intermediate, 2-naphthaldehyde (Figure 3-4). Detection of 2-naphthaldehyde has only been reported following *in vitro* incubation of 2-methylnaphthalene with recombinant mouse CYP2F2 (Shultz et al. 2001). 2-Naphthoic acid may be conjugated with either glycine or glucuronic acid (Figure 3-4). The glycine conjugate of 2-naphthoic acid forms 2-naphthuric acid, which is the most prevalent urinary metabolite of 2-methyl-naphthalene detected in exposed animals (Grimes and Young 1956; Melancon et al. 1982; Teshima et al. 1983).

Ring epoxidation at the 7,8-, 3,4-, or 5,6- positions occurs in approximately 15–20% of 2-methyl-naphthalene (Breger et al. 1983; Melancon et al. 1985). These epoxidation reactions are catalyzed by CYP isozymes that include CYP1A and CYP1B. These epoxides are proposed intermediates based on experimentally-observed metabolites, but have not been individually isolated (Figure 3-4). These epoxides may be further oxidized by epoxide hydrolase to produce dihydrodiols (the 7,8-dihydrodiol, 3,4-dihydrodiol, or 5,6-dihydrodiol of 2-methylnaphthalene) or may be conjugated with glutathione (Griffin et al. 1982; Melancon et al. 1985) by glutathione S-transferase catalysis or can proceed

Figure 3-4. Metabolism of 2-Methylnaphthalene*



[ ] = putative metabolite; CYP = cytochrome P450 enzyme(s); EH = epoxide hydrolase; GS = glutathione

*Adapted from Buckpitt and Franklin (1989), EPA (2003r); Shultz et al. (2001), and Teshima et al. (1983)
**Metabolites identified *in vitro* only

spontaneously. The hydroxy glutathionyl dihydro-2-methylnaphthalenes (Figure 3-4) have been detected after incubation of 2-methylnaphthalene with hepatic microsomes from Swiss-Webster mice or with isolated recombinant mouse CYP2F2 enzyme and glutathione S-transferase (Shultz et al. 2001). Figure 3-4 indicates six hydroxy glutathionyl 2-methylnaphthalenes; two are formed for each of the epoxide intermediates (3,4-, 5,6-, and 7,8-epoxides), and each can exist in two enantiomeric forms not shown in Figure 3-4 (Shultz et al. 2001).

Three other minor metabolites formed via the 7,8-epoxide pathway are shown in Figure 3-4. Urinary 1-glutathionyl-7-methylnaphthalene was identified in guinea pigs and by *in vitro* experiments with guinea pig microsomes (Teshima et al. 1983). 7-Methyl-1-naphthol and 7-methyl-2-naphthol were identified in the urine of rats, mice, guinea pigs, and rabbits following oral exposure (Grimes and Young 1956).

In rats administered subcutaneous injections of 2-methylnaphthalene (0.3 mg/kg 2-methyl-[8-^{14}C]-naphthalene), 2-naphthoic acid, and naphthoic acid conjugates were identified in the urine (Melancon et al. 1982). The naphthoic acid and various conjugates of the acid were estimated to account for 36–43% of the radiolabel in collected urine. Most of this (30–35% of radiolabel in urine) was found as a glycine conjugate. The urine contained 3–5% unreacted 2-methylnaphthalene; free dihydrodiols accounted for 6–8% of the label. Unidentified highly polar metabolites comprised another 36–45% of the excreted label. At least three diol derivatives of 2-methylnaphthalene were produced by hepatic microsomes from mice (Griffin et al. 1982) suggesting that the ring oxidation reactions of 2-methylnaphthalene are similar to those for naphthalene. Rat liver microsomes also produced 2-hydroxymethylnaphthalene and three diols from 2-methylnaphthalene (Breger et al. 1981, 1983; Melancon et al. 1985). The three diols were identified as 3,4-dihydrodiol, 5,6-dihydrodiol, and 7,8-dihydrodiol (Breger et al. 1983).

Metabolites isolated in the urine of guinea pigs after oral dosing with tritium labeled 2-methylnaphthalene (10 mg/kg) were 2-naphthoic acid and its glycine and glucuronic acid conjugates (Teshima et al. 1983). These metabolites accounted for 76% of the label in collected urine. Glucuronic acid and sulfate conjugates of 7-methyl-1-naphthol along with *S*-(7-methyl-1-naphthyl)cysteine accounted for 18% of the excreted label. No diol metabolites were identified.

Glutathione conjugation appears to be an important detoxication pathway for 2-methylnaphthalene. Pretreatment of male C57BL/6J mice with 625 mg/kg of diethylmaleate (a depletor of glutathione) 1 hour prior to intraperitoneal administration of 400 mg/kg of 2-methylnaphthalene resulted in mortality in 4/5 mice, whereas treatment without glutathione depletion was not fatal (Griffin et al. 1982). Bronchiolar

necrosis was not observed in male ddY mice given single intraperitoneal injections of 200 mg/kg of 2-methylnaphthalene; pretreatment with the glutathione depletor diethylmaleate (600 µL/kg) 1 hour prior to injections caused "extensive sloughing and exfoliation of bronchiolar epithelial cells" in all animals (5/5) (Honda et al. 1990). In contrast, pretreatment of male DBA/2J mice (5/group) with 625 mg/kg of diethylmaleate did not increase the severity of pulmonary necrosis induced by 400 mg/kg of 2-methylnaphthalene (Griffin et al. 1983). The observed differences among mouse strains in response to depletion of glutathione remain unexplained. Other experiments (without pretreatment) observed decreased tissue or intracellular levels of glutathione in response to exposure to high acute doses of 2-methylnaphthalene, demonstrative of glutathione conjugation (Griffin et al. 1982, 1983; Honda et al. 1990). Similarly, depletion of glutathione (by 35% compared to controls) was detected in primary cultures of female Sprague-Dawley rat hepatocytes treated with 1,000 µM of 2-methylnaphthalene (Zhao and Ramos 1998).

3.4.4 Elimination and Excretion

3.4.4.1 Inhalation Exposure

Little information is available pertaining to the excretion of naphthalene in humans after inhalation exposure to naphthalene. Workers employed in the distillation of naphthalene oil and at a coke plant had peak levels of urinary 1-naphthol 1 hour after finishing a shift. Of three workers and a nonoccupationally exposed group, naphthalene oil distribution plant workers had the highest concentrations of urinary 1-naphthol, with a mean excretion rate of 0.57% mg/hour. Investigators calculated the half-life for the urinary excretion of 1-naphthol as approximately 4 hours (Bieniek 1994). This urinary metabolite may indicate both exposure to naphthalene and low concentrations of 1-naphthol during naphthalene oil distillation (Bieniek 1994). No studies were located that documented excretion in humans after inhalation exposure to 1-methylnaphthalene or 2-methylnaphthalene.

No studies were located that documented excretion in animals after inhalation exposure to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene.

3.4.4.2 Oral Exposure

Little information is available pertaining to the excretion of orally ingested naphthalene by humans. The urine of one patient was tested for naphthalene and its derivatives. Naphthol was found at the time of hospital admission (4 days post-ingestion). Smaller quantities were present 1 day later, but naphthalene

was not detected in later specimens (Zuelzer and Apt 1949). In another instance, the urine of an 18-month-old child was found to contain 1-naphthol, 2-naphthol, 1,2-naphthoquinone, and 1,4-naphthoquinone (but no naphthalene) 9 days after exposure (Mackell et al. 1951). With the exception of the 1,4-naphthoquinone, these metabolites were still detectable on day 13, but not on day 17. These data indicate that urinary excretion of metabolites may be prolonged following exposure. It is important to note, however, that delayed dissolution and absorption from the gastrointestinal tract may also be a contributing factor. Unabsorbed naphthalene was visible in the fecal matter after ingestion of naphthalene flakes or mothballs in several individuals (Zuelzer and Apt 1949).

In nonhuman primate studies, Rhesus monkeys given naphthalene at oral doses up to 200 mg/kg did not excrete naphthalene as thioethers in urine or feces (Rozman et al. 1982). In a similar study, chimpanzees orally administered naphthalene at 200 mg/kg did not excrete naphthalene as thioethers in urine (Summer et al. 1979). These data suggest that glutathione conjugation of naphthalene may not occur to any great extent in nonhuman primates. Data from two chimpanzees indicate that most of the naphthalene excreted in this species is excreted as glucuronic acid and sulfate conjugates (Summer et al. 1979).

In rats administered radiolabelled naphthalene, the amount of label recovered in 24 hours was 77–93% in urine and 6–7% in feces (Bakke et al. 1985). There was a dose-dependent increase in urinary thioether excretion following gavage doses of naphthalene at 30, 75, and 200 mg/kg within 24 hours (Summer et al. 1979). The levels of thioethers excreted accounted for approximately 39, 32, and 26% of the three dose levels tested.

No information was located that documented excretion in humans after oral exposure to 2-methylnaphthalene. In guinea pigs, 80% of a 10 mg/kg tritium-labeled dose was excreted in the urine within 24 hours and about 10% was recovered in the feces (Teshima et al. 1983). Most of the excreted material (76%) was found as 2-naphthoic acid or its conjugates. About 18% of the recovered label was found as conjugates of 7-methyl-1-naphthol.

No studies were located that examined excretion in humans or animals after oral exposure to 1-methylnaphthalene.

3.4.4.3 Dermal Exposure

No reports have been located which discuss the excretion of naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene in humans following dermal exposure.

The dermal exposure of rats to ^{14}C-labeled naphthalene was evaluated over a 48-hour period (Turkall et al. 1994). Naphthalene (43 µg) samples were applied to shaved 13-cm^2 areas on the skin under a sealed plastic cap. Neat naphthalene or naphthalene adsorbed to the surface of sandy soil or clay soil was tested. In all three cases, excretion of the label was primarily through the urine (70–87%). With the pure naphthalene and naphthalene adsorbed to clay soil, the exhaled air accounted for 6–14% of the administered label. Exhaled air contained only 0.9% of the label in the sandy soil group. This finding was presumably related to the slower adsorption of naphthalene from the sandy soil and its more rapid metabolism to nonvolatile metabolites. Less than 0.02% of the label was exhaled as carbon dioxide in all groups. The feces contained 2–4% of the label.

The primary metabolites in the urine after dermal application of naphthalene were 2,7-dihydroxy-naphthalene, 1,2-dihydroxynaphthalene, and 1,2-naphthoquinone (Turkall et al. 1994). The ratio of these metabolites for pure naphthalene and naphthalene adsorbed to clay soil were roughly 3:2:1. For the sandy soil, the corresponding ratio was 3:2:1.5. Small amounts of 1-naphthol and 2-naphthol were also excreted. In all cases, the amount of urinary free naphthalene was less than 0.4% of the administered label.

No studies were located that documented excretion in animals after dermal exposure to 1-methyl-naphthalene or 2-methylnaphthalene.

3.4.4.4 Other Routes of Exposure

In mouse studies using the intraperitoneal or subcutaneous exposure routes, several naphthalene metabolites were excreted in the urine. After intraperitoneal administration of 100 mg/kg naphthalene, conjugates accounted for 80–95% of the urinary metabolites (Horning et al. 1980; Stillwell et al. 1982). Much of the conjugated material was present as thioethers (glutathione conjugates and their derivatives). The major oxidation products of naphthalene metabolism were 1-naphthol and trans-1,2-di-hydro-1,2-naphthalenediol.

Following subcutaneous administration of 0.3 mg/kg ^{14}C-labeled 2-methylnaphthalene, 55% was found in the urine of rats (Melancon et al. 1982). Naphthoic acid and its glycine conjugate were identified. Three other metabolites were tentatively identified as isomeric diols.

3.4.5 Physiologically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PD) Models

Physiologically based pharmacokinetic (PBPK) models use mathematical descriptions of the uptake and disposition of chemical substances to quantitatively describe the relationships among critical biological processes (Krishnan et al. 1994). PBPK models are also called biologically based tissue dosimetry models. PBPK models are increasingly used in risk assessments, primarily to predict the concentration of potentially toxic moieties of a chemical that will be delivered to any given target tissue following various combinations of route, dose level, and test species (Clewell and Andersen 1985). Physiologically based pharmacodynamic (PBPD) models use mathematical descriptions of the dose-response function to quantitatively describe the relationship between target tissue dose and toxic end points.

PBPK/PD models refine our understanding of complex quantitative dose behaviors by helping to delineate and characterize the relationships between: (1) the external/exposure concentration and target tissue dose of the toxic moiety, and (2) the target tissue dose and observed responses (Andersen and Krishnan 1994; Andersen et al. 1987). These models are biologically and mechanistically based and can be used to extrapolate the pharmacokinetic behavior of chemical substances from high to low dose, from route to route, between species, and between subpopulations within a species. The biological basis of PBPK models results in more meaningful extrapolations than those generated with the more conventional use of uncertainty factors.

The PBPK model for a chemical substance is developed in four interconnected steps: (1) model representation, (2) model parameterization, (3) model simulation, and (4) model validation (Krishnan and Andersen 1994). In the early 1990s, validated PBPK models were developed for a number of toxicologically important chemical substances, both volatile and nonvolatile (Krishnan and Andersen 1994; Leung 1993). PBPK models for a particular substance require estimates of the chemical substance-specific physicochemical parameters, and species-specific physiological and biological parameters. The numerical estimates of these model parameters are incorporated within a set of differential and algebraic equations that describe the pharmacokinetic processes. Solving these differential and algebraic equations

provides the predictions of tissue dose. Computers then provide process simulations based on these solutions.

The structure and mathematical expressions used in PBPK models significantly simplify the true complexities of biological systems. If the uptake and disposition of the chemical substance(s) are adequately described, however, this simplification is desirable because data are often unavailable for many biological processes. A simplified scheme reduces the magnitude of cumulative uncertainty. The adequacy of the model is, therefore, of great importance, and model validation is essential to the use of PBPK models in risk assessment.

PBPK models improve the pharmacokinetic extrapolations used in risk assessments that identify the maximal (i.e., the safe) levels for human exposure to chemical substances (Andersen and Krishnan 1994). PBPK models provide a scientifically sound means to predict the target tissue dose of chemicals in humans who are exposed to environmental levels (for example, levels that might occur at hazardous waste sites) based on the results of studies where doses were higher or were administered in different species. Figure 3-5 shows a conceptualized representation of a PBPK model.

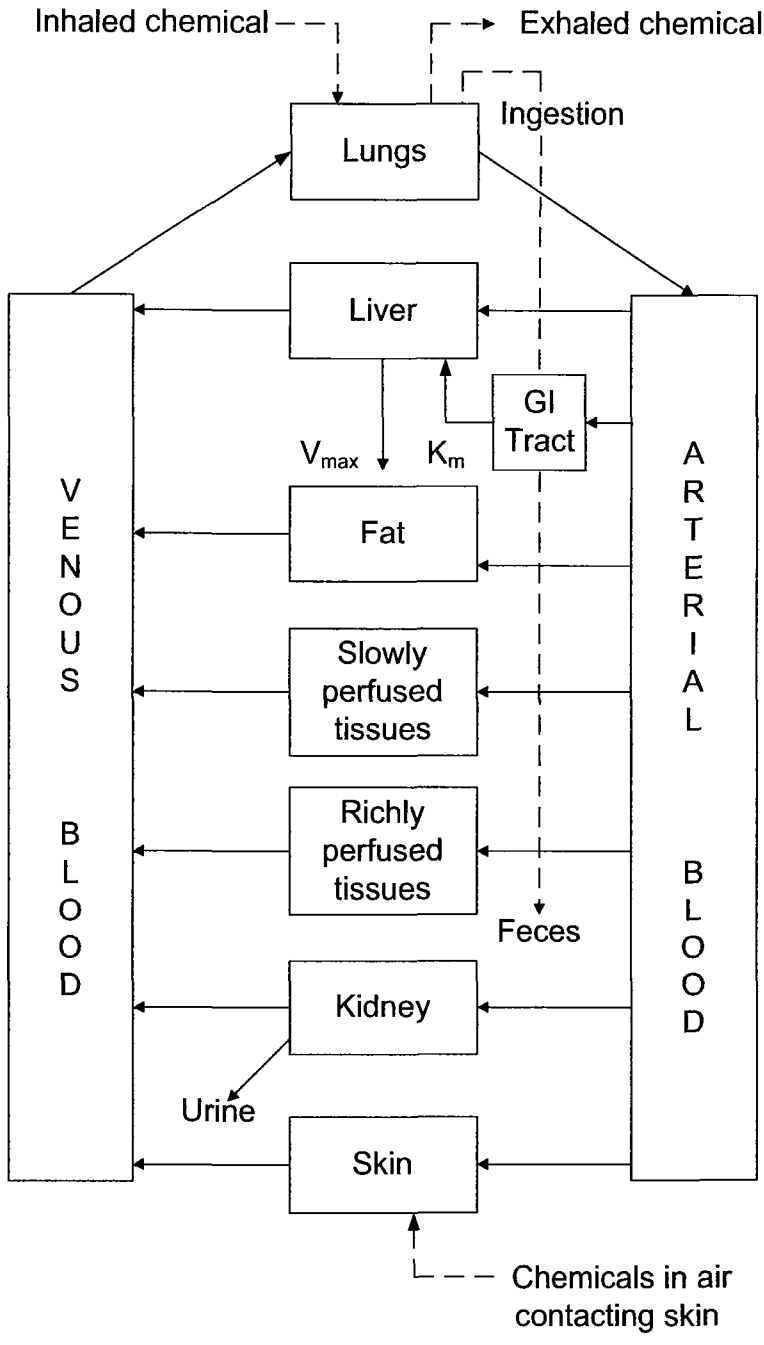
If PBPK models for naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene exist, the overall results and individual models are discussed in this section in terms of their use in risk assessment, tissue dosimetry, and dose, route, and species extrapolations.

This section will discuss the structure and application of the most recent PBPK models for naphthalene that were developed with *in vivo* data for the time-course of naphthalene in blood in rats and mice following inhalation exposure or intravenous administration (Willems et al. 2001). The inhalation data were used to select best-fitting models with the fewest assumptions possible and to optimize model parameters. The intravenous data were used to examine the validity of the final models. These models are refinements of earlier PBPK models for naphthalene in rats and mice, which were developed using parameters estimated from *in vitro* data (Ghanem and Shuler 2000; Quick and Shuler 1999; Sweeney et al. 1996). The most recent models have been used to attempt to explain why naphthalene-induced lung tumors in female B6C3F1 mice, but did not induce lung tumors in F344/N rats in chronic inhalation studies (Abdo et al. 2001; NTP 1992a, 2000). The use of these models to extrapolate dosimetry from rodents to humans is not possible until appropriate validated human physiologically based toxicokinetic (PBTK) models for naphthalene are developed.

The models do not include nasal compartments that metabolize naphthalene, because no data were available on nasal deposition and epithelial absorption of naphthalene (Willems et al. 2001). Without such data, reliable models for nasal deposition, tissue dosimetry, and nasal-tissue metabolism cannot be developed for naphthalene (models similar to those developed for other nasal toxicants such as acrylic acid [Frederick et al. 2001]). The existence of validated PBTK models with metabolizing nasal compartments would be useful to help to explain why male and female rats develop nasal tumors with chronic inhalation exposure to naphthalene, but mice do not, even though both species develop nonneoplastic lesions in the nasal tissues in which tumors developed in rats (Abdo et al. 2001; NTP 1992a, 2000). In addition, development of human models incorporating anatomical and physiological characteristics of nasal tissue will be useful to decrease uncertainty in extrapolating dose-response relationships for nasal effects in rodents to humans.

The final best-fitting models for rats and mice are comprised of two parts: (1) a diffusion-limited naphthalene submodel with compartments for arterial and venous blood, alveolar space, and tissue and capillary spaces for the lung, liver, kidney, fat, and other organs (with naphthalene metabolism occurring in the liver and lung by the same CYP isozyme with one set of Michaelis-Menten metabolic rate constants); and (2) a flow-limited 1,2- naphthalene oxide submodel describing metabolism and distribution of naphthalene oxide in the same compartments as in the naphthalene submodel (but without tissue capillary spaces) (Willems et al. 2001). Physiological parameters in both submodels (e.g., cardiac output, ventilation rates, tissue volumes, tissue capillary volumes, tissue blood flows) were taken from the literature and scaled to body weights of rats in the NTP (2000) bioassay and reference values for mice. Partition coefficients between the various compartments were calculated from octanol-water partition coefficients. Metabolic rate constants (Vmax and Km) and permeability constants (blood:fat and blood:other tissues) for naphthalene were estimated by fitting the models to naphthalene blood time-course data from the inhalation studies. The naphthalene oxide submodel was essentially the same as that developed by Quick and Shuler (1999) with *in vitro* data, with the exception that it contained a subroutine for reduced glutathione synthesis involving γ-glutamylcysteine synthetase modeled with Michaelis-Menten rate constants and noncompetitive inhibition by reduced glutathione. The metabolic fate of naphthalene oxide in the lung and liver was restricted to dihydrodiol formation via epoxide hydrolase and conjugation to glutathione via glutathione-*S*-transferase. The model did not include spontaneous conversion of naphthalene oxide to 1-naphthol or metabolic transformations to the naphthoquinones. Because no *in vivo* data were available on naphthalene oxide distribution or metabolism, the model predictions for naphthalene oxide tissue dosimetry could not be verified.

Figure 3-5. Conceptual Representation of a Physiologically Based Pharmacokinetic (PBPK) Model for a Hypothetical Chemical Substance



Source: adapted from Krishnan et al. 1994

Note: This is a conceptual representation of a physiologically based pharmacokinetic (PBPK) model for a hypothetical chemical substance. The chemical substance is shown to be absorbed via the skin, by inhalation, or by ingestion, metabolized in the liver, and excreted in the urine or by exhalation.

Under exposure conditions used in the rat (0, 10, 30, or 60 ppm) and mouse (0, 10, or 30 ppm) NTP (1992a, 2000) chronic inhalation bioassays with naphthalene (6 hours/day), the models predicted that: (1) steady-state lung concentrations of the parent compound, naphthalene, were not very different in rats and mice at equivalent exposure concentrations; (2) cumulative daily naphthalene metabolism in the lung was greater in the mouse than in the rat (by about 1.5- to 2.5-fold) at equivalent exposure concentrations; (3) cumulative daily naphthalene metabolism in the lung (64.9 mg/kg) and estimated maximal lung concentrations of naphthalene oxide (about 12 nmol/mL) for 30-ppm female mice, some of which developed lung tumors, were greater than respective values of 45.9 mg/kg and about 8 nmol/mL in 60-ppm female rats, which did not develop lung tumors; and (4) cumulative daily naphthalene metabolism in the lung was only slightly greater in 30-ppm female mice (64.9 mg/kg) than in the 30-ppm male mice (60.7 mg/kg), which did show statistically significant increased incidence of lung tumors (comparisons of lung concentrations of naphthalene oxide in female and male mice were not reported).

The model simulations are consistent with the hypothesis that the difference in lung tumor response between mice and rats may be due to a combination of greater maximal levels of naphthalene oxide or other metabolites in the mouse lung and, perhaps, a greater susceptibility of the mouse lung to epoxide-induced carcinogenesis. Results with other chemicals, such as ethylene oxide, suggest that the mouse lung may be more susceptible to epoxides than the rat lung (Willems et al. 2001). Differences in predicted cumulative lung metabolism of naphthalene in 30-ppm female mice and 30-ppm male mice were smaller than the difference noted between 30-ppm female mice and 60-ppm female rats; thus the model simulations do not explain the apparent gender difference in tumor response of the mouse lung. The formation of naphthoquinone metabolites was not included in the model. Thus, the model simulations do not provide a basis for identifying which metabolite is responsible for the nonneoplastic and neoplastic responses to naphthalene in the female mouse lung.

3.5 MECHANISMS OF ACTION

3.5.1 Pharmacokinetic Mechanisms

Absorption. No studies were located regarding the mechanisms by which naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene are absorbed from the guts, lungs, or skin. Although absorption of these compounds at these sites has been demonstrated, it is unknown if the transport is passive, active, or carried out by a facilitated diffusion mechanism. The relatively small molecular weights and lipophilicity of these compounds indicate that passive diffusion across cell membranes is a possible mechanistic path.

There is some evidence that different vehicles may influence the rate and extent of gastrointestinal or dermal absorption. Naphthalene adsorbed to organic-rich soils was absorbed across the skin more slowly than naphthalene from organic-poor soils (Turkall et al. 1994).

Distribution. As discussed in more detail in Section 3.4.2, there are limited data on the distribution of naphthalene and 2-methylnaphthalene in animals following oral or parenteral administration, but there are no data for these compounds following inhalation exposure or for 1-methylnaphthalene by any exposure route. The available data are inadequate to characterize the mechanisms by which 2-methylnaphthalene may be transported following oral exposure to the lung, the site of toxic action with acute or chronic exposure. No data are available on differences in deposition and absorption of inhaled naphthalene in nasal epithelial tissue, two of which (olfactory epithelium and respiratory epithelium) are key toxicity targets in rats and mice following chronic inhalation exposure to naphthalene.

Metabolism. As discussed in more detail in Section 3.4.3, results from *in vitro* and *in vivo* metabolic studies in mammalian systems indicate that naphthalene metabolism is complex, with multiple competing pathways leading to the formation of several reactive metabolites (e.g., 1,2-naphthalene oxide, 1,2-naphthoquinone, and 1,4-naphthoquinone) and an array of conjugated and nonconjugated metabolites that are excreted predominantly in the urine. Conjugation of the reactive metabolites is viewed as a detoxifying mechanism for the reactive metabolites. With oral exposure, the liver is expected to be the principal site of metabolism, but metabolism of naphthalene at other tissue sites, including the nasal olfactory epithelium, Clara cells in pulmonary epithelial tissue, and eye tissue, has been demonstrated. A first-pass metabolic effect due to liver metabolism is expected with oral exposure, but the degree to which a first-pass effect due to respiratory tissue metabolism occurs with inhalation exposure to naphthalene has not been studied quantitatively.

Section 3.4.3 also discusses in more detail the complexity of 2-methylnaphthalene metabolism, which, in contrast to naphthalene, involves several competing initial steps: oxidation of the methyl side group and oxidation at several positions on the rings. Oxidation of the methyl side group is the principal metabolic pathway, representing about 50–80% of administered doses in animal studies. An array of conjugated and nonconjugated metabolites that are principally excreted in the urine have been identified in animal studies. Although conjugation of metabolites (principally with glutathione) appears to be a detoxication mechanism with acute exposure in animal studies, the involvement of reactive metabolites in the development of pulmonary alveolar proteinosis from chronic exposure to 2-methylnaphthalene is

uncertain (see Section 3.5.2). No studies were located on the metabolism of 1-methylnaphthalene in humans or animals, but it is expected to be similar to 2-methylnaphthalene metabolism based on its similar chemical, physical, and toxicological properties.

Excretion. As discussed in more detail in Section 3.4.4, results from animal studies involving oral or parenteral exposure indicate that naphthalene and 2-methylnaphthalene are principally excreted as metabolites in urine. Excretion in the feces represents a minor excretion pathway for these chemicals, and the possibility of excretion via exhalation of unmetabolized parent compounds has not been examined in available studies. Data for 1-methylnaphthalene were not located, but excretion is likely to be similar to 2-methylnaphthalene given the similarity in chemical and physical properties of these chemicals.

3.5.2 Mechanisms of Toxicity

Some information on the mechanism of toxicity is available for three of the health effects associated with naphthalene exposure: hemolysis, the development of lens opacities (cataracts), and nonneoplastic and neoplastic respiratory tract lesions. Mechanistic hypotheses for these naphthalene-induced effects are discussed below, followed by a discussion of the limited mechanistic information on 1-methyl-naphthalene- and 2-methylnaphthalene-induced pulmonary alveolar proteinosis.

Naphthalene-induced Hemolysis. Humans experience red-cell hemolysis after naphthalene exposure by the inhalation, oral, and dermal routes. In general, animal species are less susceptible than humans. There are no reports of naphthalene-induced hemolysis in either rats or mice; however, hemolysis has been observed in dogs.

Chemically induced red blood cell hemolysis is caused by a breakdown of the system that protects the erythrocyte biomolecules from oxidation. In the erythrocyte, glutathione peroxidase rather than catalase is the major antioxidant enzyme. Glutathione peroxidase (Gpx) is a selenium containing metalloprotein that utilizes reduced glutathione as a cofactor. Oxidized glutathione is reduced by glutathione reductase, a nicotinamide adenine dinucleotide phosphate (NADPH)-requiring enzyme.

The primary source of erythrocyte NADPH is glucose-6-phosphate oxidation by the enzyme G6PD. Individuals who suffer from a genetic defect resulting in a modified enzyme structure (a recessive trait) have a reduced capacity to produce NADPH. Accordingly, they are more susceptible to red cell

hemolysis than individuals without this defect (Gosselin et al. 1984). There is some evidence that heterozygotes may also have an increased susceptibility to red cell hemolysis (Dawson et al. 1958).

When the red blood cell is exposed to oxidizing agents, heme iron is oxidized to the ferric state, producing methemoglobin. This in turn leads to Heinz body formation. It is believed that free radical oxygen modifies membrane lipids leading to increased membrane fragility and lysis. Destruction of the red blood cells decreases erythrocyte counts and stimulates hematopoiesis (leading to increased numbers of reticulocytes). The oxygen carrying capacity of the blood is reduced. Cell lysis releases heme and protein into the blood. Heme breakdown produces bilirubin and biliverdin, causing jaundice. Both erythrocytes and heme breakdown products (urobilinogen) spill into the urine.

Several suggestions can be made regarding the impact of naphthalene on this sequence of events. Since naphthalene is conjugated with glutathione for excretion, it can reduce the supplies of glutathione available for glutathione peroxidase and increase the vulnerability of the cell to oxidation. It is also possible that a naphthalene metabolite may act as an inhibitor for either glutathione peroxidase or glutathione reductase. Glutathione reductase activity was reduced in children who experienced hemolysis following dermal exposure to naphthalene and in related family members (Dawson et al. 1958). Both glutathione peroxidase and glutathione reductase activity were decreased in the lens of rats orally exposed to naphthalene (Rathbun et al. 1990; Tao et al. 1991).

Each of the hypotheses discussed above would serve to increase the sensitivity of any naphthalene-exposed subject to an external oxidizing agent. However, given the severity of the hemolysis that follows naphthalene exposure, it is probable that naphthalene or a naphthalene metabolite also acts as an oxidizing agent in the erythrocyte. Unfortunately, data could not be identified which would correlate the production of any particular metabolite with initiation of red cell peroxidation.

Naphthalene-induced Cataracts. Although there are reports that inhalation, oral, and dermal naphthalene exposure in humans can lead to lens opacities (Grant 1986), the case studies or industrial exposure reports that link naphthalene to cataracts in humans have not been verified by well-conducted epidemiological studies of individuals exposed to naphthalene vapors on a chronic basis. In addition, impurities present in the naphthalene may have contributed to the cataract development in all recorded human cases. Conversely, there are data from a number of well-conducted studies which demonstrate that naphthalene can induce cataracts in animals.

Much of the animal data regarding ocular effects suggest that the toxicity of naphthalene is mediated by the *in situ* formation of 1,2-naphthalenediol in the lens. It has been proposed that metabolism of naphthalene starts in the liver, yielding epoxide metabolites that are subsequently converted to stable hydroxy compounds that circulate to the lens (Van Heyningen and Pirie 1967). The 1,2-naphthalenediol metabolite is subsequently oxidized to 1,2-naphthaquinone and hydrogen peroxide. The quinone metabolite binds to constituents of the lens (protein, amino acids, and glutathione), disrupting its integrity and transparency (Rees and Pirie 1967; Uyama et al. 1955; Van Heyningen and Pirie 1967; Van Heyningen 1976, 1979; Wells et al. 1989).

Intraperitoneal administration of naphthalene (125–1,000 mg/kg), 1-naphthol (56–562 mg/kg), 1,2-naphthoquinone (5–250 mg/kg), and 1,4-naphthoquinone (5–250 mg/kg) caused a dose-related increase in cataracts in C57BL/6 mice, but administration of 2-naphthol (56–456 mg/kg) did not (Wells et al. 1989). The cataractogenic potency of the naphthoquinones was about 10 times that of naphthalene. The cataractogenic potency of 1-naphthol was intermediate to that of naphthalene and the naphthoquinones. The potency of naphthalene was increased by pretreatment with cytochrome P-450 inducers and a glutathione-depleting agent. It was inhibited by pretreatment with a cytochrome P-450 inhibitor. This suggests that the unconjugated oxidized naphthoquinone metabolites are a necessary prerequisite for cataract formation. There are differences in species and strain susceptibility to cataract formation that theoretically relate to the animals' ability to form these metabolites. Naphthalene, 1-naphthol, 1,2-naphthoquinone, and 1,4-naphthoquinone did not form cataracts in DBA/2 mice suggesting the difference between strains is not simply due to metabolite exposure (Wells et al. 1989).

Because hydrogen peroxide is also formed following the oxidation of 1,2-dihyroxynaphthalene, peroxides may play a role in naphthalene-induced ocular damage. Increased levels of ocular lipid peroxides were noted in rats given incremental doses of naphthalene which increased from 100 to 750 mg/kg/day during a 9 week period (Germansky and Jamall 1988). The antioxidants caffeic acid (527 mg/kg) and vitamin E (250 mg/kg), which have free radical protection properties, and the free radical spin trapping agent α-phenyl-N-t-butylnitrone (PBN) (518 mg/kg) diminished the incidence of cataracts in animals given 750 mg/kg naphthalene (Wells et al. 1989). There were no cataracts in the rats given only PBN.

Support for this mechanism of cataract formation was provided by a gavage study in which five rat strains (pigmented and albino) were given 500 mg/kg/day naphthalene for 3 days and 1,000 mg/kg/day for the remainder of the 28-day treatment period (Xu et al. 1992b). After 3 weeks, there was a decrease in reduced glutathione (GSH) in the lens, an increase in protein-glutathione mixed disulfides, and an

increase in high molecular weight insoluble proteins (Xu et al. 1992a, 1992b). The only metabolite detected in the aqueous humor of the lens was 1,2-dihydro-1,2-naphthalenediol. The authors hypothesized that 1,2-dihydro-1,2-naphthalenediol was oxidized to 1,2-naphthalenediol and then to 1,2-naphthoquinone. The 1,2-naphthoquinone is believed to be responsible for the chemical changes in the eyes either through crosslinking reactions or by generating free radicals (Xu et al. 1992a). All of the rats developed cataracts.

The complete mechanism for this sequence of reactions is not clear. In *in vitro* studies of cataract formation, 1,2-dihydro-1,2,naphthalenediol was the only metabolite that resulted in cataracts that were morphologically the same as those generated *in vivo* (Xu et al. 1992a). Although 1,2-naphthalenediol and naphthoquinone also formed cataracts in lens culture studies, the opacities were located in the outer layer of the cortex rather than inside the lens. Also, the permeability of the cultured lens to the metabolites in the media may have contributed to the differences in lesion location.

When the aldose reductase inhibitor, AL01576, was given to rats along with the same naphthalene doses, no cataracts developed (Xu et al. 1992a, 1992b). Aldose reductase is an enzyme found in the lens, liver, and peripheral neurons that reduces aldehyde sugars such as glucose to their corresponding alcohols (McGilvery 1983). It is believed to oxidize 1,2-naphthalenediol to 1,2-naphthoquinone; therefore, when this reaction is inhibited, the quinone hypothetically does not form and there is no eye damage (Xu et al. 1992a). Support for this hypothesis includes observations that aldose reductase inhibitors inhibit cataract formation in naphthalene-exposed rats (Tao et al. 1991; Xu et al. 1992a), dihydrodiol dehydrogenase is apparently absent in rat lens (Greene et al. 2000), and aldose reductase appears to be the only enzyme in rat lens that can transform 1,2-dihydroxy-1,2-dihydronaphthalene to 1,2-naphthoquinone (Sugiyama et al. 1999).

Naphthalene-induced Nonneoplastic and Neoplastic Respiratory Tract Lesions. The mechanisms by which naphthalene affects mouse lung epithelial tissue and mouse and rat nasal epithelial tissue are thought to involve metabolic intermediates that can react with tissue macromolecules: 1,2-naphthalene oxide, 1,2-naphthoquinone, and 1,4-naphthoquinone (Buckpitt et al. 2002). The innate reactivity of 1,2-naphthalene oxide is demonstrated by a half-life of approximately 2–3 minutes in buffer at pH 7.4; the half-life is extended by the presence of albumins to about 11 minutes (Buckpitt et al. 2002; Kanekal et al. 1991). The reactivity of 1,2-naphthoquinone has been demonstrated by its ability to form N7-adducts with deoxyguanosine under acidic conditions (McCoull et al. 1999). A second mode by which 1,2-naphthoquinone may damage tissue macromolecules involves redox cycling of the ortho-quinone

moiety and the subsequent generation of reactive oxygen species, which can lead to lipid peroxidation, consumption of reducing equivalents, oxidation of DNA, or DNA strand breaks (Bolton et al. 2000). 1,2-Naphthoquinone caused hydroxyl radical formation and DNA strand scission in buffered solutions in the presence of NADPH and $CuCl_2$ (Flowers et al. 1997), was directly mutagenic in *S. typhimurium* (Flowers-Geary et al. 1996), and directly induced sister chromatid exchanges in human mononuclear leukocytes (Wilson et al. 1996). The comparative importance of these reactive metabolic intermediates of naphthalene in producing nonneoplastic and neoplastic lesions in lung or nasal epithelial tissue is unknown, although the difference between mice and rats in susceptibility to naphthalene-induced lung damage has been associated with greater rates of naphthalene transformation to epoxides and the formation of a different enantiomeric form of 1,2-naphthalene oxide in mice compared with rats.

A fourth reactive metabolic intermediate, 1,2-dihyroxy-3,4-epoxy-1,2,3,4-tetrahydronaphthalene, has been proposed based on molecular structure characterizations of some urinary metabolites (Horning et al. 1980; Pakenham et al. 2002), but these metabolites represent minor metabolic fates of naphthalene and the potential importance of their proposed precursor in naphthalene toxicity is unstudied to date.

Mice are markedly more susceptible than rats to acute naphthalene-induced Clara cell injury (Buckpitt et al. 1992; West et al. 2001), as well as to lung inflammation and tumor development from chronic inhalation exposure (Abdo et al. 2001; NTP 1992a, 2000). The species difference in lung susceptibility has been correlated with higher rates of formation of a specific enantiomeric epoxide (1*R*,2*S*-naphthalene oxide) in lung microsomes and isolated dissected airways of mice compared with rats (Buckpitt et al. 1992, 1995). Rat, hamster, and monkey lung microsomes preferentially formed the 1*S*,2*R*-naphthalene oxide enantiomer and showed lower rates of formation of epoxides than mouse lung microsomes (Buckpitt et al. 1992). Microsomes from human lymphoblastoid cells expressing recombinant human CYP2F1 also showed preferential formation of the 1*S*,2*R*-naphthalene oxide enantiomer, providing some evidence that human transformation of naphthalene to reactive epoxides in lung tissue may be more like rats than mice (Lanza et al. 1999).

Although these observations on epoxide formation suggest that naphthalene may be metabolized to epoxide intermediates at faster rates and with different stereoselectivity in the mouse lung than in the human lung, the toxicologic significance of this species difference is uncertain. The uncertainty arises due to the possibility (and potential toxicological importance) of species differences in several steps in downstream metabolism including glutathione conjugation of the epoxide, transformation to the dihydrodiol via epoxide hydrolase, and transformations to 1,2- or 1,4-naphthoquinone. For example,

human liver microsomes have been reported to be more proficient at converting naphthalene to the dihydrodiol metabolite than rat and mouse liver microsomes (Kitteringham et al. 1996). These results suggest that epoxide hydrolase activities may be higher in humans than mice (although they do not necessarily reflect activities in the pertinent naphthalene target tissues) and that this may decrease the potential for epoxide-induced tissue damage in humans relative to mice (see Figure 3-3). However, this difference may cause relatively greater formation of 1,2-naphthoquinone (from the dihydrodiol via dihydrodiol dehydrogenase) in human tissue than in mouse tissue. While the toxicologic significance of such a difference is uncertain, it is possible that humans may be more susceptible than mice, due to the possible involvement of 1,2-naphthoquinone in naphthalene-induced lung injury as suggested by a report that 1,2-naphthoquinone was the predominant naphthalene metabolite covalently bound to proteins obtained from freshly isolated mouse Clara cells incubated for 1 hour with 0.5 mM naphthalene (Zheng et al. 1997). To date, mechanistic understanding of species differences in naphthalene bioactivation in the lung is too incomplete to definitively identify which naphthalene metabolite is responsible for the development of nonneoplastic or neoplastic lung lesions, or to rule out the possible human relevance of naphthalene-induced lung lesions in mice.

Species differences in susceptibility to naphthalene-induced nonneoplastic and neoplastic lesions in the olfactory and respiratory epithelia of the nose have not been correlated with differences in rates of transformation to 1,2-epoxide derivatives in extracts of olfactory tissue (Buckpitt et al. 1992; Plopper et al. 1992a). Rates of epoxide formation showed the order, mouse > rat > hamster, but rats were the most susceptible to acute nasal injury from naphthalene, showing olfactory epithelial necrosis and exfoliation following single intraperitoneal doses as low as 200 mg/kg naphthalene, compared with 400 mg/kg in mice and hamsters (Plopper et al. 1992a). These observations suggest that the reasons for species differences in susceptibility to naphthalene nasal toxicity are complex and do not solely involve differences in the formation of the 1,2-epoxide metabolic intermediates.

Involvement of the naphthoquinone metabolites is possible, but studies comparing species in their ability to form or accumulate reacted derivatives of naphthoquinones (or 1,2-naphthalene oxide) in nasal tissues (i.e., protein adducts) are not available. In blood of rats following gavage administration of single oral doses of naphthalene (100–800 mg/kg), levels of hemoglobin and albumin adducts with 1,2-naphthalene oxide were greater than levels of adducts of 1,2- and 1,4-naphthoquinone (Troester et al. 2002; Waidyanatha et al. 2002). These findings suggest that levels of the epoxide in the rats' blood were greater than levels of the naphthoquinones, but do not provide information on the relative amounts of these reactive metabolites in the target tissue, the nose.

Current information is inadequate to (1) identify which metabolite(s) are responsible for nonneoplastic or neoplastic nasal lesions that develop in rodents following chronic inhalation exposure, (2) explain why nasal tumors develop in rats but not in mice, or (3) rule out the possible human relevance of naphthalene-induced nasal lesions in rats or mice.

Evidence to support a nongenotoxic mode of action in naphthalene carcinogenicity involving sustained cell proliferation following repeated naphthalene-induced tissue damage includes the negative results in the genotoxicity database (see Section 3.3) suggesting that naphthalene and its metabolites (with the likely exception of 1,2-naphthoquinone) are not mutagens, and the findings that naphthalene-induced tumors in mice and rats occur in the same general tissues as those displaying nonneoplastic lesions. Evidence to support a genotoxic mode of action includes the consistently positive results for genotoxic action by 1,2-naphthoquinone and the limited and scattered positive results for genotoxic action by naphthalene in the presence of metabolic activation. Current evidence is not adequate to rule out the possibility of naphthalene genotoxic action or to determine pertinent threshold levels for genotoxic action, due to the absence of studies examining genotoxic end points in naphthalene target tissues, the nose and lung. As suggested by Moore and Harrington-Brock (2000), answering critical questions in human cancer risk assessment involves an understanding of the mode(s) of action of tumor induction in the target tissue(s) at environmentally-relevant concentrations. Such understanding can come from experiments examining genotoxic endpoints in target tissues. These data are not available for naphthalene.

In summary, the available evidence regarding the mechanism(s) by which naphthalene produces neoplastic and nonneoplastic lesions in the respiratory tract of rodents suggests the involvement of reactive metabolites. The identity of this metabolite(s), and evidence of its presence in known target tissues, remains unknown. The finding that mice are more susceptible than rats to naphthalene-induced lung toxicity may correlate with the *in vivo* generation of this reactive intermediate in target tissues. Whether the mechanism by which naphthalene produces neoplastic and nonneoplastic changes in the respiratory tract of rodents involves genotoxicity remains unknown.

1-Methylnaphthalene or 2-Methylnaphthalene-induced Pulmonary Alveolar Proteinosis. Exposure of mice to 1-methylnaphthalene or 2-methylnaphthalene in the diet for 81 weeks induced increased incidences of pulmonary alveolar proteinosis (Murata et al. 1993, 1997). The absence of nonneoplastic lesions in other lung regions or in other tissues indicates that the alveolar region of the lung is a critical and specific toxicity target of chronic oral exposure to 1-methylnaphthalene or 2-methylnaphthalene.

Increased incidences of pulmonary alveolar proteinosis have also been observed in mice exposed to dermal doses of methylnaphthalene (a 2:1 mixture of 2-methylnaphthalene and 1-methylnaphthalene) applied twice weekly for 20–61 weeks (Emi and Konishi 1985; Murata et al. 1992).

There is evidence to suggest that type II pneumocytes are specific cellular targets of the methylnaphthalenes. Pulmonary hyperplasia and hypertrophy of type II pneumocytes in alveolar regions with proteinosis was observed by light microscopy in mice that were repeatedly exposed to dermal doses of methylnaphthalene (119 mg/kg methylnaphthalene twice a week for 30 weeks [Murata et al. 1992]). In this same study, electron microscopic examination showed that alveolar spaces were filled with numerous myelinoid structures that resembled lamellar bodies of type II pneumocytes. This extracellular material was associated with mononucleated giant cells (called balloon cells) containing numerous myelinoid structures, lipid droplets, and electron dense ascicular crystals. The authors hypothesized that, in response to 1-methylnaphthalene or 2-methylnaphthalene, type II pneumocytes produce increased amounts of lamellar bodies due to hyperplasia and hypertrophy, and eventually transform into balloon cells. Balloon cell rupture has been hypothesized to lead to the accumulation of the myelinoid structures in the alveolar lumen. Ultrastructural studies of the pathogenesis of pulmonary alveolar proteinosis from chronic exposure to 2-methylnaphthalene or 1-methylnaphthalene alone were not available. However, the lesions detected by light microscopy following chronic oral exposure to 2-methylnaphthalene or 1-methylnaphthalene alone were very similar to the lesions detected following chronic dermal exposure to the mixture. These similarities suggest that the mechanistic hypotheses prompted by observations for the mixture are relevant to the individual methylnaphthalenes.

The mechanism of targeting type II pneumocytes is consistent with what is generally known regarding the etiology of pulmonary alveolar proteinosis in humans. The disease in humans, characterized by the accumulation of surfactant material in the alveolar lumen, has been hypothesized to be caused by either excessive secretion of surfactant by type II pneumocytes, or disruption of surfactant clearance by macrophages (Lee et al. 1997; Mazzone et al. 2001; Wang et al. 1997). The condition in humans has been associated with pulmonary dysfunction, characterized by decreased functional lung volume, reduced diffusing capacity, and symptoms such as dyspnea and cough. Pulmonary alveolar proteinosis has not been associated with airflow obstruction (EPA 2003; Lee et al. 1997; Mazzone et al. 2001; Wang et al. 1997).

The development of pulmonary alveolar proteinosis in mice appears to require prolonged oral exposure to 2-methylnaphthalene (or 1-methylnaphthalene). Exposure to a dietary concentration of 0.075% 2-methyl-

naphthalene for 81 weeks induced increased incidences of the lesion, but 13-week exposure to concentrations as high as 1.33% 2-methylnaphthalene did not (Murata et al. 1997). No further studies of the temporal development of methylnaphthalene-induced pulmonary alveolar proteinosis are available.

It is unknown whether the parent compounds or metabolites are responsible for the development of methylnaphthalene-induced pulmonary alveolar proteinosis. Type II pneumocytes are enriched in CYP monooxygenases (Castranova et al. 1988), which are involved in metabolizing 2-methylnaphthalene, and it is possible that metabolites may play a role in the pathogenesis of pulmonary alveolar proteinosis. Studies designed to test this hypothesis, however, have not been conducted.

In contrast to chronic oral exposure, which targets alveolar type II pneumocytes, acute intraperitoneal injection of 2-methylnaphthalene into mice targets bronchiolar Clara cells, inducing Clara cell abnormalities, focal or complete sloughing of Clara cells, or complete sloughing of the entire bronchiolar lining (Buckpitt et al. 1986; Griffin et al. 1981, 1982, 1983; Honda et al. 1990; Rasmussen et al. 1986). Mechanistic studies have not provided clear evidence that metabolites are involved in this response to acute exposure to 2-methylnaphthalene. For example, pretreatment of male C57BL/6J mice with phenobarbital (an inducer of CYP2B; 75 mg/kg, 4 days prior) or 3-methylcholanthrene (an inducer of CYP1A; 80 mg/kg, 2 days prior) prior to injection with 400 mg/kg 2-methylnaphthalene reduced the severity of bronchiolar necrosis in all mice compared to those injected without pretreatment (Griffin et al. 1982). However, CYP inhibitors, such as piperonyl butoxide (a mixed monooxygenase inhibitor; 1,000 mg/kg, 30 minutes prior) and SKF 525-A (an inhibitor of CYP1B; 25 mg/kg, 30 minutes prior), had no effect on the severity of the lung lesions. The mechanism of acute Clara cell toxicity of 2-methylnaphthalene may be similar to that of naphthalene, which involves CYP-mediated metabolism via ring epoxidation to reactive species such as the 1,2-naphthalene oxide and 1,2-naphthoquinone (Cho et al. 1995; Greene et al. 2000; Lakritz et al. 1996; Van Winkle et al. 1999). This hypothesis is supported by the finding that 2-methylnaphthalene is less acutely toxic than naphthalene (Buckpitt and Franklin 1989; Cho et al. 1995) and that only a small fraction of 2-methylnaphthalene (15-20%) undergoes metabolic ring epoxidation (Breger et al. 1983; Melancon et al. 1985). Information on the mechanism of the acute response of Clara cells is not expected to be directly related to the pathogenesis of pulmonary alveolar proteinosis from chronic oral or dermal exposure to 2-methylnaphthalene, because in mice chronically exposed to 2-methylnaphthalene or 1-methylnaphthalene for 81 weeks, no evidence for exposure-related bronchiolar Clara cell lesions was found (Murata et al. 1993, 1997). This finding is not surprising, as Clara cells have been shown to develop resistance to the acute toxicity of naphthalene (Lakritz et al.

1996). The possible development of Clara cell resistance to the acute toxicity of 2-methylnaphthalene, however, has not been studied.

Data are limited to support the hypothesis that rats are less sensitive than mice to the lung damage caused by acute exposure to 2-methylnaphthalene. Wistar rats given intraperitoneal doses of 142 mg/kg 2-methylnaphthalene did not develop lung lesions (Dinsdale and Verschoyle 1987). However, bronchiolar necrosis was induced in Swiss-Webster mice injected with the same dose (Rasmussen et al. 1986) and in C57BL/6J and DBA/2J mice injected with 100 mg/kg 2-methylnaphthalene (Griffin et al. 1981, 1982, 1983). No data are available for interspecies comparisons of the chronic toxicity of 1-methynaphthalene or 2-methylnaphthalene.

3.5.3 Animal-to-Human Extrapolations

Naphthalene-induced lesions in nasal epithelia of mice and rats appear to be the critical nonneoplastic effect (i.e., the effect occurring at the lowest exposure level) associated with inhalation exposure to naphthalene. As discussed in Section 3.5.2, studies with microsomes from human and animal cells indicate that there are species differences in specific steps of naphthalene metabolism (Buckpitt et al. 1992; Kitteringham et al. 1996; Lanza et al. 1999), but mechanistic understanding of these differences is too incomplete to effectively argue that they rule out the possible human relevance of naphthalene-induced lung lesions in mice or nasal lesions in rats or mice. Rodents and humans also display distinct differences in nasal anatomy and respiratory physiology that may cause different deposited doses, and subsequently different responses, in human nasal tissue relative to rats or mice. However, the anatomical and physiological differences alone are insufficient to rule out the possible human relevance of naphthalene-induced nasal lesions in rats or mice. For example, rat and human hybrid computational fluid dynamics and PBPK models, developed for acrylic acid, another rodent nasal toxicant, predicted that tissue concentrations of acrylic acid in human and rat nasal tissues would be similar when exposure conditions were the same (Frederick et al. 2001). Current PBPK models for naphthalene do not include nasal compartments that metabolize naphthalene, because no data were available on nasal deposition and epithelial absorption of naphthalene (Willems et al. 2001). In the absence of this type of data or a pertinent validated human PBPK model, it is reasonable to assume that naphthalene-induced nonneoplastic and neoplastic lesions observed in nasal tissues of rats and mice are relevant to humans. Development of rat, mouse, and human hybrid computational fluid dynamics and PBPK models that include metabolizing nasal compartments and the application of the models to extrapolating rat or mouse

nasal doses to humans will likely decrease uncertainty in extrapolating naphthalene health hazards from rodents to humans.

In animals orally exposed to naphthalene, the critical effects appear to be decreased weight gain and clinical signs of toxicity in pregnant rats with acute exposure and decreased body weight in rats with intermediate-duration exposure. Mechanisms associated with these effects are unstudied. Reliable data to preclude the relevance of these effects to humans were not located.

Pulmonary alveolar proteinosis induced in mice following chronic oral exposure to 1-methylnaphthalene or 2-methylnaphthalene is assumed to be relevant to humans, in the absence of data to indicate otherwise. Pulmonary alveolar proteinosis is a condition that has been described in humans, although reports noting associations with human exposure to 1-methylnaphthalene or 2-methylnaphthalene were not located.

3.6 TOXICITIES MEDIATED THROUGH THE NEUROENDOCRINE AXIS

Recently, attention has focused on the potential hazardous effects of certain chemicals on the endocrine system because of the ability of these chemicals to mimic or block endogenous hormones. Chemicals with this type of activity are most commonly referred to as *endocrine disruptors*. However, appropriate terminology to describe such effects remains controversial. The terminology *endocrine disruptors*, initially used by Colborn and Clement (1992), was also used in 1996 when Congress mandated the EPA to develop a screening program for "...certain substances [which] may have an effect produced by a naturally occurring estrogen, or other such endocrine effect[s]...". To meet this mandate, EPA convened a panel called the Endocrine Disruptors Screening and Testing Advisory Committee (EDSTAC), and in 1998, the EDSTAC completed its deliberations and made recommendations to EPA concerning *endocrine disruptors*. In 1999, the National Academy of Sciences released a report that referred to these same types of chemicals as *hormonally active agents*. The terminology *endocrine modulators* has also been used to convey the fact that effects caused by such chemicals may not necessarily be adverse. Many scientists agree that chemicals with the ability to disrupt or modulate the endocrine system are a potential threat to the health of humans, aquatic animals, and wildlife. However, others think that endocrine-active chemicals do not pose a significant health risk, particularly in view of the fact that hormone mimics exist in the natural environment. Examples of natural hormone mimics are the isoflavinoid phytoestrogens (Adlercreutz 1995; Livingston 1978; Mayr et al. 1992). These chemicals are derived from plants and are similar in structure and action to endogenous estrogen. Although the public health significance and

descriptive terminology of substances capable of affecting the endocrine system remains controversial, scientists agree that these chemicals may affect the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body responsible for maintaining homeostasis, reproduction, development, and/or behavior (EPA 1997). Stated differently, such compounds may cause toxicities that are mediated through the neuroendocrine axis. As a result, these chemicals may play a role in altering, for example, metabolic, sexual, immune, and neurobehavioral function. Such chemicals are also thought to be involved in inducing breast, testicular, and prostate cancers, as well as endometriosis (Berger 1994; Giwercman et al. 1993; Hoel et al. 1992).

No studies were located regarding endocrine disruption in human or animals after exposure to naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene.

No *in vitro* studies were located regarding endocrine disruption of naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene.

3.7 CHILDREN'S SUSCEPTIBILITY

This section discusses potential health effects from exposures during the period from conception to maturity at 18 years of age in humans, when all biological systems will have fully developed. Potential effects on offspring resulting from exposures of parental germ cells are considered, as well as any indirect effects on the fetus and neonate resulting from maternal exposure during gestation and lactation. Relevant animal and *in vitro* models are also discussed.

Children are not small adults. They differ from adults in their exposures and may differ in their susceptibility to hazardous chemicals. Children's unique physiology and behavior can influence the extent of their exposure. Exposures of children are discussed in Section 6.6, Exposures of Children.

Children sometimes differ from adults in their susceptibility to hazardous chemicals, but whether there is a difference depends on the chemical (Guzelian et al. 1992; NRC 1993). Children may be more or less susceptible than adults to health effects, and the relationship may change with developmental age (Guzelian et al. 1992; NRC 1993). Vulnerability often depends on developmental stage. There are critical periods of structural and functional development during both prenatal and postnatal life and a particular structure or function will be most sensitive to disruption during its critical period(s). Damage

may not be evident until a later stage of development. There are often differences in pharmacokinetics and metabolism between children and adults. For example, absorption may be different in neonates because of the immaturity of their gastrointestinal tract and their larger skin surface area in proportion to body weight (Morselli et al. 1980; NRC 1993); the gastrointestinal absorption of lead is greatest in infants and young children (Ziegler et al. 1978). Distribution of xenobiotics may be different; for example, infants have a larger proportion of their bodies as extracellular water and their brains and livers are proportionately larger (Altman and Dittmer 1974; Fomon 1966; Fomon et al. 1982; Owen and Brozek 1966; Widdowson and Dickerson 1964). The infant also has an immature blood-brain barrier (Adinolfi 1985; Johanson 1980) and probably an immature blood-testis barrier (Setchell and Waites 1975). Many xenobiotic metabolizing enzymes have distinctive developmental patterns. At various stages of growth and development, levels of particular enzymes may be higher or lower than those of adults, and sometimes unique enzymes may exist at particular developmental stages (Komori et al. 1990; Leeder and Kearns 1997; NRC 1993; Vieira et al. 1996). Whether differences in xenobiotic metabolism make the child more or less susceptible also depends on whether the relevant enzymes are involved in activation of the parent compound to its toxic form or in detoxification. There may also be differences in excretion, particularly in newborns who all have a low glomerular filtration rate and have not developed efficient tubular secretion and resorption capacities (Altman and Dittmer 1974; NRC 1993; West et al. 1948). Children and adults may differ in their capacity to repair damage from chemical insults. Children also have a longer remaining lifetime in which to express damage from chemicals; this potential is particularly relevant to cancer.

Certain characteristics of the developing human may increase exposure or susceptibility, whereas others may decrease susceptibility to the same chemical. For example, although infants breathe more air per kilogram of body weight than adults breathe, this difference might be somewhat counterbalanced by their alveoli being less developed, which results in a disproportionately smaller surface area for alveolar absorption (NRC 1993).

Newborns and infants are thought to be more susceptible to adverse health effects from naphthalene (e.g., hemolytic anemia from acute exposure) because hepatic enzyme systems involved in conjugation and excretion of naphthalene metabolites are not well developed shortly after birth (EPA 1987a). No studies were located, however, that specifically examined the influence of age on naphthalene toxicokinetic capabilities in humans.

Although the occurrence of hemolytic anemia in neonates of anemic, naphthalene-exposed mothers demonstrates that naphthalene and/or its metabolites can cross the placental barrier (Anziulewicz et al. 1959; Zinkham and Childs 1957, 1958), oral-exposure developmental toxicity studies in animals do not provide evidence that naphthalene was fetotoxic or impaired fetal development, even at maternally toxic dose levels as high as 450 mg/kg/day (NTP 1991a; Plasterer et al. 1985; PRI 1986).

Naphthalene has been detected in human milk samples (concentration not reported) (Pellizzari et al. 1982), but no studies were located that have specifically examined the rate or extent of naphthalene distribution to breast milk in exposed humans or animals.

Children with genetically determined glucose-6-phosphate dehydrogenase (G6PD) deficiency are expected to be especially susceptible to the hemolytic action of naphthalene (Owa 1989; Owa et al. 1993; Santucci and Shah 2000; Valaes et al. 1963). In support of this hypothesis, in 21 cases of hemolytic anemia in Greek infants exposed to naphthalene, 10 of the children had a genetically determined deficiency in G6PD (Valaes et al. 1963). In a 10-year chart review of 24 African-American children hospitalized with acute hemolytic anemia, 14 were noted to have been exposed to naphthalene-containing moth repellants (Santucci and Shah 2000). Deficiency in G6PD makes red blood cells more susceptible to oxidative damage from a wide range of causes including naphthalene exposure. Relatively high rates of genetically determined G6PD deficiency have been reported in males of certain subpopulations of Asian, Arabic, Caucasian, African, and African-American ancestry (EPA 1987a).

The limited mobility of infants when they are wearing naphthalene-treated clothing or when they are near other naphthalene-treated articles (e.g., blankets treated with naphthalene-containing moth repellants) may maximize exposure due to the development of a microenvironment with a high level of naphthalene vapor in the space around the infant. The tendency for infants and small children to place small objects, such as mothballs, in their mouths also increases their risk.

An association between elevated maternal exposure to naphthalene and increased maternal cord-blood levels of one of four T cell types, IL-4, has recently been reported (Lehmann et al. 2002). The study looked for possible associations between maternal indoor exposure to 28 volatile organic chemicals (including naphthalene) and putative immune status at birth assessed by cord-blood levels of cytokine-producing T cells [interleukin-4 (IL-4), interleukin-2 (IL-2), interferon-γ (IFN-γ), and tumor necrosis factor-α (TNF-α)]. Levels of 28 volatile organic chemicals in air samples, collected during a 4-week postnatal period in bedrooms of 85 newborn children, were measured as surrogate indices of maternal

indoor exposure. A logistic regression analysis found an elevated odds ratio (OR=2.9; 95% CI 1.0–8.2) for elevated naphthalene air concentrations (>75th percentile) and elevated percentage of IL-4-producing T cells in cord blood. The analysis adjusted for possible confounding factors of family allergic (i.e., atopic) history and maternal smoking during pregnancy. Several other statistically significant associations were found for changes in levels of different types of T cells and air levels of other chemicals, including methylcyclopentane, trichloroethylene, and tetrachloroethylene. The significance of the observed variations in cord blood T cell levels to the immune status of the newborn children is unknown. The findings from this study are inadequate to determine if maternal exposure to naphthalene may influence the immune status of newborn children.

Studies that have examined age-related effects of toxicokinetic variables specifically related to naphthalene are restricted to a study with results indicating that neonatal mice may be more susceptible than adult mice to lung injury from single intraperitoneal doses of 25, 50, or 100 mg/kg naphthalene (Fanucchi et al. 1997). Epithelial damage in terminal bronchioles (principally in the Clara cells) was observed in 7-day-old mice exposed to 25 mg/kg, but was absent in adult mice at the same dose level. In adult mice exposed to 50 mg/kg, injury was only mild and variable (from mouse to mouse) and only became consistent with exposure to 100 mg/kg. Epithelial damage in 14-day-old mice was less severe than the damage in 7-day-old mice. Activities of CYP-mediated naphthalene metabolism in bronchiolar tissues were 2.5 times lower in neonatal mice than in adult mice, suggesting that the difference in susceptibility is not explained by differences in ability to form reactive metabolites alone (e.g., 1,2-naphthalene oxide). Differences between neonates and adults in the balance between formation of reactive naphthalene metabolites and downstream transformations could potentially explain the difference in susceptibility to naphthalene toxicity, but the possibilities for specific, age-related differences in downstream enzyme activities for naphthalene (e.g., epoxide hydrolase, dihydrodiol dehydrogenase) have not been studied to date. Alternatively, toxicodynamic differences may exist between neonatal and adult mice (e.g., different target macromolecules). Based on findings that *in utero* exposure to other chemicals, which are bioactivated by CYP, caused Clara cell tumors in adult offspring, Fanucchi et al. (1997) postulated that naphthalene exposure during the neonatal period, when increased susceptibility to naphthalene-induced cytotoxicity occurs, may lead to loss of regulatory mechanisms resulting in Clara cell proliferation and tumor formation in adult animals, but direct evidence for naphthalene in support of this hypothesis is not available (e.g., demonstration that *in utero* or neonatal naphthalene exposure will cause increased incidence of lung tumors in adult mice).

No direct information was located on the relative susceptibility of children or young animals to 1-methylnaphthalene or 2-methylnaphthalene toxicity, compared with adults. However, clinical experience with humans displaying pulmonary alveolar proteinosis of unknown etiology has indicated that children with this condition experience more severe symptoms and a poor prognosis for survival than do adults (EPA 2003r; Mazzone et al. 2001).

3.8 BIOMARKERS OF EXPOSURE AND EFFECT

Biomarkers are broadly defined as indicators signaling events in biologic systems or samples. They have been classified as markers of exposure, markers of effect, and markers of susceptibility (NAS/NRC 1989).

Due to a nascent understanding of the use and interpretation of biomarkers, implementation of biomarkers as tools of exposure in the general population is very limited. A biomarker of exposure is a xenobiotic substance or its metabolite(s) or the product of an interaction between a xenobiotic agent and some target molecule(s) or cell(s) that is measured within a compartment of an organism (NAS/NRC 1989). The preferred biomarkers of exposure are generally the substance itself or substance-specific metabolites in readily obtainable body fluid(s) or excreta. However, several factors can confound the use and interpretation of biomarkers of exposure. The body burden of a substance may be the result of exposures from more than one source. The substance being measured may be a metabolite of another xenobiotic substance (e.g., high urinary levels of phenol can result from exposure to several different aromatic compounds). Depending on the properties of the substance (e.g., biologic half-life) and environmental conditions (e.g., duration and route of exposure), the substance and all of its metabolites may have left the body by the time samples can be taken. It may be difficult to identify individuals exposed to hazardous substances that are commonly found in body tissues and fluids (e.g., essential mineral nutrients such as copper, zinc, and selenium). Biomarkers of exposure to naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene are discussed in Section 3.8.1.

Biomarkers of effect are defined as any measurable biochemical, physiologic, or other alteration within an organism that, depending on magnitude, can be recognized as an established or potential health impairment or disease (NAS/NRC 1989). This definition encompasses biochemical or cellular signals of tissue dysfunction (e.g., increased liver enzyme activity or pathologic changes in female genital epithelial cells), as well as physiologic signs of dysfunction such as increased blood pressure or decreased lung

capacity. Note that these markers are not often substance specific. They also may not be directly adverse, but can indicate potential health impairment (e.g., DNA adducts). Biomarkers of effects caused by naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene are discussed in Section 3.8.2.

A biomarker of susceptibility is an indicator of an inherent or acquired limitation of an organism's ability to respond to the challenge of exposure to a specific xenobiotic substance. It can be an intrinsic genetic or other characteristic or a preexisting disease that results in an increase in absorbed dose, a decrease in the biologically effective dose, or a target tissue response. If biomarkers of susceptibility exist, they are discussed in Section 3.10, Populations That Are Unusually Susceptible.

Additional information concerning biomarkers for effects on the immune, renal, and hepatic systems can be found in the CDC/ATSDR Subcommittee Report on Biological Indicators of Organ Damage (CDC/ATSDR 1990), and on the neurological system in the Office of Technology Assessment Report on Identifying and Controlling Poisons of the Nervous System (OTA 1990). Additional details concerning the health effects caused by naphthalene can be found in Section 3.2.

3.8.1 Biomarkers Used to Identify or Quantify Exposure to Naphthalene, 1-Methylnaphthalene, and 2-Methylnaphthalene

In cases where humans have swallowed one or more mothballs, it is possible to identify the undissolved naphthalene in the stomach or duodenum by radioluminescence (Woolf et al. 1993). Thus, radiography of the abdominal area is of value in determining if exposure has occurred, especially in children who are often unreliable sources of exposure information. Of the 2,400 cases on naphthalene ingestion reported to 72 Poison Control Centers in the United States, 2,100 involve children less than 6 years old. Radioluminescence has the advantage of differentiating naphthalene-containing solids in the gastrointestinal tract from paradichlorobenzene or other materials used in moth repellants and deodorizers.

Methods are available for the determination of naphthalene in human adipose tissue (EPA 1986g; Liao et al. 1988). In the National Human Adipose Tissue Survey, 40% of the subjects surveyed had measurable levels of naphthalene with concentrations of up to 63 ng/g. Naphthalene and its metabolites can be detected in human and animal urine (Horning et al. 1980; Mackell et al. 1951; Stillwell et al. 1982). Investigators have reported strong correlations between 1-naphthol concentrations in the urine of exposed workers and naphthalene concentrations in the breathing zone air (Bieniek 1994). Peak naphthalene concentrations in the urine occurred immediately after the end of the exposure period and declined

thereafter. In some instances, 1-naphthol concentrations had returned to baseline 8 hours later. Few current data are available relating naphthalene levels in adipose tissue or urine with the human exposure concentrations.

In swine, a good correlation existed between 1-naphthol levels in hydrolyzed urine samples collected in the first and second 24 hours after dosing with as little as 7 µg/kg/day naphthalene (Keimig and Morgan 1986). Thus, 1-naphthol may be an appropriate biomarker for monitoring naphthalene exposures in the occupational setting. Some caution must be exercised in using 1-naphthol as a biomarker of naphthalene exposure in the general population since this metabolite is also excreted after exposure to the common insecticide, carbaryl (Benson and Dorough 1984).

Early work to develop biomarkers of exposure, such as naphthalene mercapturic acid derivatives in urine (Marco et al. 1993) and naphthalene hemoglobin adducts in blood (Cho et al. 1994b), has been extended to develop techniques to measure cysteinyl adducts formed from reactions of hemoglobin and albumin with reactive metabolites of naphthalene (Troester et al. 2002; Waidyanatha et al. 2002). One of the reasons for developing these techniques is that it is difficult to measure reactive metabolites of naphthalene *in vivo*. Using these techniques, hemoglobin and albumin adducts of 1,2-naphthalene oxide, 1,2-naphthoquinone, and 1,4-naphthoquinone were shown to increase with increasing dose in F344 rats given single oral doses of 0, 100, 200, 400, or 800 mg/kg naphthalene (Waidyanatha et al. 2002). The stabilities of the adducts were measured in rats following exposure to naphthalene (Troester et al. 2002). Some were found to be stable and others unstable, although they all were more stable than the reactive metabolites themselves. As such, the adducts are expected to be useful in estimating internal doses of these metabolites.

An analytical method is available to determine levels of 2-methylnaphthalene and its derivatives in rat urine (Melancon et al. 1982). This method would probably also be useful in measuring 2-methyl-naphthalene levels in human urine. Because of the lack of information for 1-methylnaphthalene, it is not possible to identify a biomarker of exposure for this substance.

3.8.2 Biomarkers Used to Characterize Effects Caused by Naphthalene, 1-Methylnaphthalene, and 2-Methylnaphthalene

Hemolytic anemia has been frequently reported to be a consequence of exposure to naphthalene. However, this effect can also occur without exposure to naphthalene, and may not be useful as a specific biomarker of effect.

Clara cell damage may be identified by the presence of naphthalene/protein adducts in lung lavage fluids (Cho et al. 1994a). Additional research is needed to improve the specificity of this technique as a biomarker of effect.

Because of the lack of information for 1-methylnaphthalene or 2-methylnaphthalene, it is not possible to identify a biomarker of effects for these chemicals.

3.9 INTERACTIONS WITH OTHER CHEMICALS

When either naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene was applied dermally in combination with benzo[a]pyrene (BaP), there was an inhibitory effect on the induction of skin tumors in female mice (Schmeltz et al. 1978). These investigators also reported that a mixture containing naphthalene (0.02%), 2-methylnaphthalene (0.02%) and 10 other methylated and ethylated naphthalenes (each at 0.02%) also appeared to inhibit the development of BaP-induced skin tumors. The authors suggested that it is likely that certain naphthalenes compete with BaP for the same enzyme sites, resulting in alteration of the BaP metabolic pathway and decreased production of the active BaP metabolite. This hypothesis is consistent with the observation that benzo(a)pyrene hydroxylase is inhibited by naphthalene (Shopp et al. 1984). Dermal application of the naphthalene mixture did not induce tumors in the absence of BaP. The results of these studies were not analyzed statistically.

Several studies have been conducted to assess factors that influence the toxicity of naphthalene. For the most part, these studies have evaluated the effects of mixed function oxidase activity (MFO) and alterations in glutathione levels on pulmonary and ocular toxicities. The effects of cyclooxygenase activity, antioxidants, and epoxide hydrolase inhibitors on the cataractogenic effect of naphthalene have also been evaluated. The administration of MFO inhibitors (SKF-525A, metyrapone) and antioxidants (caffeic acid and vitamin E) decreased ocular toxicity in mice (Wells et al. 1989). Use of ALO1576, an inhibitor of the enzyme aldose reductase, prevented cataract formation in both *in vivo* and *in vitro* studies

(Xu et al. 1992a, 1992b). On the other hand, naphthalene-induced cataracts were enhanced by pretreatment with a MFO inducer (phenobarbital) and a glutathione depletor (diethyl maleate) (Wells et al. 1989). Pulmonary damage was decreased by prior treatment with a MFO inhibitor (piperonyl butoxide), but enhanced by prior treatment with a glutathione depletor (diethyl maleate) (Warren et al. 1982). For the most part, these studies support the role for mixed function oxidase activity and glutathione conjugation in naphthalene-induced pulmonary and ocular lesions.

Mixed function oxidase inducers also affect the metabolism of 2-methylnaphthalene. Inducers that influence cytochrome P-450 increase the oxidation of the side chain and the concentration of one dihydrodiol. Induction of cytochrome P-450 increased the production of two other dihydrodiols (Melancon et al. 1985). The production of naphthoic acid in preference to the diols may explain why acute exposure to 2-methylnaphthalene is less toxic to Clara cells than acute exposure to naphthalene.

In general, interactions with environmental contaminants, such as polycyclic aromatic hydrocarbons, should be expected at hazardous waste sites. Most hazardous waste sites (with the notable exception of certain pharmaceutical sites) would not be expected to contain substantial volumes of certain types of contaminants, such as antioxidants or cytochrome P-450 inhibitors.

3.10 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

A susceptible population will exhibit a different or enhanced response to naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene than will most persons exposed to the same level of naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene in the environment. Reasons may include genetic makeup, age, health and nutritional status, and exposure to other toxic substances (e.g., cigarette smoke). These parameters result in reduced detoxification or excretion of naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene, or compromised function of organs affected by naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene. Populations who are at greater risk due to their unusually high exposure to naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene are discussed in Section 6.7, Populations with Potentially High Exposures.

The hemolytic response to naphthalene is enhanced by the presence of inherited erythrocyte G6PD deficiency. Although any human may experience acute hemolysis if exposed to a sufficiently high dose of naphthalene, this enzyme deficiency may cause some persons to be unusually sensitive. The incidence

of the deficiency among Caucasians of European origin is relatively low, while there is a higher incidence among certain groups of Asians and Middle Eastern populations. A study of hemolytic anemia in African-American children with G6PD deficiency by Shannon and Buchanan (1982) suggests that this is a population that may be susceptible to the hemolytic effects of naphthalene exposure. It was also reported that 16% of African-American males are G6PD-deficient (Calabrese 1986). According to Shannon and Buchanan (1982), a syndrome of acute severe hemolysis following exposure to oxidative stress is associated with the Mediterranean variant of the deficiency, whereas the hemolytic anemia seen in African-Americans is generally mild.

Results from a recent study indicate that female mice are more susceptible than male mice to lung injury from acute parenteral exposure to naphthalene (Van Winkle et al. 2002). Male and female Swiss-Webster mice were given intraperitoneal injections of 0 or 200 mg/kg naphthalene in corn oil, and lungs were removed at 1, 2, 3, 6, and 24 hours after treatment. Acute lung injury was determined by (1) high-resolution microscopic assessment of differential permeability to fluorescent nuclear dyes in cells along the long axis of conducting airway trees of microdissected right middle lung lobes and (2) high-resolution histopathology of sections of Karnovsky-fixed left lung lobes. Clara cell injury occurred in the terminal bronchioles of both male and female mice. Clara cell injury in terminal bronchioles, however, occurred earlier, affected cells farther up the airway tree, and showed a different temporal pattern of changes in female mice compared with male mice. Twenty-four hours after injection, Clara cell injury in the lobar bronchus of female mice was evidenced by numerous vacuolated cells, whereas normal bronchiolar epithelium containing Clara and ciliated cells was found in vehicle-control males and females, as well as in exposed male mice. Assessment of *in vitro* naphthalene metabolism in microdissected regions of airways from male and female mice by high performance liquid chromatography (HPLC) analysis indicated that the rate of formation of a dihydrodiol metabolite (1,2-dihydroxy-1,2-dihydronaphthalene) was greater in female tissue than in male tissue. This metabolic difference may be related to the apparent gender difference in susceptibility to acute lung injury from naphthalene. It is unknown whether or not the gender difference in susceptibility to acute lung injury is relevant to nasal or lung lesions formed with chronic-duration exposure to naphthalene.

There are no data that indicate whether there are populations that are unusually susceptible to the toxic effects of 1-methylnaphthalene or 2-methylnaphthalene.

3.11 METHODS FOR REDUCING TOXIC EFFECTS

This section will describe clinical practice and research concerning methods for reducing toxic effects of exposure to naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene. However, because some of the treatments discussed may be experimental and unproven, this section should not be used as a guide for treatment of exposures to naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene. When specific exposures have occurred, poison control centers and medical toxicologists should be consulted for medical advice. The following texts provide specific information about treatment following exposures to naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene:

Kurz JM. 1987. Naphthalene poisoning: Critical care nursing techniques. Dimens Crit Care Nurs 6:264-270.

Melzer-Lange M, Walsh-Kelly C. 1989. Naphthalene-induced hemolysis in a black female toddler deficient in glucose-6-phosphate dehydrogenase. Pediatr Emerg Care 5:24-26.

Siegel E, Wason S. 1986. Mothball toxicity. Pediatr Clin North Am 33:369-374.

Stutz DR, Janusz SJ. 1988. Hazardous materials injuries: A handbook for pre-hospital care. Second edition. Beltsville, MD: Bradford Communications Corporation.

3.11.1 Reducing Peak Absorption Following Exposure

If inhalation of naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene has occurred, movement to fresh air is recommended. In cases where a small amount (e.g., one mothball, 0.5–3.6 g) of naphthalene has been ingested, measures are implemented to empty the stomach contents. Syrup of Ipecac, which may be used for this purpose, is administered after ingestion to induce vomiting and is most effective if initiated within a 2-hour period after exposure (Siegel and Wason 1986). If large quantities of naphthalene have been ingested, syrup-of-ipecac-induced vomiting is usually followed by gastric aspiration using a large gauge lavaculator (to remove mothballs) (Kurz 1987). This will only be of value if the naphthalene particles are small enough to be aspirated. Measures are usually taken to protect the respiratory tract from aspiration of gastric contents. Activated charcoal can be given to bind dissolved naphthalene in the gastrointestinal tract. Further treatment with a cathartic (e.g., magnesium sulfate) to speed fecal excretion is recommended (Melzer-Lange and Walsh-Kelly 1989). Milk or fatty meals ingested within 2–3 hours after exposure may increase absorption (Siegel and Wason 1986).

In order to reduce absorption of naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene through the skin, areas of skin that have come in contact with the compound should be washed with soap and water. Application of oil based lotions should be avoided. If these compounds are splashed into the eyes, irrigation with large amounts of water for 15–30 minutes may be useful to wash away unabsorbed material (Stutz and Janusz 1988).

3.11.2 Reducing Body Burden

Some evidence exists that naphthalene metabolites may be retained in the body in adipose tissue (EPA 1986g). Naphthalene was identified in 40% of the samples evaluated for the Human Adipose Tissue Survey (EPA 1986g). Naphthalene metabolites were detected in urine up to 13 days following exposure (Mackell et al. 1951).

The most frequently documented acute toxic effect of naphthalene in humans is red cell hemolysis. In cases of clinically significant hemolysis, accelerated urinary excretion of naphthol metabolites is recommended to protect the kidney from products of hemolysis (EPA 1989d). In cases of renal failure, hemodialysis may be effective in controlling extracellular fluid (plasma) composition (EPA 1989d). It should be noted that this method is not very effective in removing lipophilic compounds from blood. Ocular effects have also been reported in humans; however, there are no specific treatments for reducing the toxic effects on the eyes. Respiratory effects have been observed in animals but these effects have not been reported in humans. Due to lack of data, it is difficult to speculate regarding the benefits of treatments that enhance elimination of naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene and their metabolites as a basis for reducing toxic effects.

3.11.3 Interfering with the Mechanism of Action for Toxic Effects

Existing data indicate that lung, nose, and eye toxicity may be mediated by reactive metabolites for naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene, although the evidence for the involvement of reactive metabolites is greater than the evidence for methylnaphthalenes. More information is needed on the bioactivation of naphthalene and transport mechanisms before methods for blocking those mechanisms can be developed.

Many of the symptoms of acute naphthalene poisoning in humans are a direct consequence of red blood cell hemolysis. Blood transfusions, packed red blood cell transfusions, and exchange transfusions (particularly in infants) can be used to replenish the concentration of red blood cells and diminish the risks of cellular anoxia (Bregman 1954; Chusid and Fried 1955; MacGregor 1954; Mackell et al. 1951). Bicarbonate is also administered to hemolysis patients to increase the alkalinity of the urine and thereby minimize deposition of hemoglobin in the kidney tubules (Chusid and Fried 1955; Gidron and Leurer 1956).

3.12 ADEQUACY OF THE DATABASE

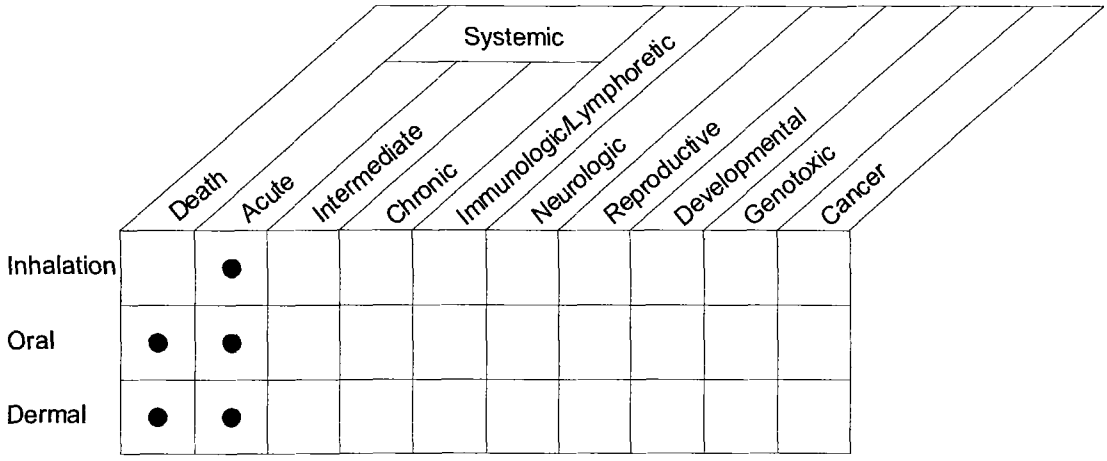
Section 104(I)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene is available. Where adequate information is not available, ATSDR, in conjunction with the National Toxicology Program (NTP), is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

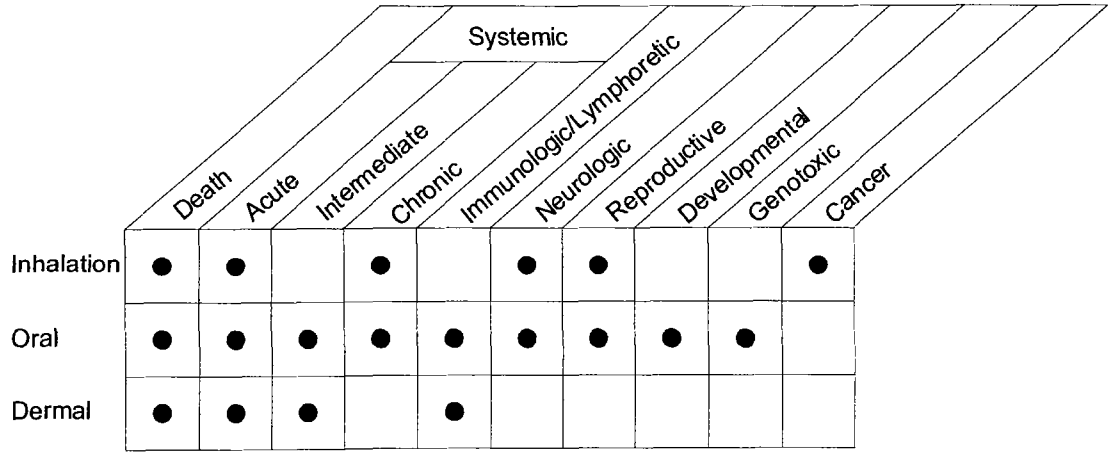
3.12.1 Existing Information on Health Effects of Naphthalene, 1-Methylnaphthalene, and 2-Methylnaphthalene

The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene are summarized in Figures 3-6, 3-7, and 3-8, respectively. The purpose of this figure is to illustrate the existing information concerning the health effects of naphthalene, 1-methylnaphthalene, and 2-methylnaphthalene. Each dot in the figure indicates that one or more studies provide information associated with that particular effect. The dot does not necessarily imply anything about the quality of the study or studies, nor should missing information in

Figure 3-6. Existing Information on Health Effects of Naphthalene



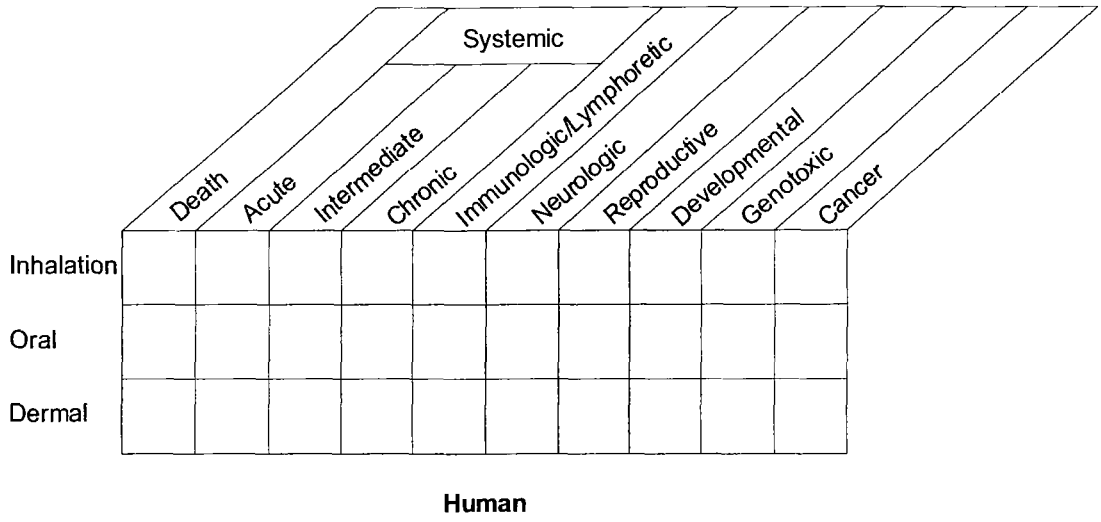
Human



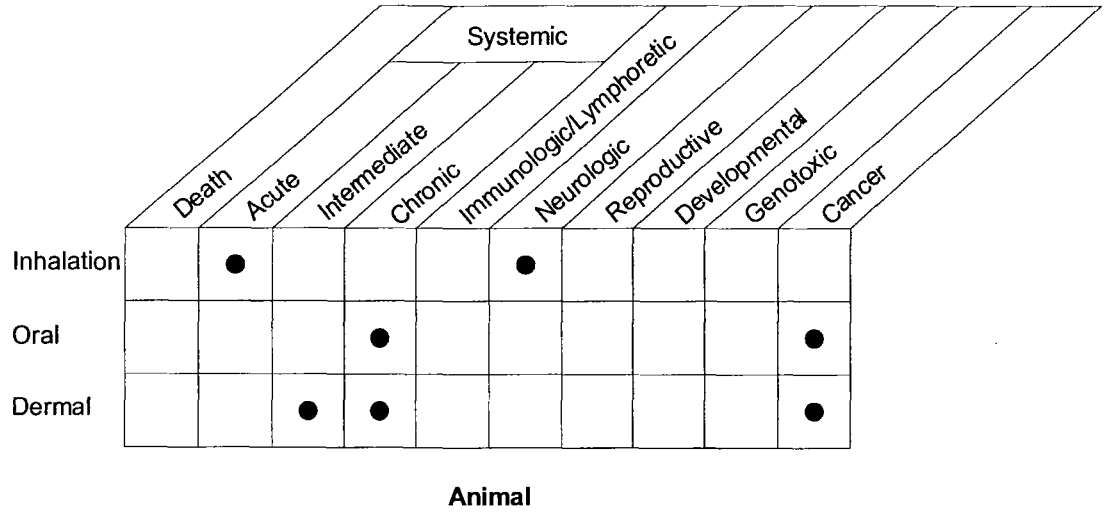
Animal

● Existing Studies

Figure 3-7. Existing Information on Health Effects of 1-Methylnaphthalene



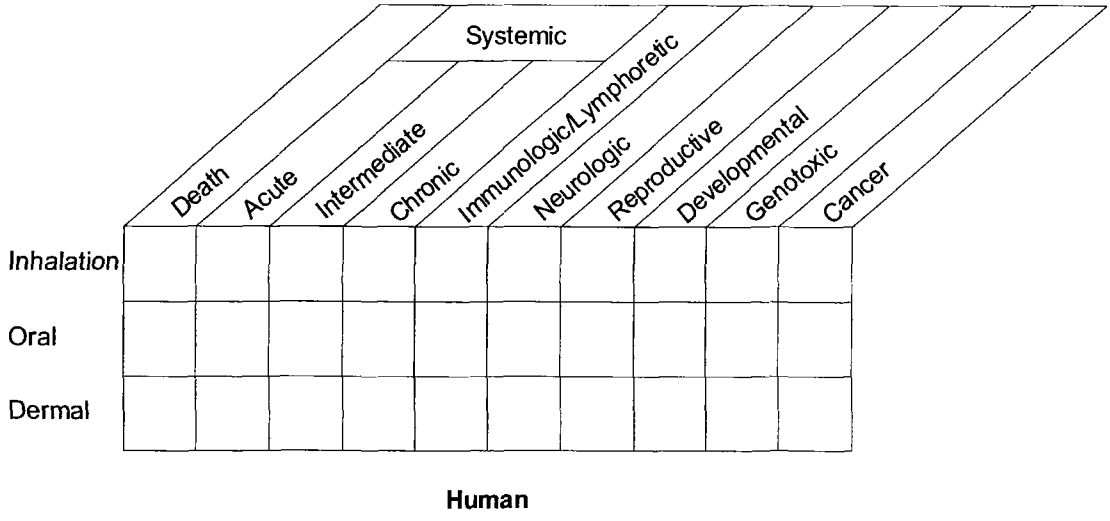
Human



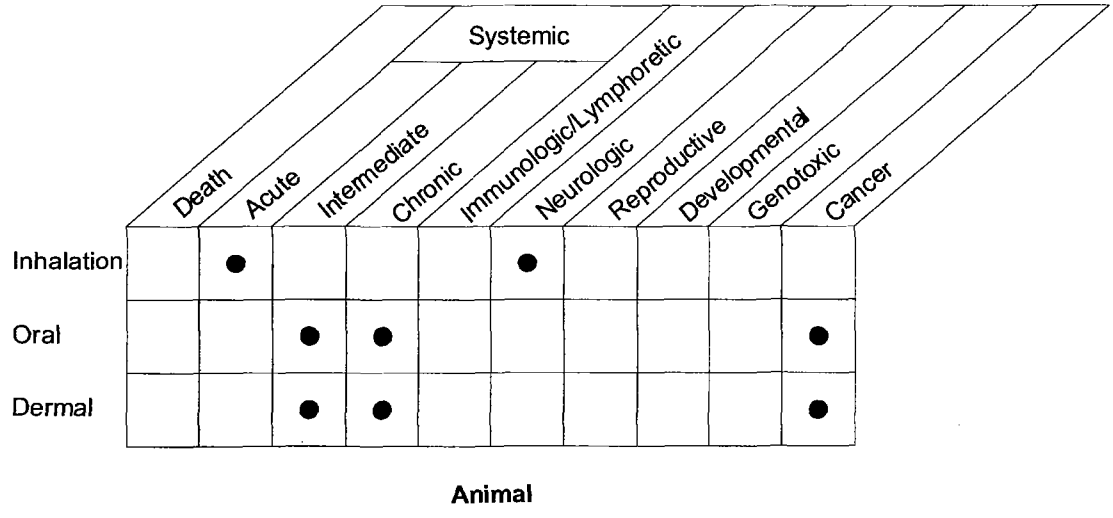
Animal

● Existing Studies

Figure 3-8. Existing Information on Health Effects of 2-Methylnaphthalene



Human



Animal

● Existing Studies

this figure be interpreted as a "data need". A data need, as defined in ATSDR's *Decision Guide for Identifying Substance-Specific Data Needs Related to Toxicological Profiles* (Agency for Toxic Substances and Disease Registry 1989), is substance-specific information necessary to conduct comprehensive public health assessments. Generally, ATSDR defines a data gap more broadly as any substance-specific information missing from the scientific literature.

Figure 3-6 shows that the database on naphthalene toxicity in humans is not extensive. There are case reports and case series of deaths, acute hemolytic anemia, and ocular effects in humans, but these reports lack quantitative information on exposure levels. Epidemiologic studies designed to examine possible associations between intermediate- or chronic-duration human exposure to naphthalene by any route of exposure and neoplastic or nonneoplastic health effects are not available. Animal data on naphthalene exist in several areas. Oral toxicity data are adequate for deriving acute- and intermediate-duration oral MRLs, but adequate chronic-duration oral toxicity studies in animals are not available. Available toxicology and carcinogenesis studies of chronic inhalation exposure to naphthalene in rats and mice are adequate for deriving a chronic-duration inhalation MRL for naphthalene and assessing the potential carcinogenicity of naphthalene, but available acute- and intermediate-duration inhalation toxicity studies are not adequate for deriving MRLs.

Figures 3-7 and 3-8 show that no information was located on the health effects of 1-methylnaphthalene or 2-methylnaphthalene in humans via inhalation, oral, or dermal exposure. These figures also reflect that data in animals are limited to cancer and toxicity studies of intermediate- and chronic-duration oral exposure of mice to 1-methylnaphthalene or 2-methylnaphthalene, a single poorly reported acute inhalation exposure study of hematologic end points in dogs exposed by inhalation to 1-methylnaphthalene or 2-methylnaphthalene, a study that reported decreased pain sensitivity, but no effects on the ability to balance on a rotating rod, in rats exposed for 4 hours by inhalation to 1-methylnaphthalene or 2-methylnaphthalene, and cancer and toxicity studies of intermediate- and chronic-duration dermal exposure of mice to a mixture of 1-methylnaphthalene and 2-methylnaphthalene.

3.12.2 Identification of Data Needs

Acute-Duration Exposure. A number of reports of human exposure to acute inhalation, oral, or dermal doses of naphthalene have established the erythrocyte as a toxicity target (Dawson et al. 1958; Haggerty 1956; Kurz 1987; Linick 1983; MacGregor 1954; Mackell et al. 1951; Melzer-Lange and

Walsh-Kelly 1989; Ojwang et al. 1985; Schafer 1951; Shannon and Buchanan 1982; Valaes et al. 1963). However, the data from these reports were not useful in predicting toxic or lethal dose levels by any of these routes because the exposure levels were not defined.

The acute oral toxicity of naphthalene has been studied in animals but there are limited data for acute inhalation and dermal exposures.

The most frequently reported adverse effects associated with acute oral exposure are ocular lesions (primarily cataracts). These have been observed in rabbits (Srivastava and Nath 1969; Van Heyningen and Pirie 1967) and rats (Kojima 1992; Murano et al. 1993; Rathburn et al. 1990; Tao et al. 1991; Yamauchi et al. 1986) and occur following exposure to high (>500 mg/kg) doses. Acute oral exposure of pregnant rats to naphthalene doses of 150 or 450 mg/kg/day (but not 50 mg/kg/day) during gestation produced maternal toxicity including clinical signs (lethargy and prone position) and marked decreases in body weight gain (NTP 1991a), but clear effects on the developing fetus have not been found at maternal oral doses as high as 450 mg/kg/day in rats (NTP 1991a), 300 mg/kg/day in mice (Plasterer et al. 1985), or 120 (NTP 1992b) or 400 mg/kg/day (PRI 1985i,1986) in rabbits. Slightly reduced numbers of mouse pups per litter were observed when naphthalene in corn oil was orally administered to pregnant mice (Plasterer et al. 1985); however, no effects were seen when pregnant rabbits were orally administered naphthalene at even higher doses but delivered in methylcellulose rather than in an oil vehicle (PRI 1986). It is unclear if these differences are due to species differences in sensitivity or to possible differences in the effects of the two vehicles on naphthalene absorption. Effects on liver (Rao and Pandya 1981) and lung (Shopp et al. 1984) weights have been reported, but no treatment-related histopathological lesions were observed in these acute oral exposure studies. Lethal doses have been identified in mice (Plasterer et al. 1985; Shopp et al. 1984) and rats (Gaines 1969).

The finding of transient clinical signs of toxicity in orally-exposed pregnant rats (NTP 1991a) serves as the basis of the acute-duration oral MRL for naphthalene. The MRL was calculated from a minimal LOAEL of 50 mg/kg/day using an uncertainty factor of 90 (3 for the use of a minimal LOAEL, 10 for extrapolation from animals to humans, and 3 for human variability). An uncertainty factor of 3 was used for human variability because the critical effect is based on effects in a sensitive animal subpopulation. Dermal or inhalation developmental toxicity studies in animals are not available. Pregnant rats appear to be more sensitive for the effects observed (clinical signs in response to gavage exposure and decreased body weight gain) than nonpregnant rats. In 13-week gavage studies with nonpregnant rats (NTP 1980b), similar persistent clinical signs were not observed following administration of doses as high as

200 mg/kg/day, but were observed at 400 mg/kg/day. In nonpregnant rats exposed for 13 weeks, significant body weight decreases occurred at 200 mg/kg/day throughout exposure, but not at 100 mg/kg/day (NTP 1980b) or in nonpregnant mice exposed for 13 weeks to 133 mg/kg/day (Shopp et al. 1984) or 200 mg/kg/day (NTP 1980a). Mice in the NTP (1980a) study showed transient signs of toxicity (lethargy, rough hair coats, and decreased food consumption), but these only occurred between weeks 3 and 5 in the 200-mg/kg/day group.

Data are inadequate for deriving an acute-duration inhalation MRL for naphthalene. Data are restricted to a 14-day (6 hours/day, 5 days/week) range-finding study in B6C3F1 mice (NTP 1992a), which only examined hematologic end points and did not histologically examine expected critical toxicity targets (lung and nasal cavity epithelial tissue) (NTP 1992a), and a study (West et al. 2001) with Swiss Webster mice and Sprague-Dawley rats, which involved single 4-hour exposure periods. The more recent study, however, only histologically examined the lung and did not examine nasal tissue. A comprehensive inhalation study involving an acute repeated exposure scenario and examining the other critical target (the nose, based on the findings from chronic mouse and rat bioassays) is not currently available. Results from such a study may be useful for deriving an acute-duration inhalation MRL for naphthalene.

Hemolysis is the best documented effect of acute naphthalene exposures in humans, but it has not been observed in studied strains of rats (F344) or mice (CD-1, B6C3F1). Dose-response data for hemolysis from a susceptible animal species (such as dogs or the Jackson Laboratory hemolytic anemia mouse) may be useful to obtain data that could be used for considering changes to the acute-duration oral MRL. Data from both inhalation and oral exposure protocols would be useful.

No acute-duration studies are available on 1-methylnaphthalene or 2-methylnaphthalene exposure in humans using the inhalation, oral, or dermal routes. Two acute inhalation studies in animals were identified. The first study reported that 1-methylnaphthalene (pure) administered in a kerosene aerosol was associated with increased reticulocyte and lymphocyte counts in splenectomized dogs and practical grade 1-methylnaphthalene was associated with increased leucocyte and neutrophil counts (Lorber 1972). Neither grade of 1-methylnaphthalene had any effect on hematocrit values. None of these parameters were affected when 2-methylnaphthalene aerosols were used. The physiological significance of these findings is not apparent and the exposure levels in the study were not clearly specified. As such, the data are not suitable for use in deriving an MRL for 1-methylnaphthalene or 2-methylnaphthalene. The second study measured decreased sensitivity to pain in rats exposed by inhalation for 4 hours to 1-methyl-naphthalene (44 ppm) or 2-methylnaphthalene (61 ppm), but found no effects on the ability to balance on

a rotating rod at exposure levels as high as 70 ppm 1-methylnaphthalene or 90 ppm 2-methylnaphthalene (Korsak et al. 1998). The biological significance of these findings is uncertain, and, in the absence of corroborative evidence of acute neurotoxicity, the findings are not suitable for deriving acute inhalation MRLs for 1-methylnaphthalene or 2-methylnaphthalene.

Parenteral studies in animals revealed that a single intraperitoneal injection of 2-methylnaphthalene (1,000 mg/kg) was lethal in mice (Griffin et al. 1981). When a glutathione-depleting agent (diethyl maleate) was administered prior to administration of 2-methylnaphthalene, a lower dose of 2-methylnaphthalene (400 mg/kg) was also lethal. A single intraperitoneal injection of 1-methylnaphthalene (426 mg/kg) was not lethal in mice (Griffin et al. 1982). Systemic effects have been reported and were limited to effects on the respiratory system (Rasmussen et al. 1986). Exfoliation of the bronchiolar epithelium in mice was reported following a single intraperitoneal injection of 2-methylnaphthalene (Buckpitt et al. 1986; Griffin et al. 1981, 1983). A single intraperitoneal injection of 2-methylnaphthalene (1,000 mg/kg) did not cause liver or kidney lesions (Griffin et al. 1981, 1983).

Because populations living near hazardous waste sites might be exposed to 1-methylnaphthalene or 2-methylnaphthalene for short periods, comprehensive toxicity studies of acute exposure in animals by the inhalation and oral routes to determine potential target tissues and dose-related effects would be useful in assessing possible health hazards to humans. The studies would be most useful if they included a battery of neurological end points and comprehensive histological examination of nasal and lung tissue.

Intermediate-Duration Exposure. Quantitative data were not provided in any intermediate-duration inhalation case studies of human naphthalene exposure and, in one case, there was simultaneous exposure to paradichlorobenzene (Harden and Baetjer 1978; Linick 1983).

The results from three intermediate-duration oral toxicity studies in animals (two in mice and one in rats) identified body weight changes as the most sensitive biologically significant effect on which to base the intermediate-duration oral MRL for naphthalene. Comprehensive intermediate-duration oral toxicity studies found no evidence for naphthalene-induced lesions in any tissue or organs in male or female Fischer 344 rats exposed to doses up to 400 mg/kg/day (NTP 1980b) or in male or female B6C3F1 mice exposed to doses up to 200 mg/kg/day (NTP 1980a). The only biologically significant effect found in these studies was decreased body weight (>10% decreased compared with control values) in rats at doses of 200 and 400 mg/kg/day. The other intermediate-duration oral study (with CD-1 mice) focused on a battery of immunologic tests, but did not include comprehensive histopathologic examination of tissues

(Shopp et al. 1984). No biologically significant effects were found except for decreases in weights of several organs (brain, liver, and spleen) in mice exposed to 133 mg/kg/day, but not to 53 or 5.3 mg/kg/day. The lack of naphthalene-induced lesions in these organs in the NTP (1980a, 1980b) studies suggests that the brain, liver, and spleen are not sensitive targets of naphthalene following intermediate-duration oral exposure. Statistically significant changes were reported in several hematological parameters, hepatic enzyme activities, and serum chemical parameters (Shopp et al. 1984), but these changes are not considered to be biologically significant or adverse. The acute-duration oral MRL was adopted as the intermediate-duration oral MRL for naphthalene, because a potential intermediate-duration oral MRL (see Section 2.3 and Appendix A) based on the NOAEL for decreased body weight changes in rats exposed by gavage 5 days/week for 13 weeks (NTP 1980b) was slightly larger than the acute MRL value.

No data were suitable for the development on an intermediate-duration inhalation MRL for naphthalene.

Intermediate-duration dermal toxicity data are restricted to an report that dermal exposure of male and female Sprague-Dawley rats (occluded exposure 6 hours/day, 5 days/week) to technical-grade naphthalene at doses up to 1,000 mg/kg/day for 13 weeks did not affect comprehensive ophthalmologic, hematologic, serum chemistry, or urinalysis parameters (Frantz et al. 1986). In addition, exposure did not produce increased incidences of histological lesions in 34 tissues that were examined (however, the nasal cavity was not included). The only exposure-related effect found was an increased incidence of excoriated skin and papules at the site of exposure at the highest dose level (1,000 mg/kg/day).

Intermediate-duration studies on 1-methylnaphthalene or 2-methylnaphthalene exposure in humans or animals using the inhalation, oral, or dermal routes are restricted to a study that found no pulmonary alveolar proteinosis in male or female mice exposed to diets containing up to 1.33% 2-methylnaphthalene for 13 weeks (Murata et al. 1997). The reporting of the experimental protocol and results from this study, however, is too limited to reliably use the results as a basis for an intermediate-duration oral MRL for 2-methylnaphthalene. New intermediate-duration toxicity studies using the inhalation route of exposure may be the most useful to better assess the health hazard of intermediate-duration exposure to naphthalene, based on the findings that the alveolar region of the lung is the most sensitive tissue in mice chronically exposed to 1-methylnaphthalene or 2-methylnaphthalene in the diet (Murata et al. 1993, 1997).

Chronic-Duration Exposure and Cancer. There is one report of cataracts occurring in humans following chronic-duration inhalation exposure to naphthalene (Ghetti and Mariani 1956) but no information on effects from exposures by the oral or dermal routes. The only studies of cancer in humans exposed to naphthalene are two case series reports of cancer; one report of four laryngeal cancer cases (all of whom were smokers) among workers in a naphthalene purification plant in East Germany (Wolf 1976, 1978), and another report of 23 cases of colorectal carcinoma admitted to a hospital in Nigeria (Ajao et al. 1988). NTP (2002b), EPA (2002b), and IARC (2002) concurred that these studies provide inadequate evidence of naphthalene carcinogenicity in humans. No cohort mortality or morbidity studies or case-control studies examining possible associations between naphthalene exposure and increased risk of cancer (or other health effects) are available.

There are two comprehensive chronic-duration inhalation toxicology and carcinogenicity studies of naphthalene in animals, one in rats (Abdo et al. 2001; NTP 2000) and one in mice (NTP 1992a). These studies identify respiratory tissues as the most sensitive toxicity targets of chronic-duration exposure to inhaled naphthalene in animals: nonneoplastic and neoplastic lesions in the nose of rats, nonneoplastic lesions in the nose of mice, and nonneoplastic and neoplastic lesions in the lungs of mice. Exposure-related lesions in other tissues were not found in these studies. NTP (2002b) and IARC (2002) concurred that these studies provide sufficient evidence of naphthalene carcinogenicity in animals. The chronic-duration inhalation MRL for naphthalene is based on the LOAEL of 10 ppm for nonneoplastic lesions in the olfactory epithelium and respiratory epithelium of the nose of rats.

No appropriate studies were located for deriving an MRL for chronic-duration oral exposure to naphthalene. One chronic study was located that examined the toxicity of naphthalene in rats (Schmahl 1955). No treatment-related effects were reported at a dose level of 41 mg/kg/day for 700 days. The study was not suitable as the basis for deriving a chronic MRL or for assessing carcinogenicity because only one dose level was evaluated (apparently below the maximum tolerated dose), histopathological examination was limited, and dosing was not precisely controlled.

New chronic oral or dermal toxicity studies would be useful to better determine the possible carcinogenicity and noncancer toxicity of naphthalene via these routes of exposure.

Epidemiology studies, case reports, or controlled-exposure studies examining the potential health effects of human chronic exposure to 1-methylnaphthalene or 2-methylnaphthalene by any route of exposure are not available.

No chronic-duration studies are available on 1-methylnaphthalene or 2-methylnaphthalene exposure in animals using the inhalation routes.

A chronic-duration study of 1-methylnaphthalene in the diet that identified a LOAEL of 71.6 mg/kg/day for the occurrence of pulmonary alveolar proteinosis in mice (Murata et al. 1993) was used as the basis of the oral MRL for 1-methylnaphthalene. A chronic-duration oral study of 2-methylnaphthalene in the diet (Murata et al. 1997) that identified a LOAEL of 50.3 mg/kg/day for pulmonary alveolar proteinosis in mice was the basis of the chronic oral MRL for 2-methylnaphthalene. Support for pulmonary alveolar proteinosis as the critical effect for the chronic oral MRLs for 1-methylnaphthalene and 2-methylnaphthalene comes from dermal chronic-duration studies with methylnaphthalene (a mixture of 1- and 2-methylnaphthalene), which reported increased incidences of this lesion in mice dermally exposed to 30 or 119 mg/kg of methylnaphthalene for 30–61 weeks (Emi and Konishi 1985; Murata et al. 1992). Increased incidences of lung adenomas were found in several exposed groups in the oral chronic-duration studies, but the evidence for carcinogenicity is considered to be limited. The tumorigenic response was predominantly benign and was only consistently seen in male mice exposed to 1-methylnaphthalene. The available data on the methylnaphthalenes appear inadequate to determine the potential carcinogenicity in humans.

A new chronic-duration oral study in rats or another animal species may help to better assess the potential carcinogenicity and noncancer toxicity of the methylnaphthalenes. Because the lung is the most sensitive toxicity target of the methylnaphthalenes in mice exposed orally or dermally, it is plausible that chronic inhalation exposure may also target the lung. The availability of repeated-exposure inhalation carcinogenicity and toxicity studies would help to better determine this possibility.

Genotoxicity. As discussed in Section 3.3, results in bacterial mutation assays were predominantly negative (see Table 3-4 for citations) with the exceptions that the metabolite, 1,2-naphthoquinone, was mutagenic in *S. typhimurium* without metabolic activation (Flowers-Geary 1996), and naphthalene was mutagenic in *V. fischeri* with metabolic activation (Arfsten et al. 1994).

Results from a limited number of *in vitro* eukaryotic genotoxicity assays are mixed. Negative results were obtained for mutations and sister chromatid exchanges in cultured human cells exposed to naphthalene, for DNA single strand breaks and unscheduled DNA synthesis in rat hepatocytes, and for cell transformation in several types of mammalian cells (see Table 3-3 for citations). Positive results

included increased chromosomal aberrations in Chinese hamster ovary cells and preimplantation whole mouse embryos exposed to naphthalene, and increased sister chromatid exchanges in human mononuclear leukocytes exposed to 1,2- or 1,4-naphthoquinone and in Chinese hamster ovary cells exposed to naphthalene (see Table 3-3 for citations). Other studies in cell-free systems reported that 1,2-naphthoquinone formed N7 adducts with deoxyguanosine (McCoull et al. 1999) and caused DNA strand scission in the presence of NADPH and copper via reactive oxygen species from an oxidation/reduction cycle (Flowers et al. 1997).

In vivo genotoxicity assays with naphthalene are also limited and do not provide consistently negative or positive results for naphthalene genotoxicity. Positive results were obtained for somatic mutations in *D. melanogaster*, micronuclei in salamander larvae erythrocytes, and DNA fragmentation in liver and brain tissue from mice and rats orally exposed to naphthalene (see Table 3-3 for citations). Negative results were obtained for micronuclei formation in bone marrow of mice given oral or intraperitoneal injections of naphthalene, DNA single strand breaks and unscheduled DNA synthesis in hepatocytes of rats given oral doses of naphthalene, and neoplastic transformations in liver cells of partially hepatectomized rats given oral doses of naphthalene (see Table 3-3 for citations).

The available data suggest that genotoxic action by the naphthalene metabolite, 1,2-naphthoquinone, is plausible and that the mutagenic/genotoxic potential of naphthalene and its metabolites may be weak. Assays of possible genotoxic action in sensitive target tissues of naphthalene in rodents (lung and nasal epithelial tissue), however, are not available. New studies examining genotoxic end points in lung and nasal epithelial tissue following inhalation exposure to naphthalene would help to better determine the potential genotoxicity of naphthalene and it metabolites.

For the methylnaphthalenes, data in humans are limited to one study that reported no effects on human chromosomes in tests evaluating the effects of 1-methylnaphthalene or 2-methylnaphthalene on human peripheral lymphocytes *in vitro* (Kulka et al. 1988). 1-Methylnaphthalene and 2-methylnaphthalene were also determined to be nonmutagenic in four strains of *S. typhimurium* (Florin et al. 1980). Additional mutagenicity studies using an *in vivo* approach would be useful to better assess the genotoxicity potentials of 1-methylnaphthalene and 2-methylnaphthalene.

Reproductive Toxicity. No information is available on the reproductive effects of naphthalene in humans, although the occurrence of hemolytic anemia in the neonates of anemic, naphthalene-exposed mothers demonstrates that naphthalene and/or its metabolites can cross the placental barrier (Anziulewicz

et al. 1959; Zinkham and Childs 1957, 1958). Animal studies involving naphthalene exposure during gestation reported no reproductive effects in rabbits administered doses of up to 120 mg/kg/day by gavage or in rats given doses of up to 450 mg/kg/day, although doses of 150 mg/kg/day and greater were maternally toxic to rats. There was a decrease in the number of live mouse pups per litter with a dose of 300 mg/kg/day given during gestation (Plasterer et al. 1985) and *in vitro* studies of naphthalene embryotoxicity in the presence of liver microsomes support the concept that naphthalene metabolites may be harmful to the developing embryo (Iyer et al. 1991). No exposure-related lesions in reproductive tissues were found in intermediate-duration oral exposure studies in rats (NTP 1980b) and mice (NTP 1980a) or in chronic inhalation studies in rats (Abdo et al. 2001; NTP 2000) or mice (NTP 1992a). One- or two-generation reproductive toxicity studies evaluating reproductive performance variables in male and female animals exposed to naphthalene are not available. Results from such studies may help to better determine the potential reproductive toxicity of naphthalene.

No studies are available on the reproductive toxicity of 1-methylnaphthalene or 2-methylnaphthalene in humans or animals following inhalation, oral, or dermal exposure, with the exceptions of the reports that 81-week oral exposure to 1-methylnaphthalene or 2-methylnaphthalene did not induce lesions in reproductive tissues of male or female mice (Murata et al. 1993; 1997). One- or two-generation reproductive toxicity studies evaluating reproductive performance variables in male and female animals exposed to 1-methylnaphthalene or 2-methylnaphthalene are not available. Results from such studies may help to better determine the potential reproductive toxicity of the methylnaphthalenes.

Developmental Toxicity. There is no information on the potential developmental effects of naphthalene in humans, although, as mentioned previously, naphthalene and/or its metabolites can cross the placental barrier and cause hemolytic anemia in newborns (Anziulewicz et al. 1959; Zinkham and Childs 1957, 1958). Studies of the developmental effects of orally administered naphthalene in rats (NTP 1991a), mice (Plasterer et al. 1985), and rabbits (NTP 1992b; PRI 1985i, 1986) have been negative, except for a slight nonsignificant increase in fused sternebrae in female rabbit pups from a small number of litters at doses of 80 and 120 mg/kg/day (NTP 1992b). No developmental toxicity studies involving inhalation or dermal exposure to naphthalene are available. The availability of such studies would help to better determine the developmental toxicity potential of naphthalene.

No studies are available on the developmental toxicity of 1-methylnaphthalene or 2-methylnaphthalene in humans or animals following inhalation, oral, or dermal exposure.

Immunotoxicity. There have been no comprehensive studies of the immunotoxicity of naphthalene in humans exposed by the inhalation, oral, or dermal routes. The animal oral exposure data indicate that naphthalene did not affect humoral or cell-mediated immunity in mice (Shopp et al. 1984). Minor effects on the thymus and spleen were noted in mice and rats (NTP 1980b; Shopp et al. 1984), but in no case were animals of both sexes affected. Because there are few data pertaining to the immunotoxicity of naphthalene, a battery of *in vitro/in vivo* screening assays of immune function may be useful to determine whether more detailed and longer-term studies are needed.

No studies are available on the immunotoxicity of 1-methylnaphthalene or 2-methylnaphthalene in humans or animals following inhalation, oral, or dermal exposure. However, the reported increase in the level of monocytes in mice following long-term oral exposure to 1-methylnaphthalene (Murata et al. 1993) may deserve additional study. As with naphthalene, a battery of *in vitro/in vivo* screening assays of immune function may be useful to determine whether more detailed and longer-term studies are needed.

Neurotoxicity. The direct effects of naphthalene on the central nervous system have not been investigated in either humans or animals. Neurotoxic effects seen in humans exposed to naphthalene via inhalation or oral exposure may be a consequence of the diminished oxygen-carrying capacity of the blood which results from red cell hemolysis (Bregman 1954; Gupta et al. 1979; Kurz 1987; Linick 1983; MacGregor 1954; Ojwang et al. 1985; Zuelzer and Apt 1949). Persistent clinical signs of toxicity (lethargy and prone position) were seen in pregnant rats following gavage administration of naphthalene at dose levels of 150 or 450 mg/kg/day; at 50 mg/kg/day, the signs were only observed during the first 2 days of dose administration (NTP 1991a). Comparable effects were not observed in F344/N rats exposed to doses of up to 400 mg/kg/day for 13 weeks or in B6C3F1 mice at doses of up to 200 mg/kg/day (NTP 1980a, 1980b). With inhalation exposure, no treatment-related gross or histopathological lesions of the brain were observed in mice (NTP 1992a) or rats (Abdo et al. 2001; NTP 2000) exposed for 2 years to naphthalene concentrations as high as 30 or 60 ppm, respectively. Clinical observations revealed no gross behavioral changes indicative of neurological impairment. Additional studies involving batteries of neurological end points following oral and/or inhalation exposure may help to better determine the potential neurotoxicity of naphthalene and explain why pregnant rats appear to be more susceptible to the behavioral effects of acute-duration exposures to naphthalene.

No studies on the neurotoxicity of 1-methylnaphthalene or 2-methylnaphthalene in humans following inhalation, oral, or dermal exposure were located with the exception of a single study that found decreased sensitivity to pain in rats exposed by inhalation for 4 hours to 1-methylnaphthalene (44 ppm) or

2-methylnaphthalene (61 ppm), but no effects on rotarod performance at exposure levels as high as 70 ppm 1-methylnaphthalene or 90 ppm 2-methylnaphthalene (Korsak et al. 1998). The biological significance of these findings is uncertain. Additional studies involving batteries of neurological end points may help to better determine the potential neurotoxicity of the methylnaphthalenes.

Epidemiological and Human Dosimetry Studies. A small number of reports have equivocally suggested that workers exposed to naphthalene for long periods of time may have an elevated risk of cataract development (Ghetti and Mariani 1956; Lezenius 1902). This information, coupled with the cataractogenic effects of naphthalene in orally exposed rats (Kojima 1992; Xu et al. 1992b; Yamauchi et al. 1986) and rabbits (Rossa and Pau 1988; Srivastava and Nath 1969; Van Heyningen and Pirie 1967) in acute- and intermediate-duration studies, suggests that studies of occupationally-exposed workers would help to determine its potential to produce ocular toxicity in humans. The incidence of tumors, anemia, and reproductive problems in this population could be determined at the same time. Available case reports of cancer in naphthalene-exposed humans provide inadequate evidence of naphthalene carcinogenicity. Currently, no cohort mortality or morbidity studies or case-control studies examining possible associations between naphthalene exposure and increased risk of cancer (or other health effects) are available. If human populations that are specifically and repeatedly exposed to naphthalene can be identified, epidemiological studies of these populations may help to better assess the potential chronic-duration toxicity and carcinogenicity of naphthalene.

No epidemiological or human dosimetry studies on the effects of 1-methylnaphthalene or 2-methylnaphthalene were located. Exposure to these compounds, particularly through dermal contact or inhalation, can occur in workplaces where the compounds are produced or used. Populations living near hazardous waste sites can potentially be exposed by the oral, inhalation, and dermal routes. If an appropriate population can be identified, it may be helpful to conduct epidemiological studies to determine if there are toxic effects (particularly on the lungs) resulting from exposure to these substances.

Biomarkers of Exposure and Effect.

Exposure. There are methods to determine the presence of naphthalene in adipose tissue and these methods have been used in a national monitoring program for the analysis of naphthalene in the adipose tissue of the general population (EPA 1986g). Metabolites of naphthalene, such as naphthols and naphthoquinones, have been detected in the urine of a patient 4 days after ingestion of naphthalene (Zuelzer and Apt 1949), but not in another patient at 17 days after ingestion (Mackell et al. 1951).

1-Naphthol is present in the urine of workers occupationally exposed to naphthalene. Maximum 1-naphthol levels occurred immediately after the end of the work period and in some cases had returned to baseline levels 8 hours later (Bieniek 1994). New techniques have been developed to measure cysteinyl adducts formed from reactions of hemoglobin and albumin with reactive metabolites of naphthalene (Troester et al. 2002; Waidyanatha et al. 2002). The adducts are expected to be useful in estimating internal doses of these metabolites, and with further development, they may become useful biomarkers of exposure.

Effect. There are no known specific biomarkers of effects for naphthalene, 1-methylnaphthalene, or 2-methylnaphthalene. Hemolytic anemia has been frequently associated with human exposure to naphthalene, but may also be the result of exposure to other chemicals. Pulmonary alveolar proteinosis in mice has been associated with chronic oral exposure to 1-methylnaphthalene and 2-methylnaphthalene. The condition has been described in humans, but has not been associated with human exposure to 1-methylnaphthalene or 2-methylnaphthalene. Currently, these effects (hemolytic anemia or pulmonary alveolar proteinosis) do not hold promise as specific biomarkers of effect for naphthalene or methyl-naphthalenes. Identification of specific biomarkers of effect such as particular protein adducts in naphthalene-affected target tissues in animals (e.g., nasal epithelium tissue) may be useful to test whether similar biomarkers of effect may exist in naphthalene-exposed human populations.

Absorption, Distribution, Metabolism, and Excretion. Although human absorption of naphthalene has not been quantitatively characterized, case reports indicate that humans can absorb toxicologically significant amounts of this compound by the oral, inhalation, or dermal routes (Bregman 1954; Chusid and Fried 1955; Dawson et al. 1958; Gidron and Leurer 1956; Gupta et al. 1979; Haggerty 1956; Kurz 1987; Linick 1983; MacGregor 1954; Mackell et al. 1951; Ojwang et al. 1985; Santhanakrishnan et al. 1973; Schafer 1951; Shannon and Buchanan 1982; Valaes et al. 1963; Zuelzer and Apt 1949). Laboratory animals such as rats, mice, and rabbits also absorb the chemical via their skin and gastrointestinal and respiratory tracts (NTP 1992a; Rao and Pandya 1981; Shopp et al. 1984; Srivastava and Nath 1969; Turkall et al. 1994; van Heyningen and Pirie 1967). Naphthalene adsorbed to organic-rich soils is absorbed across the skin more slowly than naphthalene from organic-poor soils (Turkall et al. 1994). The compound apparently partitions between the soil organic carbon and the hydrophobic components of the epidermis and dermis. More information concerning the mechanism of absorption (facilitated versus passive transport) across nasal and pulmonary epithelial membranes, the gastrointestinal tract, and the skin may be helpful in estimating the effect of dose on absorption coefficients and in better determining the effect of the medium of exposure (water, oil, food, etc.) on oral

or dermal absorption. Empirical measurements of permeability coefficients for naphthalene in blood or air with various tissues from various species may be useful to further develop PBPK models for naphthalene.

As discussed in Sections 3.4.3 and 3.5.2, extensive research on the bioactivation and metabolic transformations of naphthalene in mammalian systems has identified several reactive metabolites that are potentially responsible for the nasal, pulmonary, and ocular toxicity of naphthalene (1,2-naphthalene oxide, 1,2-naphthoquinone, and 1,4-naphthoquinone), but the relative importance of these metabolites in affecting these toxicity targets remains uncertain. Because nasal respiratory and olfactory epithelia are the most sensitive targets in rodents following acute or chronic inhalation exposure, better understanding of the deposition, absorption, and metabolism of inhaled naphthalene in different regions of nasal epithelia, and the degree to which species (particularly rodents and primates) differ in these processes, may be useful for decreasing uncertainty in extrapolating human health hazards from data for rodents exposed to naphthalene. *In vivo, in vitro,* and modeling research approaches are likely to create better understanding of these processes, which may also provide explanations for observed species differences in response to naphthalene. For example, both rats and mice developed nonneoplastic nasal lesions following chronic inhalation exposure to naphthalene concentrations as low as 10 ppm, but only rats developed nasal tumors (Abdo et al. 2001; NTP 1992a, 2000). Other examples are the findings that *in vitro* rates of epoxide formation from naphthalene in extracts of nasal olfactory tissue showed the order, mouse>rat>hamster, but rats were more susceptible to acute nasal injury from naphthalene than mice or hamsters (Buckpitt et al. 1992; Plopper et al. 1992a). Mechanistic explanations for these differences are not currently available.

The most recently developed PBPK models for naphthalene in mice and rats (Willems et al. 2001) do not include nasal compartments that metabolize naphthalene and do not include the spontaneous conversion of 1,2-naphthalene oxide to 1-naphthol or metabolic transformations to the naphthoquinones. Additional toxicokinetic data are needed to further refine these models to include these potentially important processes. Application of such further refined models, and the development of comparable models for humans, may be useful to decrease uncertainty in extrapolating dose-response relationships for nasal effect in rodents to humans.

No studies were located on the absorption, metabolism, and excretion of 1-methylnaphthalene in humans or animals following inhalation, oral, or dermal exposure. There was one study of 2-methylnaphthalene in guinea pigs (Teshima et al. 1983). Parenteral studies in animals show that 2-methylnaphthalene is

converted to both monohydrated compounds and dihydrodiols (Breger et al. 1981, 1983; Melancon et al. 1982). In addition, 2-naphthoic acid and the glycine or the cysteine conjugates were identified in rats (Melancon et al. 1982) and guinea pigs (Teshima et al. 1983). Studies by relevant exposure routes would further characterize the toxicokinetics of these compounds and may enhance the understanding of the potential risk associated with exposure to these compounds.

Comparative Toxicokinetics. Data suggest that there are strain- and species-specific effects associated with naphthalene toxicity. Laboratory animals, such as rats and mice, do not exhibit red cell hemolysis after exposure to naphthalene, while humans and dogs do (NTP 1980a, 1980b, 1992a; Shopp et al. 1984; Zuelzer and Apt 1949). Mice and rats both develop nonneoplastic nasal lesions after chronic inhalation exposure to naphthalene, but only rats develop nasal tumors, and only mice develop nonneoplastic lung lesions or lung tumors (Abdo et al. 2001; NTP 1992a; 2000). There are differences in susceptibility to the acute pulmonary toxicity of naphthalene among mice, rats, hamsters, and guinea pigs (Buckpitt et al. 2002; Plopper et al. 1992a, 1992b). Differences in the susceptibility of rats and mice, and of different mouse strains, to the cataractogenic properties of naphthalene have also been reported (Wells et al. 1989). These differences may relate to differences in tissue distribution of specific CYP isoenzymes, rates of formation of reactive metabolites, rates of transformation of reactive metabolites to nonreactive metabolites, or partitioning of the parent compound or metabolites within and between tissues. For example, the difference in susceptibility to the acute pulmonary toxicity of naphthalene between mice and rats has been correlated with higher rates of metabolic formation and different stereoselectivity of epoxide metabolites in mice compared with rats (Buckpitt et al. 1992; 1995; 2002). In contrast, differences among rat, mice and hamsters in susceptibility to naphthalene-induced nasal lesions were not correlated with species differences in rates of epoxide formation from naphthalene in extracts of olfactory epithelial tissue (Plopper et al. 1992; see Section 3.5.2). Further evaluation of these differences and comparative studies of distribution and metabolic patterns among species may help to decrease uncertainty in extrapolating estimates of human health hazards from data for animals exposed to naphthalene.

There are no data available concerning the toxicokinetics of 1-methylnaphthalene or 2-methylnaphthalene in humans following inhalation, oral, or dermal exposure. There are no data from studies of 1-methylnaphthalene in animals, but there are limited data for 2-methylnaphthalene (Breger et al. 1983; Griffin et al. 1982; Melancon et al. 1982, 1985; Teshima et al. 1983). New studies that evaluate toxicokinetic parameters in several animal species may be useful to decrease uncertainty in the chronic oral MRLs for

1-methylnaphthalene and 2-methylnaphthalene, which are based on the occurrence of pulmonary alveolar proteinosis in mice.

Methods for Reducing Toxic Effects. Available methods are sufficient for reducing peak absorption of naphthalene following ingestion (Melzer-Lange and Walsh-Kelly 1989; Siegel and Wason 1986; Stutz and Janusz 1988). No antidotal methods are available that would be useful for treatment of naphthalene exposure based on any proposed hypothesis pertaining to the mechanism of action. Additional studies to characterize the metabolic activation of naphthalene and the role of circulating reactive metabolites from nontarget tissues may be useful in developing methods for interfering with the mechanism of action. Further studies to identify ways to reduce or prevent accumulation of toxic metabolites in target tissues may be warranted when mechanisms of naphthalene toxic action are better understood.

There are no compound-specific methods for reducing the toxic effects of 1-methylnaphthalene and 2-methylnaphthalene. Additional information on the toxicokinetics and mechanism of action for these compounds may be beneficial in identifying possible approaches for reducing compound toxicity.

Children's Susceptibility. Data needs relating to both prenatal and childhood exposures, and developmental effects expressed either prenatally or during childhood, are discussed in detail in the Developmental Toxicity subsection above.

As discussed in Section 3.7, cases of naphthalene-induced hemolytic anemia in children have been frequently reported (Owa 1989; Owa et al. 1993; Santucci and Shah 2000; Valaes et al. 1963). Newborns and infants are thought to be more susceptible than older people because hepatic enzymes involved in conjugation and excretion of naphthalene metabolites are not well developed after birth, and children with genetically determined G6PD deficiency are thought to be especially susceptible to chemically-induced hemolytic anemia (EPA 1987a). There are no studies that have specifically examined the influence of age on naphthalene toxicokinetic capabilities in humans. Although the availability of such studies may increase the understanding of the specific physiological basis for the apparent susceptibility of newborns, they are unlikely to be conducted. Experiments examining the most sensitive targets in animals (see below) are likely surrogates.

Although naphthalene and/or its metabolites can cross the placental barrier (Anziulewicz et al. 1959; Zinkham and Childs 1957, 1958), oral-exposure developmental toxicity studies in animals do not provide

evidence that naphthalene was fetotoxic or impaired fetal development, even at maternally toxic dose levels as high as 450 mg/kg/day (NTP 1991a; Plasterer et al. 1985; PRI 1986). Additional developmental toxicity studies in animals with inhalation or dermal exposure would determine if naphthalene exposure by these routes represents a greater developmental hazard than oral exposure.

Neonatal mice (7 days old) appear to be more susceptible than adult mice to lung injury induced by acute intraperitoneal injection of naphthalene (Fanucchi et al. 1997). The mechanistic basis of this difference is currently unknown, but does not appear to be explained by differences in CYP catalytic capabilities to produce epoxide metabolites, since CYP activities were 2.5 time lower in neonates than in adults. Downstream metabolic capabilities, however, were not examined in this study. Comparison of neonatal and adult tissues in these metabolic steps may help to explain this apparent susceptibility of neonatal mice. Based on findings that *in utero* exposure to other CYP-bioactivated chemicals caused Clara cell tumors in adult offspring, Fanucchi et al. (1997) postulated that naphthalene exposure during the neonatal period may lead to loss of regulatory mechanisms resulting in Clara cell proliferation and tumor formation in adult animals. Direct evidence for naphthalene in support of this hypothesis, however, is not available. Additional research may help to determine whether or not *in utero* or neonatal naphthalene exposure will cause increased incidence of lung tumors in adult mice.

Child health data needs relating to exposure are discussed in Section 6.8.1, Identification of Data Needs: Exposures of Children.

3.12.3 Ongoing Studies

Dr. Alan Buckpitt and colleagues at the University of California, Davis have been conducting studies in several areas related to naphthalene toxicology including (1) identifying specific naphthalene-protein adducts in lungs of mice, rats, and Rhesus macaques and characterizing the time course of their generation and disappearance; (2) identifying cellular and molecular events involved in the development of naphthalene-induced acute lung injury by comparing lung tissue from rodents, Rhesus macaques, and humans; and (3) comparing the cellular distribution and catalytic activities of CYP monooxygenases in lung tissues from various species.

Dr. Charles Plopper and colleagues at the University of California, Davis have been conducting studies comparing acute naphthalene-induced lung injury in neonatal mice and adult mice and the biochemical

effects of *in utero* or neonatal exposure to lung toxicants on the development of bronchiolar repair capabilities. This work is part of an effort to increase understanding of molecular mechanisms involved in lung diseases that may originate in childhood exposures.

Dr. Leena Nylander French and colleagues at the University of North Carolina, Chapel Hill have been conducting studies to test the hypothesis that low levels of exposure to benzene or naphthalene can be detected using samples of keratinized epidermis removed by tape stripping.

Dr. Y. Awasthi and colleagues at the University of Texas, Galveston are studying the roles of glutathione S-transferases in protecting against ocular cytotoxicity and apoptosis caused by several oxidants, including naphthalene. Studies include the use of genetically altered knock-out mice strains, which are deficient in specific types of glutathione-*S*-transferases.

Dr. Barry Stripp and colleagues at the University of Pittsburgh are studying the role of proliferative cells originating from the neuroepithelial body in repair of airway epithelial cell damage in mice exposed to ozone or naphthalene.

Dr. John Markley and colleagues at the University of Wisconsin, Madison are studying the 1-, 2-, and 3-dimensional molecular structures of toluene 4-monooxygenase, an enzyme that catalyzes NADH- and O_2-dependent conversion of toluene to p-cresol, as well as the oxidation of numerous hydrocarbons, including naphthalene.

TOXICITY SUMMARY
FOR
TOLUENE

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RESTORATION PROGRAM

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EXECUTIVE SUMMARY

Toluene is a colorless liquid widely used as raw material in the production of organic compounds and as a solvent (EPA, 1990). It is readily absorbed from the gastrointestinal and respiratory tracts and, to a lesser degree, through the skin. Toluene is distributed throughout the body, with accumulation in tissues with high lipid content. It is metabolized in the liver, primarily to hippuric acid and benzoyl glucuronide, compounds that are rapidly excreted in the urine (EPA, 1990; ATSDR, 1989).

In humans and animals, the primary effect associated with inhalation exposure to toluene is central nervous system (CNS) depression. Short-term exposure of humans to 100–1500 ppm has elicited CNS effects such as fatigue, confusion, incoordination, and impairments in reaction time, perception, and motor control and function (NTP, 1990). Exposure to concentrations ranging from 10,000–30,000 ppm has resulted in narcosis and deaths (WHO, 1985). Prolonged abuse of toluene or solvent mixtures containing toluene has led to permanent CNS effects. Exposure to high concentrations of toluene (1500 ppm) has produced hearing loss in rats (Pryor et al., 1984). Hepatomegaly and impaired liver and kidney function have been reported in some humans chronically exposed to toluene (Askergren, 1984; Szilard et al., 1978; Greenburg et al., 1942). Toluene vapors may cause eye irritation (Andersen et al., 1983), and prolonged or repeated dermal contact may produce drying of skin and dermatitis (ATSDR, 1989; NIOSH, 1973).

In experimental animals, subchronic inhalation exposure to $\geq$ 2500 ppm toluene resulted in increased liver and kidney weights (rats and mice), increased heart weights (rats), increased lung weights, and centrilobular hypertrophy of the liver (mice) (NTP, 1990). Chronic inhalation exposure to 600 or 1200 ppm for 2 years produced degeneration of olfactory and respiratory epithelia of rats and minimal hyperplasia of bronchial epithelia in mice (NTP, 1990).
Subchronic oral administration of toluene at doses ranging from 312 to 5000 mg/kg/day produced clinical signs of neurotoxicity at $\geq$ 2500 mg/kg in rats and mice. Other effects observed at higher doses in rats included increased relative liver, kidney, and heart weights (females only) and necrosis of the brain and hemorrhage of the urinary bladder (NTP, 1990).

Equivocal evidence shows that exposure to toluene in utero causes an increased risk of CNS abnormalities and developmental delay in humans (Goodwin, 1988; Hersh et al., 1985; Holmberg, 1979). Animal studies, in which toluene was administered by inhalation, showed that exposure results in fetotoxicity and delayed skeletal development but does not cause internal or external malformations in rats (Courtney et al., 1986; Litton Bionetics, 1978). An oral study noted an increased incidence of embryonic deaths, cleft palate, and maternal toxicity in mice administered 1 mL/kg toluene during gestation (Nawrot and Staples, 1979).

An oral reference dose (RfD) of 2 mg/kg/day for subchronic exposure (EPA, 1993) and 0.2 mg/kg/day for chronic exposure (EPA, 1992) to toluene was calculated based on a no-observed-adverse-effect level (NOAEL) of 223 mg/kg/day and a lowest-observed-adverse-effect level (LOAEL) of 446 mg/kg/day from a 13-week subchronic gavage study in rats (NTP, 1990). Increased liver and kidney weights in males were identified as the critical effects. A subchronic (EPA, 1993) and chronic inhalation reference concentration (RfC) of 0.4 mg/m^3 (EPA, 1992) was calculated based on results of a battery of neurological tests with occupationally exposed female subjects (Foo et al., 1990).

An increased incidence of hemolymphoreticular neoplasms was reported in rats exposed to 500

mg/kg of toluene by gavage for 2 years (Maltoni et al., 1985); however, results from two long-term inhalation studies (NTP, 1990; Gibson and Hardisty, 1983) indicate that toluene is not carcinogenic at concentrations up to 1200 ppm. Based on U.S. Environmental Protection Agency (EPA) guidelines, toluene was assigned to weight-of-evidence group D, not classifiable as to human carcinogenicity (EPA, 1992).

1. INTRODUCTION

Toluene ($C_6H_5CH_3$; CAS No. 108-88-3), also known as methylbenzene and phenylmethane, is a colorless liquid with a sweet pungent odor (HSDB, 1992). It has a molecular weight of 92.15, a density of 0.8669 g/mL at 20°C, and an octanol/water partition coefficient of 2.79 (Lide, 1991; Mabey et al., 1982). Toluene is isolated by distillation of reformed or pyrolized petroleum and coal tar; however, most of the toluene produced remains as a benzene-toluene-xylene (BTX) mixture for use in gasoline. The primary use of isolated toluene is in the production of benzene and for backblending into gasoline to increase octane ratings (EPA, 1990). Toluene is also used as raw material in the production of benzyl chloride, benzoic acid, phenol, cresols, vinyl toluene, TNT, and toluene diisocyanate (U.S. Air Force, 1989); as a solvent for paints and coatings; and in adhesives, inks, and pharmaceuticals (EPA, 1990).

Inhalation is the primary route of toluene exposure for the general population and for occupationally exposed individuals. Evaporation of gasoline and automobile exhaust is the largest source of toluene in the environment, and industries that use toluene as a solvent are the second largest source (EPA, 1984). Toluene is also a common indoor contaminant due to releases from common household products and from cigarette smoke (ATSDR, 1989). Nonatmospheric releases of toluene are relatively small (e.g., to water and soil) and are estimated to comprise less than 1% of total toluene releases (ATSDR, 1989). In the atmosphere, toluene is degraded by reaction with hydroxyl radicals, with a typical half-life of about 13 hours. It is highly volatile, and volatilization is likely to be the predominant removal process from soil and water. Toluene is also subject to microbial degradation. Because of volatilization and biodegradation, toluene levels in the environment are not expected to increase over time (EPA, 1990; ATSDR, 1989).

2. METABOLISM AND DISPOSITION

2.1 ABSORPTION

Toluene is readily absorbed from the respiratory and gastrointestinal tracts and, to a lesser extent, through the skin. Animal studies suggest that absorption from the gastrointestinal tract is complete. Absorption data for humans and animals indicate that pulmonary absorption is 85–90% during brief exposures but nearer to 50% during extended exposures (< 1 hour). In humans, toluene has been detected in the arterial blood within 10 seconds after initiation of inhalation exposures; exercise greatly increases the absorption of toluene (EPA, 1990). Cutaneous absorption is approximately 1% of that absorbed by the lungs when there is exposure to the vapor; however, dermal absorption of the liquid may be higher. Because toluene evaporates readily, it is unlikely that significant absorption will occur by this route.

2.2 DISTRIBUTION

Distribution of toluene following absorption occurs throughout the body, with accumulation in adipose tissue, other tissues with high fat content, and highly vascular tissues. High levels of toluene were found in the brain and liver of an individual who had died following an episode of glue sniffing (Paterson and Sarvesvaran, 1983). Autoradiography studies using mice indicate that

immediately after inhalation exposure, a high level of radioactivity is present in the body fat, bone marrow, spinal nerves, spinal cord, and white matter of the brain. Radioactivity was also observed in the blood, kidney, and liver but at lower levels (Bergman, 1979). In one individual who died 30 minutes after ingestion of toluene, the liver had the highest concentration of toluene, followed by the pancreas, brain, heart, blood, body fat, and cerebrospinal fluid (Ameno et al., 1989). Since retention time of toluene is usually considered to be less than 24 hours, bioaccumulation of toluene is unlikely (EPA, 1990).

2.3 METABOLISM

The initial step in toluene metabolism is side-chain hydroxylation to benzyl alcohol by P-450 enzymes in the liver, followed by oxidation to benzaldehyde by alcohol dehydrogenase and subsequently to benzoic acid by aldehyde dehydrogenase. Benzoic acid is then conjugated with glycine to form hippuric acid, the major urinary metabolite. Benzoic acid can also react with glucuronic acid to form benzoyl glucuronide (ATSDR, 1989). Ring hydroxylation to *o*- and *p*-cresol is considered a minor metabolic pathway (EPA, 1990).

2.4 EXCRETION

Toluene excretion in humans and animals is dose-dependent and clearance from the body is rapid. Toluene is primarily excreted in the urine as the metabolite, hippuric acid, which accounts for 60–70% of absorbed toluene. Excretion of hippuric acid is usually complete within 24 hours after exposure. The glucuronide conjugate of benzoic acid excreted in the urine represents 10–20% of absorbed toluene. Elimination of unchanged toluene by the lungs and possibly by the skin may also account for 10–20% of the absorbed dose (EPA, 1990).

3. NONCARCINOGENIC HEALTH EFFECTS

3.1 ORAL EXPOSURES

3.1.1 Acute Toxicity

3.1.1.1 Human

Ingestion of approximately 60 mL toluene was fatal to a male mental patient, with death occurring within 30 minutes of ingestion (Ameno et al., 1989). Autopsy results showed constriction and necrosis of myocardial fibers, a markedly swollen liver, congestion and hemorrhage of the lungs, and acute tubular necrosis. Severe depression of CNS function was thought to be the probable cause of death.

3.1.1.2 Animal

The acute oral toxicity of toluene in rats appears to be age-dependent. For adult rats, the reported LD_{50} values range from 5.5 to 7.3 g/kg. For younger adult, 14-day-old, or newborn rats, the LD_{50} values are 5.3–5.9, 2.6, or <1 g/kg, respectively (EPA, 1990).

3.1.2 Subchronic Toxicity

3.1.2.1 Human

Information on the subchronic oral toxicity of toluene in humans was not available.

3.1.2.2 Animal

F344 and Sprague-Dawley rats administered daily doses of 620 mg/kg by gavage for 4 weeks developed hearing loss that was attributed to damage of the outer hair cells of the inner ear (Sullivan, 1986).

Depressed immune responses were reported in mice exposed to toluene in drinking water. Male mice administered doses of 105 mg/kg/day of toluene for 28 days had decreased thymus weights, mixed lymphocyte culture responses, and antibody plaque-forming cell responses (Hsieh et al., 1989). Mitogen-stimulated lymphocyte proliferation and interleukin-2 immunity were decreased at doses of 22 and 105 mg/kg/day. Other effects included increased levels of neurotransmitters in the brain at doses of 5, 22, or 105 mg/kg/day and increased liver weights at 105 mg/kg/day.

In an National Toxicology Program (NTP) study (1990), F344/N rats and $B6C3F_1$ mice of both sexes were administered toluene in corn oil by gavage at doses of 0, 312, 625, 1250, 2500, or 5000 mg/kg, 5 days/week for 13 weeks. All rats receiving 5000 mg/kg died within the first week, all mice receiving 5000 mg/kg died, and 40% of mice receiving 2500 mg/kg also died. Rats exposed to doses $\geq$ 2500 mg/kg of toluene exhibited prostration, hypoactivity, ataxia, piloerection, lacrimation, excess salivation, and body tremors. In male rats, absolute and relative liver and kidney weights were significantly ($p < 0.05$) increased at doses $\geq$ 625 mg/kg. In females, absolute and relative liver, kidney, and heart weights were all significantly increased at doses $\geq$ 1250 mg/kg ($p < 0.01$ for all comparisons except $p < 0.05$ for absolute kidney and heart weights at 1250 mg/kg). Histopathologic lesions were seen in the liver, kidneys, brain, and urinary bladder of rats. Hepatocellular hypertrophy occurred at $\geq$ 2500 mg/kg. Nephrosis was observed in rats that died, and damage to the tubular epithelium of the kidney occurred in terminally sacrificed rats. In the brain, mineralized foci and necrosis of neuronal cells were observed in male and female rats at 5000 mg/kg and males at 2500 mg/kg. Hemorrhage of the bladder (mucosa and muscularis) was seen in male and female rats at 5000 mg/kg and males at 2500 mg/kg. Signs of toxicity seen in mice receiving $\geq$ 2500 mg/kg included subconvulsive jerking, prostration, impaired grasping reflex, bradypnea, hypothermia, ataxia, and hypoactivity. By week 13, the mean body weight of males given 2500 mg/kg was significantly ($p < 0.05$) lower than that of controls. No adverse effects were reported in rats exposed to the lowest dose, 312 mg/kg/day, or in mice exposed to doses < 2500 mg/kg/day.

In an early subchronic gavage study, Wolf et al. (1956) observed no adverse effects in female Wistar rats treated with 0, 118, 354, or 590 mg/kg of toluene in olive oil, 5 days/week for 27–28 weeks (Wolf et al., 1956).

3.1.3 Chronic Toxicity

Information on the chronic oral toxicity of toluene in humans or animals was not available.

3.1.4 Developmental and Reproductive Toxicity

3.1.4.1 Human

Information on the developmental and reproductive toxicity of toluene in humans following oral exposure was not available.

3.1.4.2 Animal

Oral administration of a single dose of 2350 mg/kg/day of toluene on gestational days 7–14 had no effect on the number of viable litters of mice and single doses of 1800 or 2350 mg/kg/day did not cause developmental effects (Seidenberg et al., 1986; Smith, 1983).

Kostas and Hotchin (1981) exposed female NYLAR mice to 16, 80, or 400 ppm toluene in drinking water beginning at the mating period and continuing throughout gestation and lactation. Upon weaning, the offspring were exposed to the same drinking water solutions until the time of behavioral testing—45–55 days of age. Rotorod performance was affected in all toluene-exposed groups, but there was an inverse dose-relationship. Decreased open-field activity was seen at 400 ppm. Offspring mortality rate, development of eye or ear openings, and surface-righting response of offspring was not affected.

Nawrot and Staples (1979) administered 0.3, 0.5, or 1.0 mL/kg (260, 433, or 867 mg/kg) of toluene in cottonseed oil by gavage 3 times/day on days 6–15 of gestation or 1.0 mL/kg (867 mg/kg) on days 12–15 of gestation to pregnant CD-1 mice. Increased embryonic lethality was reported in all groups treated with toluene on days 6–15 of gestation. Fetal weight was reduced in the mid- and high-dosed groups, and the incidence of cleft palate was increased in high-dosed fetuses. Maternal toxicity (decreased weight gain) was the only effect noted in mice treated on days 12–15 of gestation.

3.1.5 Reference Dose

3.1.5.1 Subchronic

ORAL RfD: 2 mg/kg/day (U.S. EPA, 1993)
NOAEL: 223 mg/kg/day
LOAEL: 446 mg/kg/day
UNCERTAINTY FACTOR: 100

PRINCIPAL STUDY: NTP, 1990

COMMENTS: The same study, described in Subsect. 3.1.2.2, was used for the derivation of the subchronic and chronic RfD. The dose was adjusted for discontinuous exposure (5 days/week). An uncertainty factor of 100 was applied to account for interspecies extrapolation (10) and intraspecies variability (10).

3.1.5.2 Chronic

ORAL RfD: 0.2 mg/kg/day (U.S. EPA, 1992)
NOAEL: 223 mg/kg/day
LOAEL: 446 mg/kg/day
UNCERTAINTY FACTOR: 1000
CONFIDENCE:
Study: High
Data Base: Medium

RfD: Medium

VERIFICATION DATE: 6/20/90

PRINCIPAL STUDY: NTP, 1990

COMMENTS: The RfD is based on a gavage study with rats exposed to toluene for 13 weeks, with increased liver and kidney weights as critical effect. The dose was adjusted for discontinuous exposure (5 days/week). An uncertainty factor of 1000 was applied to account for interspecies extrapolation (10), intraspecies variability (10), and for the use of a subchronic study for chronic RfD derivation (10). Confidence in the data base and RfD is rated medium because the available oral studies are all subchronic and because of a lack of reproductive toxicity studies (EPA, 1992).

3.2 INHALATION EXPOSURES

3.2.1 Acute Toxicity

3.2.1.1 Human

Acute toxicity data of toluene in humans come from experimental exposures, case reports of intentional abuse (glue sniffing), and accidental occupational exposures. The major acute effects of toluene in humans are CNS dysfunction and neurological impairment. Studies reviewed by NTP (1990) showed that individuals developed fatigue, drowsiness, impaired cognitive function, incoordination, and irritation of the eyes and throat after a single exposure to toluene at concentrations ranging from 50 to 1500 ppm for 3–8 hours. These effects increased in severity with increases in concentration and progressed to nausea, staggering gait, confusion, extreme nervousness, muscular fatigue, and insomnia lasting for several days (NTP, 1990). Exposure to concentrations ranging from 10,000 to 30,000 ppm have resulted in narcosis and death (WHO, 1985).

In a controlled exposure study, Andersen et al. (1983) exposed human subjects to 0, 10, 40, or 100 ppm toluene for 6 hours on each of 4 consecutive days. Eye and nose irritation occurred at 100 ppm, without affecting nasal mucous flow or lung function. The subjects frequently reported headaches, dizziness, and a feeling of intoxication. These effects were not reported in the 10- or 40-ppm exposure groups. No effects were seen in performance tests.

3.2.1.2 Animal

LC_{50} values for 6- to 7-hour exposures are 12,200 ppm for rats and 5300–7000 ppm for mice (EPA, 1990). Central nervous system effects are the primary toxic effects following acute inhalation exposure to toluene. The CNS response is biphasic, with an initial excitable phase followed by depression.

Rats exposed to 10,000 to 15,000 ppm toluene for 60 minutes exhibited an initial increase in locomotor activity; however, at continued exposure, locomotor activity decreased and eventually ceased (Hinman, 1987). Rats exposed to 125, 250, or 500 ppm toluene for 4 hours showed a decline in trained neuromuscular responses 20 hours after exposure (Kishi et al., 1988). Exposure of weanling or young rats to 7550 mg/m^3 (~2000 ppm), 8 hours/day for 3 days or to 5660 mg/m^3

(~1500 ppm) for 14 hours resulted in hearing loss (Pryor et al., 1984). Acute exposure of monkeys caused impaired cognitive and motor abilities when exposed to 1000 or 2000 ppm, concentrations that were below those causing overt clinical signs of neurotoxicity such as ataxia and tremors (Taylor and Evans, 1985).

3.2.2 Subchronic Toxicity

3.2.2.1 Human

Echeverria et al. (1989) exposed volunteers to 0, 74, or 151 ppm toluene for 7 hours over 3 days. This exposure sequence was repeated for a total of 42 exposures over a 3-month period. A battery of performance tests showed that visual perception was affected and manual dexterity differed from control values at both exposure levels. However, psychomotor test results were unaffected by toluene exposure. Subjective symptoms such as eye irritation, headache, and somnolence increased with exposure.

Individuals who had abused toluene for at least 1 year reported disturbed behavior; slow thought and speech; illusionary misinterpretations; tactile, auditory, and visual hallucinations; and delusional ideas (Evans and Raistrik, 1987).

3.2.2.2 Animal

Pryor et al. (1984) found irreversible high frequency hearing loss in rats exposed to toluene at concentrations of 1200 ppm, 12 hours/day for 5 weeks. Rats exposed at weaning age exhibited a more pronounced hearing loss than young adult rats.

Ungvary et al. (1980) exposed male and female CFY rats to 1000 mg/m^3 (265 ppm) toluene 6 hours/day, 5 days/week for 6 months. No adverse effects were seen in males; however, females exhibited increased cytochrome P-450 levels, decreased body weights, and increased liver-to-body weight ratios. Exposure to 3500 mg/m^3 (928 ppm) (males only), 8 hours/day, 5 days/week for 6 months produced effects similar to those elicited in females at the lower dose.

In an NTP (1990) study, F344/N rats and B6C3F$_1$ mice were exposed to 0, 100, 652, 1250, 2500, or 3000 ppm toluene 6.5 hours/day, 5 days/week for 15 weeks (rats) or 14 weeks (mice). All female rats survived exposure to 3000 ppm, but 8/10 male rats died within 2 weeks at this exposure level. Decreased body weights and increased relative liver, kidney, and heart weights were seen in rats exposed to the two higher concentrations compared with those of controls. All female mice and 5/10 male mice exposed to 3000 ppm and 7/10 female mice exposed to 2500 ppm died during the first 2 weeks. The body weights of all exposed groups were lower than those of controls. Relative liver weights were increased in mice exposed to $\geq$ 625 ppm. Increased relative lung weights were seen at $\geq$ 1250 ppm and increased relative kidney weights at $\geq$ 1250 ppm (females only). Centrilobular atrophy of the liver occurred in all male mice exposed to 2500 ppm and in 70% of male mice exposed to 3000 ppm.

No effects on the kidneys, lungs, spleen, or heart were observed in rats, guinea pigs, dogs, or monkeys continuously exposed to 107 ppm toluene for 90 days (Jenkins et al., 1970). In addition, no treatment-related effects were observed on the brain and spinal cord of dogs and monkeys, and no significant changes were observed in hematological parameters in any of the species tested.

3.2.3 Chronic Toxicity

3.2.3.1 Human

Occupational exposure studies that have investigated the potential neurotoxicity of toluene have not shown severe neurological effects. Rotogravure printers exposed to an estimated 117 ppm toluene for up to 22 years exhibited no clinically significant adverse effects on the nervous system (Juntunen et al., 1985). Occupational studies by Yin et al. (1987) and Lee et al. (1988) reported subjective symptoms such as headaches, sore throats, and dizziness following exposure to approximately 100 ppm toluene. Foo et al. (1990) conducted a cross-sectional study involving 30 female workers employed at an electronic assembly plant where toluene was emitted from glue. The toluene workers were employed for an average of 5.7 years and exposed to time-weighted-average (TWA) air concentrations of 88 ppm (332 mg/m^3) toluene; a control group was exposed to 13 ppm (49 mg/m^3) (TWA). A battery of eight neurobehavioral tests showed that the exposed group had a poorer performance in 6 of 8 tests administered when compared with the control group.

Cerebellar dysfunction, mental retardation, abnormal encephalograms, brain atrophy, and visual impairment were observed in long-term abusers of pure toluene (6–14 years) (NTP, 1990). Clinical studies of toluene sniffers suggest that ototoxicity as well as vestibular deficits may occur after prolonged inhalation exposure (Winneke, 1992).

Some studies have reported effects on the kidney and liver following inhalation exposure to toluene. Askergren (1984) reported increased protein excretion and increased excretion of erythrocytes and leukocytes/tubular epithelial cells in construction workers exposed to toluene. Renal tubular effects, indicated by metabolic acidosis (hypokalemia, hypophosphatemia, and hyperchloremia), have been associated with abusers of toluene-containing solvents (NTP, 1990). Krusell et al. (1985), however, indicated that there is no causal relationship between toluene exposure alone and renal injury. Hepatomegaly was observed in airplane painters exposed to 100–1150 ppm toluene in air for up to 5 years (Greenburg et al., 1942) and in 20–50% of workers exposed to toluene at 53–80 ppm for 2–14 years (Szilard et al., 1978).

Although early studies (before the mid-1950s) have associated chronic exposure to toluene with myelotoxic effects, most recent studies generally indicate that toluene does not cause toxic effects in blood and bone marrow. The previously observed hematologic effects are now attributed to concurrent exposure to benzene, a common contaminant of toluene at that time (NTP, 1990; ATSDR, 1989).

3.2.3.2 Animal

F344/N rats and B6C3F_1 mice were exposed by inhalation to 0, 600, or 1200 ppm toluene 6.5 hours/day, 5 days/week for 15 months or 2 years (NTP, 1990). Mean body weights and survival of rats and mice were generally similar to those seen in controls throughout the 2-year study. All rats exhibited nephropathy, with an increased severity in toluene-exposed animals. At 15 months, goblet cell hyperplasia and degeneration of olfactory and respiratory epithelium were increased in exposed rats. At 2 years, erosion of the olfactory epithelium and degeneration of respiratory epithelium were significantly ($p < 0.05$) increased in males and females at both doses. Mice exposed to 1200 ppm exhibited minimal hyperplasia of the bronchial epithelium. No other biologically important increases in non-neoplastic lesions were seen in exposed mice. The lesions observed in this study were considered mild and are not unusual with solvent exposures.

In an earlier 2-year inhalation bioassay, male and female F344 rats were exposed to 0, 30, 100,

or 300 ppm toluene, 6 hours/day, 5 days/week (Gibson and Hardisty, 1983). Except for a dose-related decrease in hematocrit values in females exposed to 100 and 300 ppm and increased corpuscular hemoglobin concentrations in high-dosed females, all clinical chemistry, hematology, and urinalysis values were normal at the termination of the study. No other adverse effects were observed.

3.2.4 Developmental and Reproductive Toxicity

3.2.4.1 Human

Evidence for human developmental effects from case reports and occupational exposure studies is equivocal because these studies are confounded by exposure to multiple organic solvents during pregnancy. A retrospective study of 14 women exposed to mixed solvents, including toluene, suggested an increased risk of CNS abnormalities and defects of neural tube closure in children exposed in utero (Holmberg, 1979). In another study, microcephaly, CNS dysfunction, attentional deficits, minor craniofacial and limb abnormalities, developmental delay, and variable growth were observed in three children exposed in utero to toluene as a result of maternal solvent abuse (Hersh et al., 1985). A third study reported growth retardation and dysmorphism in five infants whose mothers were chronic paint sniffers (Goodwin, 1988).

3.2.4.2 Animal

Retarded bone ossification and growth inhibition were observed in fetuses of Charles River rats exposed to 400 ppm toluene, 6 hours/day on days 6–15 of gestation (Litton Bionetics, 1978), but no teratogenic effects were observed in the study. No compound-related effects on sperm or adverse effects on estrous cycle were seen in Fischer 344 rats or $B6C3F_1$ mice exposed to toluene at concentrations ranging from 100 to 3000 ppm, 6.5 hours/day, 5 days/week for 15 weeks (rats) or 14 weeks (mice) (NTP, 1990).

Pregnant CD-1 mice, exposed daily to 200 or 400 ppm toluene for 7 hours during gestational days 7–16, showed a significant increase in dilated renal pelves at 200 ppm but not at 400 ppm (Courtney et al., 1986). At 400 ppm, a significant shift in the fetal rib profile was observed. Both exposure concentrations caused maternal toxicity. Hudak and Ungvary (1978) observed decreased body weights but no malformations in fetuses of CFLP mice continuously exposed by inhalation to 133 ppm toluene on days 6–13 of gestation. Retarded skeletal development resulting in poorly ossified sternebrae, split vertebral centra, and shortened free ribs was reported in CFY rats continuously exposed to 230 or 399 ppm toluene on days 1–8 of development (Hudak and Ungvary, 1978). Fetuses of rats exposed to 399 ppm on days 9–14 of gestation exhibited extra ribs and fused sternebrae. No increases in visceral or external malformations were identified in mice or rats.

Deaths, but no teratogenic effects, were observed in fetuses of New Zealand rabbits continuously exposed to 266 ppm toluene on days 6–20 of gestation (Ungvary and Tatrai, 1985).

3.2.5 Reference Concentration

3.2.5.1 Subchronic

INHALATION RfC: 0.4 mg/m^3 (U.S. EPA, 1993)
LOAEL: 332 mg/m^3
UNCERTAINTY FACTOR: 300

PRINCIPAL STUDY: Foo et al., 1990

COMMENTS: The chronic inhalation RfC was adopted as the subchronic inhalation RfC. The study is described in Subsect. 3.2.3.1.

3.2.5.2 Chronic

INHALATION RfC: 0.4 mg/m^3 (U.S. EPA, 1992)
LOAEL: 332 mg/m^3
UNCERTAINTY FACTOR: 300

PRINCIPAL STUDY: Foo et al., 1990

CONFIDENCE:
Study: Medium
Data Base: Medium
RfC: Medium

COMMENTS: The chronic RfC was based on results of a battery of neurological tests in occupationally exposed females. Adverse neurological effects at atmospheric concentrations of 332 mg/m^3 were considered the lowest-observed-adverse-effect level (LOAEL). An uncertainty factor (UF) of 300 was used to account for intraspecies variability (10), for the use of a LOAEL (10), and for data base deficiencies (3). The data base and RfC were given a medium rating because long-term data in humans are not available for neurotoxicity endpoints and the reproductive/developmental studies in animals were not comprehensive.

3.3 OTHER ROUTES OF EXPOSURE

3.3.1 Acute Toxicity

3.3.1.1 Humans

Eye irritation has been reported in humans following exposure to toluene vapors (Andersen et al., 1983). The liquid splashed in the eyes has caused a transient disturbance of the eyes, with healing complete within 48 hours (Grant, 1986).

3.3.2.2 Animals

The LD_{50} value reported for New Zealand rabbits following a single dermal application is 14.1 mL/kg (12.2 g/kg); for Wistar rats, the LD_{50} following an intraperitoneal injection is 1.64 g/kg (EPA, 1990).

Undiluted toluene applied to intact and abraded skin of rabbits for 24 hours produced moderate skin irritation (Guillot et al., 1982). Direct application of toluene to the conjunctiva has resulted in slight to moderately severe irritation of rabbit eyes (ATSDR, 1989).

3.3.2 Subchronic Toxicity

3.3.2.1 Human

Prolonged or repeated skin contact may cause drying and dermatitis due to the degreasing action of toluene and its removal of protective skin oils (ATSDR, 1989; NIOSH, 1973).

3.3.2.1 Animal

Information on the subchronic toxicity of toluene by other routes of exposure in animals was not available.

3.3.3 Chronic Toxicity

Information on the chronic toxicity of toluene by other routes of exposure in humans or animals was not available.

3.3.4 Developmental and Reproductive Toxicity

Information on the developmental or reproductive toxicity of toluene by other routes of exposure in humans or animals was not available.

3.4 TARGET ORGANS/CRITICAL EFFECTS

3.4.1 Oral Exposures

3.4.1.1 Primary Target Organs

1. Central nervous system: Subchronic exposure to toluene caused necrosis and mineralization of brain cells and hearing loss in rats and altered brain levels of neurotransmitters in mice. Pre- and post-natal exposure affected rotorod performance and open-field activity in mice.

2. Kidneys: Subchronic exposure to toluene produced nephrosis, damage to tubular epithelium, and increased kidney weights in rats.

3. Liver: Subchronic exposure to toluene produced increased liver weights in rats and mice and hepatocellular hypertrophy in rats.

4. Reproduction: Embryonic deaths, reduced fetal weights, and cleft palates were observed in mice exposed to toluene during gestation.

3.4.1.2 Other Target Organs

1. Immune system: Depressed immune responses were observed in rats following subchronic exposure to toluene.

2. Urinary bladder: Hemorrhage of the bladder mucosa and muscularis were observed in rats following subchronic exposure to toluene.

3.4.2 Inhalation Exposures

3.4.2.1 Primary Target Organs

1. Central nervous system: Chronic occupational exposure to toluene has resulted in headaches, dizziness, and impaired neurobehavioral performance. Brain dysfunction, abnormal encephalograms, brain atrophy, mental retardation, and visual and hearing impairment have been reported in long-term abusers of toluene. Subchronic exposure of rats produced a high frequency hearing loss.

2. Kidneys: Chronic exposure of workers to toluene has resulted in abnormalities of kidney function. Renal tubular effects have been associated with abuse of toluene-containing solvents. Chronic exposure to toluene has caused nephropathy in rats.

3. Liver: Hepatomegaly has been reported in workers chronically exposed to toluene. Increased liver weights were reported in rats following subchronic exposure to toluene.

4. Respiratory system: Sore throat was one of the symptoms reported in workers chronically exposed to toluene. Chronic exposure of rats has produced lesions in olfactory and respiratory epithelia.

3.4.2.2 Other Target Organs

Reproduction: Equivocal evidence shows that exposure to toluene in utero causes an increased risk of CNS abnormalities and developmental delay in humans. Exposure during gestation has resulted in delayed skeletal maturation in rats and mice.

3.4.3 Other Routes of Exposure

Skin: Repeated or prolonged contact may cause drying and dermatitis.

4. CARCINOGENICITY

4.1 ORAL EXPOSURES

4.1.1 Human

Information on the carcinogenicity of toluene in humans following oral exposure was not available.

4.1.2 Animal

In a 2-year gavage study, Maltoni et al. (1985) administered 500 mg/kg of toluene, 4 to 5 days/week to 40 male and 40 female Sprague-Dawley rats. At the end of the study, 8% of the treated males and 17.5% of the treated females developed hemolymphoreticular neoplasms compared with 7% of the treated males and 3% of the female controls, respectively.

4.2 INHALATION EXPOSURES

4.2.1 Human

Svensson et al. (1990) studied a cohort of 1020 rotogravure workers exposed to toluene and employed for a minimum of 3 months in eight plants from 1925 to 1985. The overall incidence of tumors during the time period 1958–1985 was not increased. Among specific tumors, only those of the respiratory tract were significantly increased (16 observed vs 9 expected). However, statistical significance was not attained when only workers with an exposure period of at least 5 years and a latency period of at least 10 years were considered. Results of a retrospective cohort mortality study of 1008 male oil refinery workers exposed to toluene and other chemicals indicated that worker mortality due to all causes of death and to cancer were lower than that for the general population (Wen et al., 1985).

4.2.2 Animal

Two long-term bioassays found no evidence of carcinogenicity in rats and mice following inhalation of toluene. Compared with controls, the incidence of treatment-related neoplastic lesions was not increased in male and female F344 rats exposed to 30, 100, or 300 ppm, 6 hours/day, 5 days/week for 24 months (Gibson and Hardisty, 1983). Similarly, there was no evidence of carcinogenic activity in male and female F344/N rats or male and female $B6C3F_1$ mice exposed to 600 or 1200 ppm toluene, 6.5 hours/day, 5 days/week for 24 months (NTP, 1990).

4.3 OTHER ROUTES OF EXPOSURE

4.3.1 Human

Information on the carcinogenicity of toluene in humans by other routes of exposure was not available.

4.3.2 Animal

Several studies examined the carcinogenicity of toluene following repeated dermal application in mice. Toluene applied to the shaved skin of male A/He, C3HeB, and SRW mice, three times weekly for life produced no carcinogenic response (Poel, 1963). No skin papillomas or carcinomas were observed in albino mice that received twice weekly dermal applications of toluene for 50 weeks (Coombs et al., 1973). One skin papilloma and one skin carcinoma was reported in a group of mice treated twice weekly for 72 weeks with 1 drop of a 0.2% solution of toluene (Lijinsky and Garcia, 1972). In initiation/promotion studies, toluene was reported to have little or no promoting activity after initiation with 7,12-dimethylbenz(α)anthracene (DMBA) (EPA, 1990). Toluene inhibited skin carcinogenesis in mice in the two-stage model using benzo[*a*]pyrene or DMBA as tumor initiators and phorbol-12-myristate-13-acetate as a tumor promoter (Weiss et al., 1986).

4.4 EPA WEIGHT-OF-EVIDENCE

Classification—Group D; not classifiable as to human carcinogenicity (EPA, 1992)
Basis: No human data and inadequate animal data. Toluene did not produce positive results in the majority of genotoxicity assays.

4.5 CARCINOGENICITY SLOPE FACTORS

No carcinogenicity slope factors were calculated.

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Attachment C3

Superfund Technical Support Center
Provisional Toxicity Values

2. HEALTH EFFECTS

2.1 INTRODUCTION

The primary purpose of this chapter is to provide public health officials, physicians, toxicologists, and other interested individuals and groups with an overall perspective of the toxicology of polycyclic aromatic hydrocarbons (PAHs). It contains descriptions and evaluations of toxicological studies and epidemiological investigations and provides conclusions, where possible, on the relevance of toxicity and toxicokinetic data to public health.

A glossary and list of acronyms, abbreviations, and symbols can be found at the end of this profile.

2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

To help public health professionals and others address the needs of persons living or working near hazardous waste sites, the information in this section is organized first by route of exposure-inhalation, oral, and dermal; and then by health effect-death, systemic, immunological, neurological, reproductive, developmental, genotoxic, and carcinogenic effects. These data are discussed in terms of three exposure periods-acute (14 days or less), intermediate (15-364 days), and chronic (365 days or more).

Levels of significant exposure for each route and duration are presented in tables and illustrated in figures. The points in the figures showing no-observed-adverse-effect levels (NOAELs) or lowest-observed-adverse-effect levels (LOAELs) reflect the actual doses (levels of exposure) used in the studies. LOAELs have been classified into "less serious" or "serious" effects. "Serious" effects are those that evoke failure in a biological system and can lead to morbidity or mortality (e.g., acute respiratory distress or death). "Less serious" effects are those that are not expected to cause significant dysfunction or death, or those whose significance to the organism is not entirely clear. ATSDR acknowledges that a considerable amount of judgment may be required in establishing whether an end point should be classified as a NOAEL, "less serious" LOAEL, or "serious" LOAEL, and that in some cases, there will be insufficient data to decide whether the effect is indicative of significant dysfunction. However, the Agency has established guidelines and policies that are used to classify these end points. ATSDR believes that there is sufficient merit in this approach to warrant an attempt

at distinguishing between "less serious" and "serious" effects. The distinction between "less serious" effects and "serious" effects is considered to be important because it helps the users of the profiles to identify levels of exposure at which major health effects start to appear. LOAELs or NOAELs should also help in determining whether or not the effects vary with dose and/or duration, and place into perspective the possible significance of these effects to human health.

The significance of the exposure levels shown in the Levels of Significant Exposure (LSE) tables and figures may differ depending on the user's perspective. Public health officials and others concerned with appropriate actions to take at hazardous waste sites may want information on levels of exposure associated with more subtle effects in humans or animals (LOAELs) or exposure levels below which no adverse effects (NOAELs) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels or MRLs) may be of interest to health professionals and citizens alike.

Levels of exposure associated with carcinogenic effects (Cancer Effect Levels, CELs) of PAHs are indicated in Tables 2-1, 2-2, and 2-3 and Figures 2-l and 2-2. Because cancer effects could occur at lower exposure levels, Figure 2-2 also shows a range for the upper bound of estimated excess risks, ranging from a risk of 1 in 10,000 to 1 in 10,000,000 (10^{-4} to 10^{-7}), as developed by EPA.

Estimates of exposure levels posing minimal risk to humans (Minimal Risk Levels or MRLs) have been made for PAHs. An MRL is defined as an estimate of daily human exposure to a substance that is likely to be without an appreciable risk of adverse effects (noncarcinogenic) over a specified duration of exposure. MRLs are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive health effect(s) for a specific duration within a given route of exposure. MRLs are based on noncancerous health effects only and do not consider carcinogenic effects. MRLs can be derived for acute, intermediate, and chronic duration exposures for inhalation and oral routes. Appropriate methodology does not exist to develop MRLs for dermal exposure.

Although methods have been established to derive these levels (Barnes and Dourson 1988; EPA 1990), uncertainties are associated with these techniques. Furthermore, ATSDR acknowledges additional uncertainties inherent in the application of the procedures to derive less than lifetime MRLs. As an example, acute inhalation MRLs may not be protective for health effects that are delayed in development or are acquired following repeated acute insults, such as hypersensitivity reactions,

asthma, or chronic bronchitis. As these kinds of health effects data become available and methods to assess levels of significant human exposure improve, these MRLs will be revised.

A User's Guide has been provided at the end of this profile (see Appendix A). This guide should aid in the interpretation of the tables and figures for Levels of Significant Exposure and the MRLs.

PAHs are a group of chemicals that are formed during the incomplete burning of coal, oil, gas, wood, garbage, or other organic substances, such as tobacco and charbroiled meat. PAHs can either be synthetic or occur naturally. Most of these chemicals as individual compounds (i.e., not as part of a combustion product) have no known use except for research purposes. A few PAHs are used in medicines and to make dyes, plastics, and pesticides. Others are contained in asphalt used in road construction. They are found throughout the environment in the air, water, and soil. There are more than 100 different PAH compounds and the health effects of the individual PAHs are not exactly alike.

Fifty-four PAHs have been identified at one or more NPL hazardous waste sites. These 54 are acenaphthene, acenaphthylene, 2-acetoaminofluorene, anthracene, 9, 10-anthracenedione, benz[a]anthracene, benzo[a]pyrene, benzo[e]pyrene, benzo[a]fluoranthene, benzo[b]fluoranthene, benzo[b]fluorene, benzofluoranthene, benzo[j]fluoranthene, benzo[k]fluoranthene, benzo[g,h,i]fluoranthene, benzoperylene, benzo[g,h,i]perylene, benzophenanthrene, benzopyrene, benzothiophene, benzo[b]thiophene, chrysene, 4H-cyclopenta[d,e,f]phenanthrene, dibenz[a,j]anthracene, dibenz[a,h]anthracene, 7,12-dimethylbenz[a]anthracene, 2,7-dimethylbenzo[b]thiophene, 1,4-dimethoxyanthracene, dimethyl phenanthrene, 2,5dimethyl phenanthrene, dodecachlorodecahydrotrim, fluoranthene, fluorene, indeno[1,2,3-c,d] pyrene, 12-methylbenz[a]anthracene, methyl anthracene, 9-methylanthracene, 3-methylcholanthrene, methylfluorene, methylphenanthrene, 2-methylphenanthrene, 1-methylphenanthrene, 4-methylphenanthrene, methylpyrene, phenanthrene, phenanthridine, phenanthroline, pyrene, perylene, 6,7-tetrahydropyrene, tetramethylphenanthrene, 3,4,5,6-tetramethylphenanthrene, and trimethylphenanthrene.

However, only 17 PAHs are discussed in this profile. These 17 PAHs are:

- acenaphthene
- acenaphthylene
- anthracene

- benz[a]anthracene
- benzo[a]pyrene
- benzo[e]pyrene
- benzo[b]fluoranthene
- benzo[j]fluoranthene
- benzo[g,h,i]perylene
- benzo[k]fluoranthene
- chrysene
- dibenz[a,h]anthracene
- fluoranthene
- fluorene
- indeno[l,2,3-c,d]pyrene
- phenanthrene
- pyrene

These 17 PAHs were selected using the following four criteria:

(1) toxicity
(2) potential for human exposure
(3) frequency of occurrence at NPL hazardous waste sites
(4) extent of information available.

The 17 PAHs were combined into one profile to avoid repetition across multiple profiles on the individual PAHs since these chemicals often occur together in the environment and many have similar toxicological effects, environmental fate, etc. Instances in which it is known that the various PAHs differ with regard to toxicological effects or environmental fate will be pointed out. For example, PAHs can be classified as "alternant" (e.g., benzo[a]pyrene, benz]a]anthracene, chrysene, dibenz[a,h]anthracene) or "nonalternant" (e.g., fluoranthene, benzo[k]fluoranthene, benzol[j]fluoranthene, indeno[1,2,3-c,d]pyrene). This distinction is based on the electron density associated with the molecule. Altemant PAHs have an equally distributed electron density, whereas nonalternant PAHs behave almost as if they were two different molecules because of an uneven distribution of electron density from one portion of the molecule to another. The toxicological significance of this difference is that alternant and nonalternant PAHs appear to behave differently, for example, with regard to how they are metabolized to ultimate carcinogens (see Section 2.3.3, Metabolism).

Reliable health-based and environmental information exists on only a few of the 17 PAHs discussed in this profile, and the potential health effects of the other less well-studied PAHs must be inferred from this information. By combining all 17 PAHs in one profile, these comparisons and inferences can

easily be made. Although a large toxicity database exists on complex mixtures that contain PAHs (such as crude oils, various high boiling point distillates, complex petroleum products, coal tars, creosote, and the products of coal liquification processes), these data generally have not been used in this profile. It is difficult to ascertain the toxicity of the component PAHs in these mixtures because of the potential interactions that could occur and the presence of other toxic substances in the mixtures. Furthermore, ATSDR has developed a profile on one of these complex mixtures, creosote, and the reader is referred to this profile for information on this complex mixture (ATSDR 1994). However, most of the available information on the health effects of PAHs in humans must be inferred from studies that reported the effects of exposure to complex mixtures that contain PAHs. Several epidemiologic studies have shown increased mortality due to lung cancer in humans exposed to coke oven emissions, roofing-tar emissions, and cigarette smoke. Each of these mixtures contains benzo[a]pyrene, chrysene, benz[a]anthracene, benzo[b]fluoranthene, and dibenz[a,h]anthracene as well as other potentially carcinogenic PAHs and other carcinogenic and potentially carcinogenic chemicals, tumor promoters, initiators, and co-carcinogens such as nitrosamines, coal tar pitch, and creosote. It is thus impossible to evaluate the contribution of any individual PAH to the total carcinogenicity of these mixtures in humans because of the complexity of the mixtures and the presence of other carcinogens. Despite these limitations, reports of this nature provide qualitative evidence of the potential for mixtures containing PAHs such as benzo[a]pyrene, chrysene, benz[a]anthracene, benzo[b]fluoranthene, and dibenz[a,h]anthracene to cause cancer in humans. For this reason, and also because of the lack of data on the effects of individual PAHs in humans, such information has been included in this profile on PAHs.

2.2.1 Inhalation Exposure

2.2.1.1 Death

No studies were located regarding death in humans following inhalation exposure to any of the 17 PAHs discussed in this profile. However, a dose-related decrease in survival was noted in hamsters after 60 weeks of inhalation exposure to 46.5 mg/m^3 benzo[a]pyrene for 109 weeks (Thyssen et al. 1981). The authors attributed this reduced survival in part to toxic and carcinogenic effects induced by this PAH (e.g., tumors in the pharynx and larynx that could have inhibited food intake).

2.2.1.2 Systemic Effects

No studies were located regarding cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, dermal, or ocular effects in humans or animals following inhalation exposure to any of the 17 PAHs discussed in this profile. The systemic effects observed after inhalation exposure are discussed below.

The highest NOAELs for respiratory and renal effects in each species and duration category are recorded in Table 2-1 and plotted in Figure 2-1.

Respiratory Effects. Only one study was located regarding respiratory effects in humans following inhalation exposure to PAHs, specifically, benzo[a]pyrene. The respiratory health of 667 workers in a rubber factory was investigated (Gupta et al. 1993). Respiratory health was evaluated and examined for correlations to length of employment at the factory. In addition, total suspended particulate matter and benzo[a]pyrene concentrations were monitored in various parts of the factory and examined for possible correlation with the respiratory health of the workers in the same area of the factory. Statistically significant decrements in ventilatory function occurred following prolonged exposure as assessed by duration of employment. When different sections of the factory were considered, workers in the compounding section were the most affected, which was associated with the highest exposure to particulate matter and benzo[a]pyrene. Workers in the compounding section exhibited radiographic abnormalities including patch opacities, prominent bronchiovascular markings, and pleural effusions. Other symptoms included bloody vomit, breathing problems, chest pains, chest irritation, throat irritation, and cough. Workers in other areas of the plant exposed to lower levels of particulate matter and benzo[a]pyrene were similarly affected although to a lesser degree and in fewer numbers (Gupta et al. 1993). No attempt was made to separate the effects of exposure to benzo[a]pyrene and particulate matter, or to identify possible simultaneous exposure to other toxic chemicals.

Groups of 40 Fischer-344/Crl rats/sex were exposed nose-only to an aerosol of benzo[a]pyrene (7.7 mg/m^3) 2 hours/day, 5 days/week, for 4 weeks (Wolff et al. 1989a). Nasal and left lung sections were examined histopathologically. No treatment-related lesions were noted in the lungs or nasal cavities of the animals exposed to benzo[a]pyrene. Although this was a well-conducted inhalation toxicity study, it is not appropriate for use in risk assessment because only one concentration was

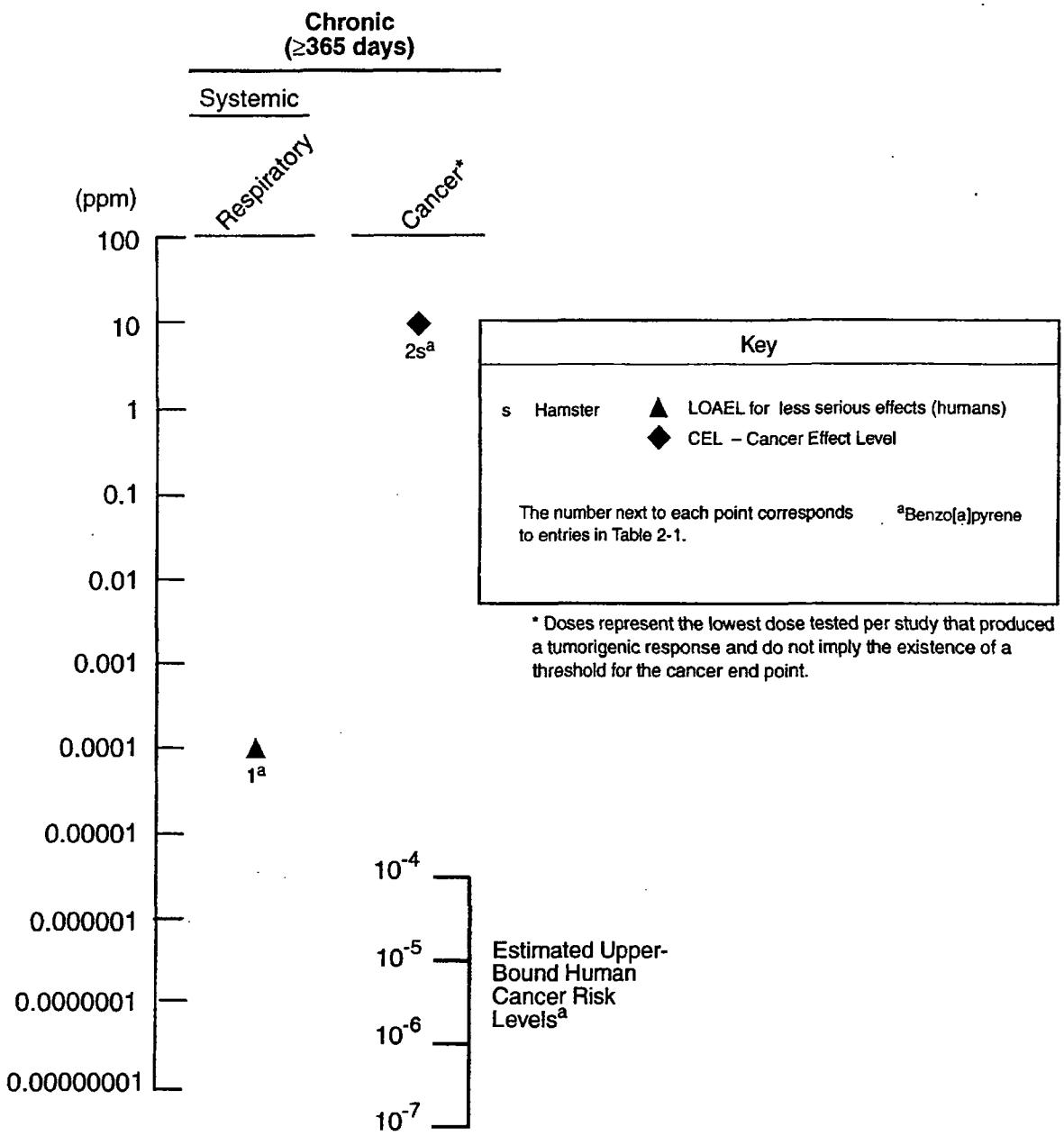
TABLE 2-1. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons - Inhalation

Key to[a] figure	Species/ (strain)	Exposure/ duration/ frequency	System	NOAEL (mg/m3)	LOAEL Less serious (mg/m3)	LOAEL Serious (mg/m3)	Reference
CHRONIC EXPOSURE							
Systemic							
1	Human	6 mo - >6 yr	Resp			0.0001 NS (reduced lung function, abnormal chest x-ray, cough, bloody vomit, throat and chest irritation.	Gupta et al. 1993 benzo[a]pyrene
Cancer							
2	Hamster (Syrian golden)	109 wk 7 d/wk 3-4.5 hr/d				9.5 M (CEL: 34.6% increase in respiratory tract tumors; neoplasms of the upper digestive tract in 26.9%)	Thyssen et al. 1981 benzo[a]pyrene

[a]The number corresponds to entries in Figure 2-1.

CEL = cancer effect level; d = day(s); hr = hour; LOAEL = lowest-observed-adverse-effect level; M = male; mo = month; NOAEL = no-observed-adverse-effect level; NS = not specified; Resp = respiratory; wk = week(s); yr = year(s)

Figure 2-1. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons – Inhalation



studied (thereby precluding the assessment of a dose-response relationship); no adverse treatment-related effects were observed; and the only parts of the respiratory tract examined histopathologically were the lungs and nose.

Renal Effects. No studies were located regarding renal effects in humans following inhalation exposure to any of the 17 PAHs discussed in this profile.

Groups of 40 Fischer-344/Crl rats/sex were exposed nose-only to an aerosol of benzo[a]pyrene 2 hours/day, 5 days/week, for 4 weeks (Wolff et al. 1989a). Kidney sections were examined histopathologically. No treatment-related lesions were noted in the kidneys of the animals exposed to benzo[a]pyrene.

2.2.1.3 Immunological and Lymphoreticular Effects

Humoral immunity was monitored in male iron foundry workers in Poland (Szczeklik et al. 1994). Coke oven workers (199) were compared to cold-rolling mill workers (76). The groups were similar with respect to age, length of employment, and smoking habits. The results showed that coke oven workers, exposed to high concentrations of atmospheric PAHs, including fluoranthene, perylene, pyrene, benzo[a]pyrene, chrysene, benz[a]anthracene, dibenz[a,h]anthracene, and benzo[g,h,i]perylene, had reduced levels of serum immunoglobins. The workers most exposed to PAHs worked at the topside area of the coke ovens. Benzo[a]pyrene exposure was used as a reference point. Coke oven workers, exposed to 0.0002-0.50 mg/m^3 benzo[a]pyrene, were compared to cold-rolling mill workers, whose exposure to benzo[a]pyrene was 3-5 orders of magnitude less. Average length of employment was 15 years. IgG, IgA, IgM, and IgE concentrations were measured. Coke oven workers exhibited a marked depression of mean serum IgG and IgA, compared to mill workers. IgM tended to decrease, whereas IgE tended to increase in the coke oven workers. The biological significance of this finding is unclear and is not addressed by the authors. However, the authors suggest that serum immunoglobulin levels may be a useful biomarker for PAH exposure. The authors note, however, that the coke oven workers were exposed to higher levels of sulfur dioxide and carbon monoxide than were the cold-rolling mill workers, and they suggest that this additional exposure may have potentiated the effects of the PAH exposure. The potential contribution of the smoking habits of the subjects was not investigated.

2. HEALTH EFFECTS

No studies were located regarding the following effects in humans or animals following inhalation exposure to any of the 17 PAHs discussed in this profile:

2.2.1.4 Neurological Effects

2.2.1.5 Reproductive Effects

2.2.1.6 Developmental Effects

2.2.1.7 Genotoxic Effects

Becher et al. (1984) evaluated urine and blood samples from 15 aluminum plant workers (average age, 29 years; average years employed, 3.8) exposed to an estimated total PAH concentration of 1 mg per 8-hour work shift. The main PAH components identified by air sampling and also detected in the urine samples included phenanthrene, fluoranthene, pyrene, benz[a]anthracene, chrysene, benzo[e]pyrene, and benzo[a]pyrene. Results of the cytogenetic analysis of peripheral lymphocytes of the exposed workers indicated that the frequency of sister chromatid exchange was not influenced by the presence of large amounts of PAHs. These findings were reported to be consistent with the negligible increase in lung cancer found in epidemiological studies of aluminum workers. The investigators, therefore, questioned the relevance of PAH air monitoring as a measure of the occupational hazards associated with PAH exposure. Alternatively, it is possible that there are no occupational hazards associated with PAH exposure at these levels. Similar results were obtained with iron factory workers (length of employment: 2 46 years) exposed to 0.0005-0.00 mg/m^3 benzo[a]pyrene (Perera et al. 1993), who exhibited an increased rate of mutations in peripheral lymphocytes that were not correlated with PAH exposure. These authors suggest that both biomonitoring and personal monitoring may be necessary to evaluate exposure.

The high lung cancer rate in Xuan Wei, China, is associated with smokey coal use in unvented homes, but not with wood or smokeless coal use (Mumford et al. 1993). Smoky coal combustion emits higher PAH concentrations than wood combustion. This study evaluated PAH-DNA adducts in placentas, and in peripheral and cord white blood cells (WBC) from Xuan Wei women burning smoky coal or wood and from Beijing women using natural gas. Exposures were based on benzo[a]pyrene concentrations determined by personal monitors. Women in Xuan Wei burning smoky coal without a chimney were

exposed to 0.383 mg/m^3 benzo[a]pyrene, those burning smoky coal with chimneys were exposed to 0.184 mg/m^3, and women burning wood or using natural gas (Beijing) had no detectable exposure to benzo[a]pyrene. Positive results (detection of PAH-DNA adducts) were found in 58, 47, and 5% of the placentas from Xuan Wei women burning smoky coal without a chimney, with a chimney, and Beijing women using natural gas, respectively. Positive results were found in 46, 6.5, 56, and 25% of placentas from Xuan Wei women who lived in houses without and with chimneys, Xuan Wei women burning wood, and Beijing controls, respectively. Peripheral WBC samples were positive in 7 of 9, 8 of 9, and 3 of 9 for the Xuan Wei women who lived in houses without and with chimneys and Beijing women, respectively. No dose-response relationship was observed between the air benzo[a]pyrene concentrations and DNA adduct levels or percentage of detectable samples. However, using the fluorescent color assay, there was a significant association between DNA adduct detection in the placenta and cooking methods. Moreover, individual comparisons of the data revealed a significant difference between both smokey coal groups (chimney, no chimney) and natural gas cooking. The results of this study suggest that DNA adducts can be used as a biomarker to assess human exposure to combustion emissions.

Thirty-four workers in an electrode paste plant were monitored for response to exposure (Ovrebo et al. 1994). Exposure to benzo[a]pyrene was 0.9 μg/m^3; exposure to pyrene was 3.5μg/m^3. 1-Hydroxypyrene was measured in the urine, and PAH-DNA adducts were measured in white blood cells to demonstrate their relationship to the exposure. Results from these workers were compared to two reference control groups: research and development (R&D) workers and nickel refinery workers. Mean values of PAH-DNA adducts in the white blood cells from randomly selected participants in the three groups were only marginally different, with the exception of two smokers in the electrode plant, who had the highest levels. Mean PAH-DNA adduct levels were 10.9 adducts per 108 nucleotides for the electrode workers, 10.8 adducts per 10^8 nucleotides for the R&D personnel, and 10.0 adducts per 10^8 nucleotides for nickel plant workers not occupationally exposed to PAHs. No correlation was found between PAH-DNA adducts and 1-hydroxypyrene in the urine.

In an ongoing comprehensive evaluation of biological markers, workers in or near an iron foundry with varying exposures to PAHs were examined for response to exposure (Santella et al. 1993). Exposure to benzo[a]pyrene, determined by personal monitors, was 2-60 ng/m^3, which are the lowest levels yet analyzed in foundry workers. 1-Hydroxypyrene was measured in the urine, and PAH-DNA adducts were measured in white blood cells to demonstrate their relationship to the exposure.

Cigarette smoking, but not age or charbroiled food, influenced the level of 1-hydroxypyrene but not PAH-DNA adducts. When workers were classified into three categories of exposure (low, <.0005 mg/m^3; medium, 0.0005-0.0012 mg/m^3; high, >0.0012 mg/m^3), PAH-DNA adducts showed an increasing trend, with exposure from 5.2 to 6.2-9.6 adducts per 10^8 nucleotides in the low-, medium, and high-exposure groups, respectively. However, the three exposure groups did not differ significantly from each other, and no independent control group was used.

In order to evaluate the correlation between peripheral blood leukocyte DNA adducts as an indicator of exposure to PAHs and the airborne contamination of PAH at the workplaces, a survey of 69 coke oven workers was carried out (Assennato et al. 1993). In each workplace, total PAH and specific (benz[a]anthracene, benzo[a]pyrene, chrysene) PAH airborne concentrations were measured. Job titles included supervisor, door maintenance, machine operator, gas regulators, temperature operators, and top side workers. For the workplaces evaluated, the range of airborne concentrations (μg/m^3) for benz[a]anthracene, benzo[a]pyrene, and chrysene, respectively, were: supervisor (0.41, 0.29, 0.32), door maintenance (4.26-14.79, 2.31-6.37, 2.34 6.53), machine operator (0.11-33.19, 0.08-13.17, 0.03-12.63), gas regulators (0.21-2.10, 0.12-1.61, 0.13-1.60), temperature operators (1.77-10.07, 1.37-5.03, 0.98 4.78), and top side workers (0.45-3.40, 0.47-4.73, 0.23-2.42). Mean values (fmol/μg DNA) for PAH-DNA adducts in leukocytes by job title were: supervisor (0.059), door maintenance (0.174) machine operator (0.065), gas regulators (0.081), and temperature operators (0.071). Levels of exposure were correlated with PAH-DNA adduct formation. However, the differences were not statistically significant. The major limitations of the study included no record of length of exposure, no independent control group, no reporting of expected background levels of adducts, and no estimation of the length of time individual workers were exposed to particular levels of the PAHs. Other genotoxicity studies are discussed in Section 2.4.

2.2.1.8 Cancer

No studies were located regarding cancer in humans following inhalation exposure to any of the 17 PAHs discussed in this profile. However, epidemiologic studies have shown increased mortality due to lung cancer in humans exposed to coke oven emissions (Lloyd 1971; Mazumdar et al. 1975; Redmond et al. 1976), roofing-tar emissions (Hammond et al. 1976), and cigarette smoke (Maclure and MacMahon 1980; Wynder and Hoffmann 1967). Each of these mixtures contains benzo[a]pyrene, chrysene, benz[a]anthracene, benzo[b]fluoranthene, and dibenz[a,h]anthracene as well as other

potentially carcinogenic PAHs and other carcinogenic and potentially carcinogenic chemicals, tumor promoters, initiators, and co-carcinogens such as nitrosamines, coal tar pitch, and creosote. It is thus impossible to evaluate the contribution of any individual PAH to the total carcinogenicity of these mixtures in humans because of the complexity of the mixtures and the presence of other carcinogens. Furthermore, the levels of individual or total PAHs were not quantified in any of these reports. Despite these limitations, reports of this nature provide qualitative evidence of the potential for mixtures containing PAHs such as benzo[a]pyrene, chrysene, benz[a]anthracene, benzo[b]fluoranthene, and dibenz[a,h]anthracene to cause cancer in humans.

Several inhalation studies for animals given benzo[a]pyrene were located. Shulte et al. (1993) found a significant increase in all lung tumors and a dose-dependent increase in malignant lung tumors for mice exposed to PAH-enriched exhausts containing 0.05 or 0.09 mg/m^3 benzo[a]pyrene. The chronic study of Thyssen et al. (1981) provides clear-cut evidence of a dose-response relationship between inhaled benzo[a]pyrene particles (99% of the benzo[a]pyrene particles were between 0.2 and 0.54 microns in diameter) and respiratory tract tumorigenesis. Respiratory tract tumors were induced in the nasal cavity, pharynx, larynx, and trachea in a dose-related manner in hamsters exposed to 9.5 mg/m^3 or 46.5 mg/m^3 for 109 weeks. No lung tumors were found, and the reason for the absence of lung tumors is not known. Furthermore, the particle sizes were reported to be within the respirable range (0.2-0.5 microns in diameter). Tumors were also observed following exposure to 46.5 mg/m^3 in the esophagus and forestomach (presumably as a consequence of mucocilliary particle clearance) (Thyssen et al. 1981). These tumor types consisted of papillomas, papillary polyps, and squamous cell carcinomas.

The CEL from the Thyssen et al. (1981) study is recorded in Table 2-1 and plotted in Figure 2-1.

2.2.2 Oral Exposure

2.2.2.1 Death

No studies were located regarding death in humans after oral exposure to any of the 17 PAHs discussed in this profile.

Oral exposure to 120 mg/kg/day benzo[a]pyrene has resulted in decreased survival time in two strains of mice (DBA/2N and AKR/N) whose hepatic aryl hydrocarbon hydroxylase (AHH) activity is not induced by PAHs ("nonresponsive" mice) (Robinson et al. 1975). AHH is a microsomal enzyme believed to be responsible for the metabolism of benzo[a]pyrene. All of the mice in the treatment group died, with at least half the deaths occurring within 15 days of dosing. Only three mice in the control group died. Death appeared to be caused by bone marrow depression (aplastic anemia, pancytopenia), leading to hemorrhage or infection. In contrast, only 6 of 90 (7%) mice with inducible AHH activity ("responsive" mice) similarly exposed to benzo[a]pyrene died over the same period of time. The authors concluded that the decreased survival in the nonresponsive mice was associated with a single gene difference encoding aromatic hydrocarbon responsiveness and was dependent on route of exposure. Benzo[a]pyrene was not as rapidly metabolized by the liver and excreted following oral administration in nonresponsive mice as in responsive mice. Therefore, more benzo[a]pyrene was available to reach the target tissue (i.e., bone marrow) in the nonresponsive mice, resulting in bone marrow depression and death.

A LOAEL for death for intermediate-duration exposure in mice is recorded in Table 2-2 and plotted in Figure 2-2.

2.2.2.2 Systemic Effects

No studies were located regarding respiratory, cardiovascular, hematological, musculoskeletal, hepatic, dermal, or ocular effects in humans following oral exposure to any of the 17 PAHs discussed in this profile. The systemic effects observed in humans or animals after oral exposure are discussed below.

The highest NOAEL values and all LOAEL values from each reliable study for each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2.

Respiratory Effects. Male and female mice were exposed to 0, 175, 350, or 700 mg/kg/day acenaphthene by gavage for 13 weeks (EPA 1989c). No signs of respiratory distress were seen during life for any dose group, and no gross or microscopic damage was seen upon necropsy. Similar findings were reported after 13-week administration of 1,000 mg/kg/day anthracene, and 500 mg/kg/day fluoranthene, or 500 mg/kg/day fluorene (EPA 1988e, 1989d, 1989e).

TABLE 2-2. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons - Oral

Key to[a] figure	Species/ (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference
	ACUTE EXPOSURE						
	Systemic						
1	Rat (Wistar/Af/Han/Mol/ Kuo)	4 d 1 x/d (G)	Gastro	150M			Nousiainen et al. 1984 benz[a]anthracene
			Hepatic	150M			
			Renal	150M			
2	Rat (Wistar/Af/Han/Mol/ Kuo)	4 d 1 x/d (G)	Gastro	150M			Nousiainen et al. 1984 benzo[a]pyrene
			Hepatic	150M			
			Renal	150M			
	Reproductive						
3	Mouse (CD-1)	10 d Gd 7-16 (G)		40 F		160 F (reduced pregnancy)	Mackenzie and Angevine 1981 benzo[a]pyrene
	Developmental						
4	Mouse (B6AKF1, AKR/J)	8 d Gd 2-10 (F)				120 F (fetal resorption in Ahd/Ahd)	Legraverend et al. 1984 benzo[a]pyrene
5	Mouse (CD-1)	10 d Gd 7-16 (G)		10 F		40 F (reduced pup weight at 20 days)	Mackenzie and Angevine 1981 benzo[a]pyrene
	Cancer						
6	Mouse (CFW Swiss)	1-7 d ad lib (F)		13.3		33.3 (CEL: gastric neoplasms)	Neal and Rigdon 1967 benzo[a]pyrene

TABLE 2-2. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons - Oral (continued)

Key to figure[a]	Species/ (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference
	INTERMEDIATE EXPOSURE						
	Systemic						
7	Mouse (CD-1)	13 wk 1 x/d (GO)	Resp	700			EPA 1989c acenaphthene
			Cardio	700			
			Gastro	700			
			Hemato	700			
			Musc/skel	700			
			Hepatic		175[b]	(increased relative liver weight)	
			Renal	700			
			Endocr	700			
			Dermal	700			
			Ocular	700			
			Bd Wt	700			
8	Mouse (CD-1)	13 wk 1 x/d (GO)	Resp	1000			EPA 1989d anthracene
			Cardio	1000			
			Gastro	1000			
			Hemato	1000			
			Musc/skel	1000			
			Hepatic	1000[c]			
			Renal	1000			
			Endocr	1000			
			Dermal	1000			
			Ocular	1000			
			Bd Wt	1000			

TABLE 2-2. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons - Oral (continued)

Key to figure[a]	Species/ (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference
9	Mouse (DBA/2,ARR/ N); (C57B1/b, C3H/HeN, BALB/cAnN)	6 mo (F)	Hemato			120 (aplastic anemia)	Robinson et al. 1975 benzo[a]pyrene
			Hepatic		120 (increased liver weight)		
10	Mouse (CD-1)	13 wk 1 x/d (GO)	Resp	500			EPA 1988e fluoranthene
			Cardio	500			
			Gastro	500			
			Hemato	125 F 500 M	250 F (decrease in packed cell volume)		
			Musc/skel	500			
			Hepatic		125[d] M (increased relative liver weight)		
				125 F	250 F (increased relative liver weight; centrilobular pigmentation, increased enzymes)		
			Renal	250 M 125 F	500 M (renal tubular 250 F regeneration; interstitial lymphocytic infiltrates and/or fibrosis)		
			Endocr	500			
			Dermal	500			
			Ocular	500			
			Bd Wt	500			

TABLE 2-2. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons - Oral (continued)

Key to[a] figure	Species/ (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference
11	Mouse (CD-1)	13 wk 1 x/d (GO)	Resp	500			EPA 1989e fluorene
			Cardio	500			
			Gastro	500			
			Hemato	125	250 (decreased PCV and MCHC in males; decreased RBC, PCV, MCH, and MCHC in females)		
			Musc/skel	500			
			Hepatic		125[e] (increased relative liver weight)		
			Renal	250 M 500 F	500 M (increased absolute and relative kidney weight)		
			Endocr	500			
			Dermal	500			
			Ocular	500			
			Bd Wt	500 M 250 F	500 F (increased body weight)		
	Immunological/Lymphoreticular						
12	Mouse (CD-1)	13 wk 1 x/d (GO)		700			EPA 1989c acenaphthene
13	Mouse (CD-1)	13 wk 1 x/d (GO)		1000			EPA 1989d anthracene
14	Mouse (CD-1)	13 wk 1 x/d (GO)		500 F	500 M (increased serum globulin values)		EPA 1988e fluoranthene

TABLE 2-2. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons - Oral (continued)

Key to figure[a]	Species/ (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference
15	Mouse (CD-1)	13 wk 1 x/d (GO)		125	250 M (increased spleen weight)		EPA 1989e fluorene
	Neurological						
16	Mouse (CD-1)	13 wk 1 x/d (GO)		700			EPA 1989e acenaphthene
17	Mouse (CD-1)	13 wk 1 x/d (GO)		1000			EPA 1989d anthracene
18	Mouse (CD-1)	13 wk 1 x/d (GO)		500			EPA 1988 fluoranthene
19	Mouse (CD-1)	13 wk 1 x /d (GO)		500			EPA 1989e fluorene
	Reproductive						
20	Mouse (CD-1)	13 wk 1 x/d (GO)		700 M 350 F	700 F (decreased ovary weights correlated with increased incidence and degree of inactivity of the ovary and uterus)		EPA 1989c acenaphthene
21	Mouse (CD-1)	13 wk 1 x/d (GO)		1000			EPA 1989d anthracene

TABLE 2-2. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons - Oral (continued)

Key to figure[a]	Species/ (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)		Reference
22	Mouse (White Swiss)	19-29 d ad lib (F)		133.3 F				Rigdon and Neal 1965 benzo[a]pyrene
23	Mouse (CD-1)	13 wk 1 x/d (GO)		500				EPA 1988 fluoranthene
24	Mouse (CD-1)	13 wk 1 x/d (GO)		500				EPA 1989e fluorene
	Cancer							
25	Mouse (CFW Swiss)	30-197 d ad lib (F)		1.3		2.6	(CEL: gastric tumor)	Neal and Rigdon 1967 benzo[a]pyrene
26	Mouse (Swiss)	23-238 d ad lib (F)				33.3	(CEL: papillomas; squamous cell carcinomas)	Rigdon and Neal 1966 benzo[a]pyrene

TABLE 2-2. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons - Oral (continued)

Key to[a] figure	Species/ (Strain)	Exposure/ Duration/ Frequency (Specific Route)	System	NOAEL (mg/kg/day)	LOAEL				Reference
					Less Serious (mg/kg/day)		Serious (mg/kg/day)		
27	Mouse (Swiss)	80-140 d ad lib (F)					33.3	(CEL: tumors of the forestomach in 69/108)	Rigdon and Neal 1969 benzo[a]pyrene

[a]The number corresponds to entries in Figure 2-2.

[b]Used to derive an intermediate-duration oral minimal risk level (MRL) of 0.6 mg/kg/day for acenaphthene; dose divided by an uncertainty factor of 300 (3 for use of a LOAEL, 10 for extrapolation from animals to humans and 10 for human variability)

[c]Used to derive an intermediate-duration oral MRL of 10 mg/kg/day for anthracene; dose obtained by dividing the NOAEL value by 100 (10 for extrapolation from animals to humans and 10 for human variability)

[d]Used to derive an intermediate-duration oral MRL of 0.4 mg/kg/day for fluoranthene; dose divided by an uncertainty factor of 300 (3 for use of a minimal LOAEL, 10 for extrapolation from animals to humans and 10 for human variability)

[e]Used to derive an intermediate-duration oral MRL of 0.4 mg/kg/day for fluorene; dose divided by an uncertainty factor of 300 (3 for use of a minimal LOAEL, 10 for extrapolation from animals to humans and 10 for human variability)

ad lib = ad libitum; BaP = benzo(a)pyrene; Bd Wt = body weight; Cardio = cardiovascular; CEL = cancer effect level; d = day(s); Endocr = endocrine; F = female; (F) = feed; (G) = gavage; Gastro = gastrointestinal; Gd = gestation day(s); (GO) = gavage (oil); Hemato = hematological; LOAEL = lowest-observed-adverse-effect level; M = male; MCH = mean cell hemoglobin; MCHC = mean cell hemoglobin concentration; mo = month(s); Musc/skel = musculoskeletal; NOAEL = no-observed-adverse-effect level; PCV = packed cell volume; RBC = red blood cells; Resp = respiratory; TPA = tetradecanoyl phorbol acetate; wk = week(s); x = time(s)

Figure 2-2. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons – Oral

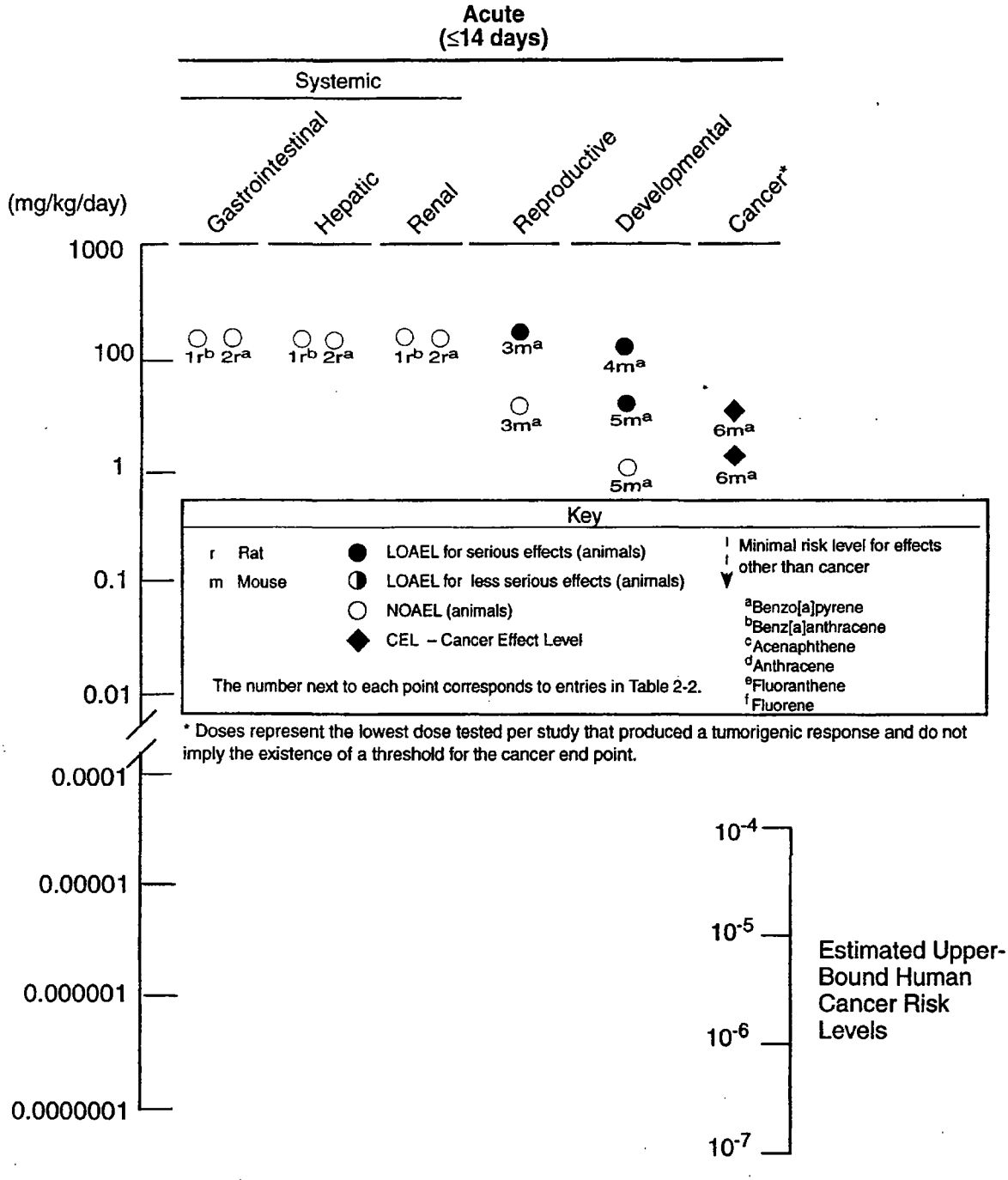
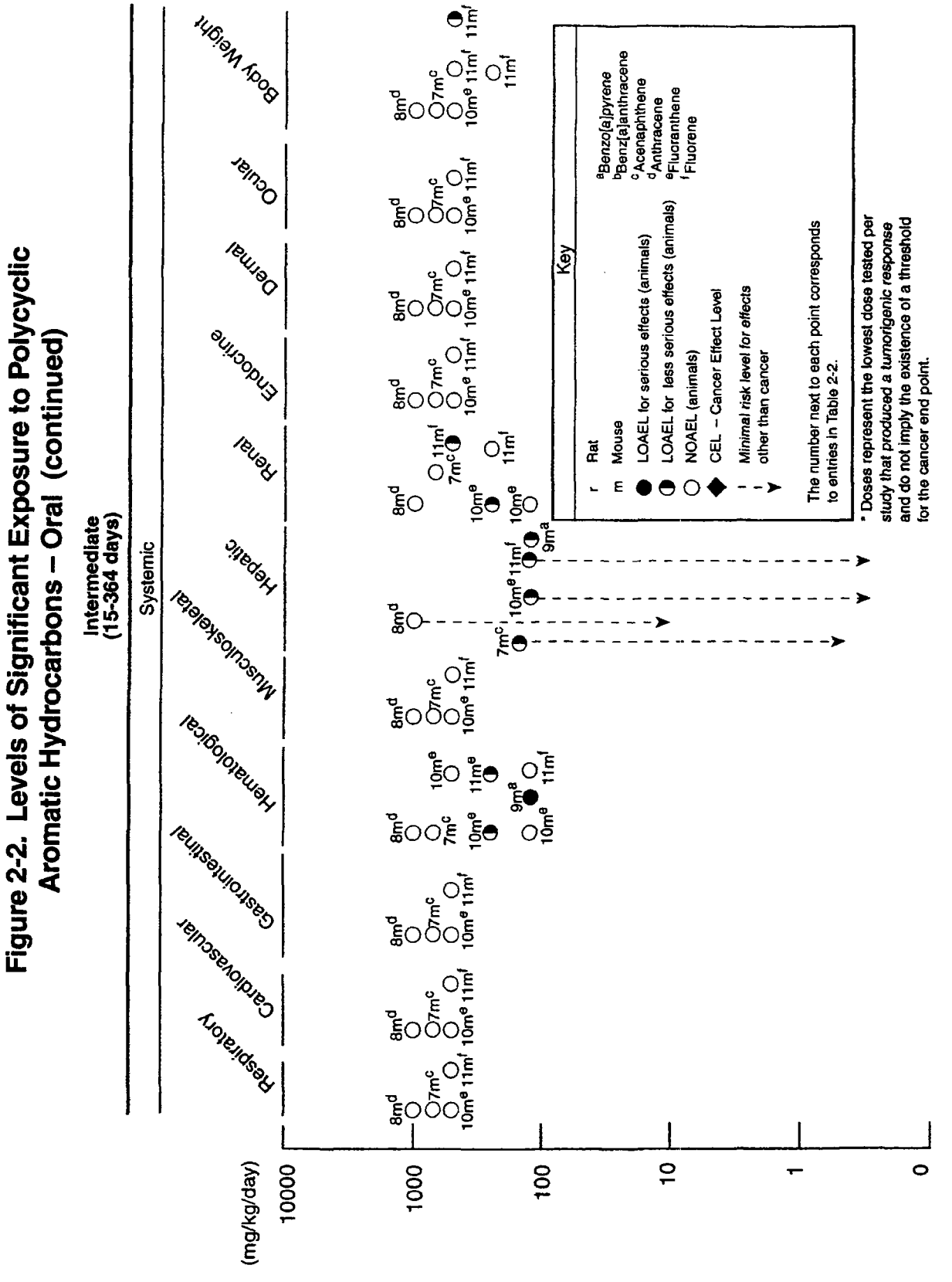
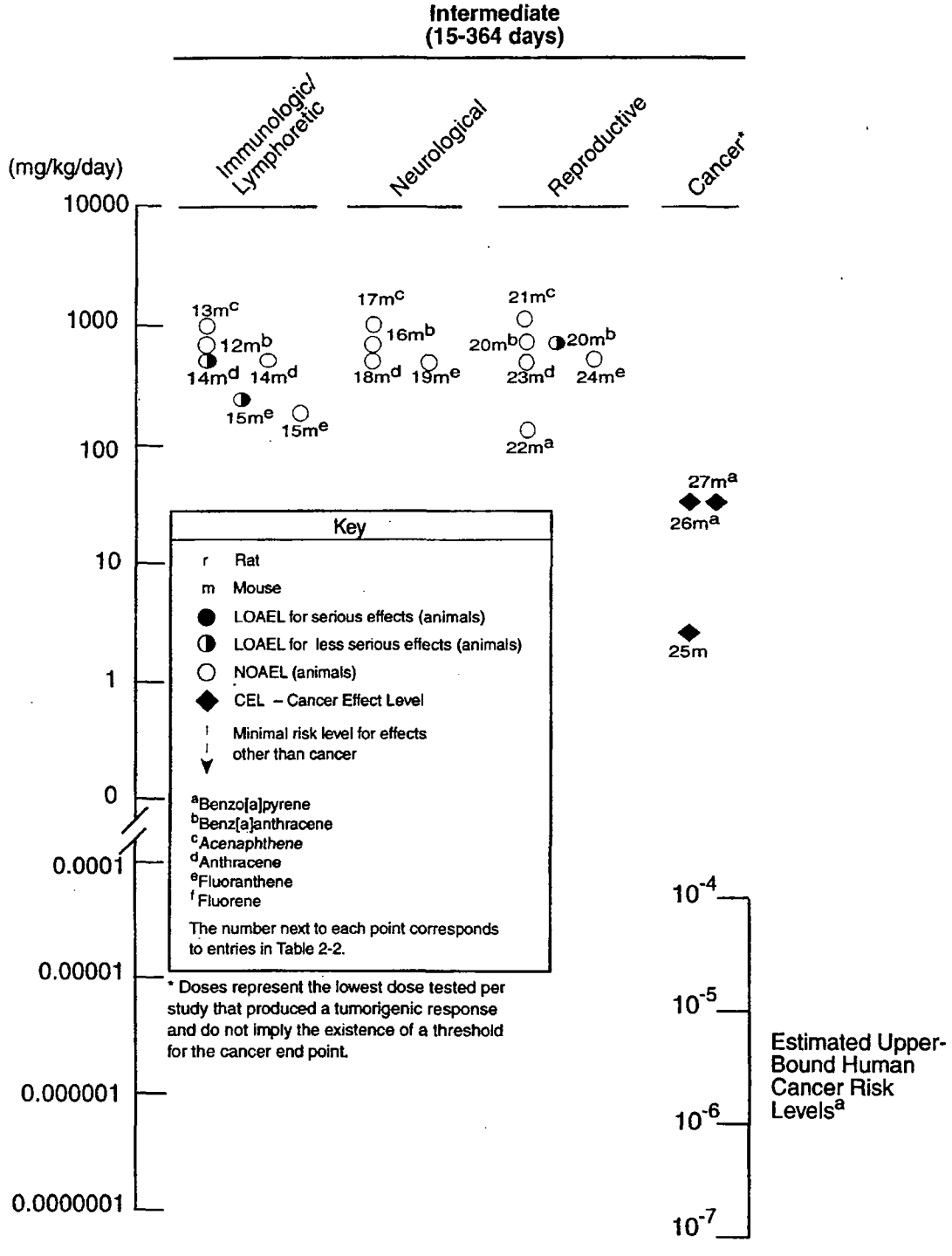


Figure 2-2. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons – Oral (continued)



* Doses represent the lowest dose tested per study that produced a tumorigenic response and do not imply the existence of a threshold for the cancer end point.

Figure 2-2. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons – Oral (continued)



Cardiovascular Effects. Male and female mice were exposed to 0, 175, 350, or 700 mg/kg/day acenaphthene by gavage for 13 weeks (EPA 1989c). No signs of cardiovascular distress were seen during life for any dose group, and no gross or microscopic damage was seen upon necropsy. Similar findings were reported after 13-week administration of 1,000 mg/kg/day anthracene, and 500 mg/kg/day fluoranthene, or 500 mg/kg/day fluorene (EPA 1988e, 1989d, 1989e).

Gastrointestinal Effects. Minimal information is available on the gastrointestinal effects of human oral exposure to PAHs. In one study, humans that consumed anthracene-containing laxatives (the anthracene concentration was not specified) for prolonged periods of time were found to have an increased incidence of melanosis of the colon and rectum (i.e., unusual deposits of black pigments in the colon and rectum) compared to patients who did not consume anthracene laxatives. However, no definitive conclusions can be drawn from these results because of study limitations that include possible misclassification of patients with respect to the level of anthracene laxative use over 30 years and no accounting for other factors involved in the pathogenesis of melanosis (Badiali et al. 1985).

Enzyme alterations in the mucosa of the gastrointestinal tract have been observed in animals acutely exposed to anthracene, benz[a]anthracene, benzo[a]pyrene, or phenanthrene. In rats, acute intragastric administration of 50 or 150 mg/kg/day benz[a]anthracene or benzo[a]pyrene, respectively, for 4 days resulted in suppression of carboxylesterase activity in the intestinal mucosa (reduction of activity by 30% and 44%, respectively); rats exposed to 100 mg/kg/day of anthracene or phenanthrene exhibited carboxylesterase activity that was increased by 13% and 30%, respectively (Nousiainen et al. 1984). Enzyme alteration in the absence of other signs of gastrointestinal toxicity is not considered an adverse health effect, but it may precede the onset of more serious effects. Based on this very limited information, it would appear that acute ingestion of anthracene, benz[a]anthracene, benzo[a]pyrene, or phenanthrene at these doses may not adversely affect the gastrointestinal tract of animals; however, exposed animals exhibited biochemical changes and it is possible that more serious effects could occur at high doses.

Male and female mice were exposed to 0, 175, 350, or 700 mg/kg/day acenaphthene by gavage for 13 weeks (EPA 1989c). No adverse effects on the gastrointestinal system were seen during life for any dose group, and no gross or microscopic damage was seen upon necropsy. Similar findings were reported after 13-week administration of 1,000 mg/kg/day anthracene, 500 mg/kg/day fluoranthene, or mg/kg/day fluorene (EPA 1988e, 1989d, 1989e).

Hematological Effects. Male and female mice were exposed to 0, 175, 350, or 700 mg/kg/day acenaphthene by gavage for 13 weeks (EPA 1989). No hematological effects were seen during life for any dose group, and no gross or microscopic damage was seen upon necropsy. Similar findings were reported after 13-week administration of 1,000 mg/kg/day anthracene (EPA 1989d). Administration of 250 mg/kg/day fluoranthene by gavage for 13 weeks to mice resulted in decreased packed cell volume in females, but not in males, given doses up to 500 mg/kg/day (EPA 1988e). Both male and female mice exposed to 250 mg/kg/day fluorene exhibited hematologic effects, including decreased packed cell volume and hemoglobin content (EPA 1989e).

Adverse hematopoietic effects (e.g., aplastic anemia, pancytopenia) that ultimately led to death were reported in the Ah-nonresponsive strains of mice, DBA/2N and AKR/N, following oral exposure to 120 mg benzo[a]pyrene/kg/day for 180 days. Death was attributed to hemorrhage or infection that resulted from pancytopenia (Robinson et al. 1975). Similar results were obtained by Legraverend et al. (1983). The Ah gene encodes a cytosolic receptor (Ah receptor) that regulates the induction of the cytochrome P-450 enzymes. Differences in this gene locus determine whether the Ah receptor will be "high-affinity" (i.e., will allow for the induction of the cytochrome P-450 enzymes [more specifically, AHH] and is found in responsive mice) or "low-affinity" (i.e., does not allow for the induction of the AHH and is found in nonresponsive mice). Mice with a high-affinity Ah receptor (i.e., responsive mice) were administered 120 mg/kg/day benzo[a]pyrene in the diet for 3 weeks and exhibited no myelotoxicity. However, all nonresponsive mice that were treated according to the same regimen died from myelotoxic effects within 3 weeks (Legraverend et al. 1983). These results support the results of Robinson et al. (1975).

Musculoskeletal Effects. Male and female mice were exposed to 0, 175, 350, or 700 mg/kg/day acenaphthene by gavage for 13 weeks (EPA 1989c). No signs of musculoskeletal effects were seen during life for any dose group, and no gross or microscopic damage was seen upon necropsy. Similar findings were reported after 13-week administration of 1,000 mg/kg/day anthracene, 500 mg/kg/day fluoranthene, or 500 mg/kg/day fluorene (EPA 1988e, 1989d, 1989e).

Hepatic Effects. The induction of foci of altered hepatocytes is often seen in rats and mice that also develop liver tumors. These foci have altered enzyme activities and higher rates of cell proliferation than normal hepatocytes. A 1-day intragastric administration of 200 mg/kg of benzo[a]pyrene or dibenz[a,h]anthracene, or of 180 mg/kg benz[a]anthracene to rats was followed by a

diet containing 2-acetylaminofluorene (2-AAF) and carbon tetrachloride induced gamma-GT foci (Tsuda and Farber 1980). Partially hepatectomized rats and sham hepatectomized rats were used, to provide proliferating and non-proliferating hepatocytes, respectively. Partially hepatectomized rats were more responsive to treatment than the sham-operated animals. For partially hepatectomized rats, benzo[a]pyrene was a more potent foci inducer than either benz[a]anthracene or dibenz[a,h]anthracene. Increased relative liver weight was seen in male mice and increased absolute and relative liver weight was seen in female mice given 175 mg/kg/day acenaphthene daily by gavage for 13 weeks; these effects were unaccompanied by other hepatic effects (EPA 1989c). Increased absolute and relative liver weight correlated with hepatocellular hypertrophy was seen in male and female mice given 350 mg/kg/day acenaphthene daily by gavage for 13 weeks (EPA 1989c). Increased serum cholesterol was also seen in females receiving 350 mg/kg/day acenaphthene (EPA 1989c). Increased liver weight and dose-related centrilobular pigmentation accompanied by an increase in liver enzymes were observed in both male and female mice receiving 250 mg/kg/day fluoranthene by gavage for 13 weeks (EPA 1988e). Male mice exposed to 125 mg/kg/day fluoranthene exhibited a slight increase in centrilobular pigmentation, and an increase in relative liver weight (EPA 1988e). Increased relative liver weight was observed in all treated groups, whereas increased absolute and relative liver weight was observed in the mid- and high-dose animals receiving 0, 125, 250, and 500 mg/kg/day fluorene for 13 weeks (EPA 1989e). However, there were no accompanying histopathological changes. No statistically significant effects of treatment were reported after 13-week administration of 1,000 mg/kg/day anthracene (EPA 1989d)

The ability to induce aldehyde dehydrogenase (ADH) in animals has been correlated with carcinogenic potency. Rats that were intragastrically administered 100 mg/kg/day of benzo[a]pyrene, benz[a]anthracene, anthracene, chrysene, or phenanthrene for 4 days exhibited cytosolic ADH induction (Torronen et al. 1981). However, benzo[a]pyrene and benz[a]anthracene were much more effective than phenanthrene, chrysene, or anthracene. Exposure to benzo[a]pyrene and benz[a]anthracene also increased the relative liver weights by 27% and 19%, respectively (Torronen et al. 1981). The authors concluded that anthracene, phenanthrene, and chrysene, which have been characterized as either noncarcinogens or equivocal carcinogens (see Section 2.2.2.8), are poor ADH inducers (Torronen et al. 1981).

The induction of carboxylesterase activity has also been observed in animals exposed to PAHs (Nousiainen et al. 1984). Benzo[a]pyrene, benz[a]anthracene, and chrysene were moderate inducers of

hepatic carboxylesterase activity in rats that were intragastrically administered 50, 100, and 150 mg/kg/day (100 mg/kg/day for chrysene), respectively, for 4 days. However, rats administered 100 mg/kg/day anthracene or phenanthrene did not exhibit induction of hepatic carboxylesterase activity. Induction of hepatic microsomal enzymes generally results in enhanced biotransformation of other xenobiotics (to either more or less toxic forms).

Increases in liver weight following partial hepatectomy have also been examined following acute oral exposure to various PAHs. Partially hepatectomized rats were fed diets containing various PAHs for 10 days. Administration of 51.4 mg/kg/day acenaphthene or 180 mg/kg/day fluorene resulted in statistically significant increases in liver weight compared to controls, which may have indicated an effect on regeneration, although rates of cell proliferation were not determined. Administration of 15.4 mg/kg/day acenaphthene, 51.4 mg/kg/day benzo[a]pyrene, or 51.4 mg/kg/day pyrene, anthracene, or phenanthracene had no effect. Diets containing 51.4 mg/kg/day acenaphthene or dibenz[a,h]anthracene, 180 mg/kg/day anthracene or phenanthracene, or 437 mg/kg/day pyrene produced no increase in the liver-to-body-weight ratio. Rats that were fed a diet containing 514 mg/kg/day chrysene exhibited equivocal results: in one trial, a significant increase in liver weight gain was noted, while in another trial, no increase in. liver-to-body-weight ratio was observed (Gershbein 1975). Thus, both suspected carcinogenic and noncarcinogenic PAHs can affect liver weights, although much higher doses are required for noncarcinogenic PAHs. The livers of rats administered single doses of ,fluorene by gavage in dimethyl sulfoxide (DMSO) were evaluated for the promotion of growth (i.e., cell proliferation as determined by organ weight and mitotic index) (Danz et al. 1991). The authors claimed that liver weight was increased in a dose-dependent manner to 20% over control values, and that the mitotic index of the hepatocytes was increased by 6-fold after 48 hours. However, the organ weight data were not presented, and the mitotic index data presented graphically in the text do not indicate a 6-fold increase over controls.

Ah-responsive strains of mice (C57BL/6, C3H/HeN, BALB/cAnN) that were orally administered 120 mg benzo[a]pyrene/kg/day in their diet for 180 days exhibited a 13% increase in relative liver weights (Robinson et al. 1975).

The hepatic effects observed in animals following oral exposure to PAHs are generally not considered serious. However, the enzyme alterations, gamma-GT foci induction, liver regeneration, and increased liver weight may precede the onset of more serious hepatic effects.

Renal Effects. The kidney microsomal carboxylesterase activity of rats was moderately induced by 50-150 mg/kg of benzo[a]pyrene following 4 days of intragastric administration; however, rats administered 100 mg/kg/day of anthracene or phenanthrene and 50-150 mg/kg benz[a]anthracene did not exhibit increased activity. The authors conclude that anthracene, phenanthrene, and benz[a]anthracene are not inducers of kidney carboxylesterase activity (Nousiainen et al. 1984). Enzyme induction is considered an adverse effect when observed concurrently with more serious effects such as impaired renal function and/or histopathological changes of the kidney.

Increasing dietary doses of pyrene ranging from 1,000 mg/kg food (127 mg/kg/day) up to 25,000 mg/kg food (917 mg/kg/day) for a mean dose of 426.6 mg/kg/day over a 25-day study produced dilation of the renal tubules in an unspecified number of mice. This effect was not observed until the highest dose was administered (Rigdon and Giannukos 1964). The limitations of this study (e.g., doses changed throughout exposure period and no statistical analyses performed) render these results of questionable toxicological significance.

Male and female mice were exposed to 0, 175, 350, or 700 mg/kg/day acenaphthene by gavage for 13 weeks (EPA 1989c). No signs of renal toxicity were seen during life for any dose group, and no gross or microscopic damage was seen upon necropsy. Similar findings were reported after 13-week administration of 1,000 mg/kg/day anthracene (EPA 1989d). Increased absolute and relative kidney weight was observed in males, but not females receiving 500 mg/kg/day fluorene for 13 weeks (EPA 1989e). Renal tubular regeneration, and interstitial lymphocytic infiltrates and/or fibrosis were observed after 13-week oral administration of fluoranthene to female mice at 250 mg/kg/day, and male mice at 500 mg/kg/day (EPA 1988e).

Endocrine Effects. Male and female mice were exposed to 0, 175, 350, or 700 mg/kg/day acenaphthene by gavage for 13 weeks (EPA 1989c). No signs of endocrine imbalance were seen during life for any dose group, and no gross or microscopic damage was seen upon necropsy. Similar findings were reported after 13-week administration of 1,000 mg/kg/day anthracene, 500 mg/kg/day fluoranthene, or 500 mg/kg/day fluorene (EPA 1988e, 1989d, 1989e).

Dermal Effects. Male and female mice were exposed to 0, 175, 350, or 700 mg/kg/day acenaphthene by gavage for 13 weeks (EPA 1989c). No signs of dermal effects were seen during life for any dose group, and no gross or microscopic damage was seen upon necropsy. Similar findings

were reported after 13-week administration of 1,000 mg/kg/day anthracene, 500 mg/kg/day fluoranthene, or 500 mg/kg/day fluorene (EPA 1988e, 1989d, 1989e).

Ocular Effects. Male and female mice were exposed to 0, 17.5, 350, or 700 mg/kg/day acenaphthene by gavage for 13 weeks (EPA 1989c). No signs of ocular toxicity were seen during life for any dose group, and no gross or microscopic damage was seen upon necropsy. Similar findings were reported after 13-week administration of 1,000 mg/kg/day anthracene, 500 mg/kg/day fluoranthene, or 500 mg/kg/day fluorene (EPA 1988e, 1989d, 1989e).

Body Weight Effects. Male and female mice were exposed to 0, 175, 350, or 700 mg/kg/day acenaphthene by gavage for 13 weeks (EPA 1989c). No adverse effects on body weight were seen during life or upon necropsy. Similar findings were reported after 13-week administration of 1,000 mg/kg/day anthracene, and 500 mg/kg/day fluoranthene (EPA 1988e, 1989d). After administration of 500 mg/kg/day fluorene for 13 weeks; however, female mice exhibited increased body weight, although male mice showed no effect at the same dose level (EPA 1989e).

Other Systemic Effects. The number of thymic glucocorticoid receptors in 6-week-old rats treated once with 2 mg/kg benzo[a]pyrene was measured (Csaba et al. 1991). It is assumed that administration was by oral gavage, but this was never explicitly stated. The number of these receptors was decreased by 40% in females and unaffected in males relative to the vehicle control animals. The statistical significance of these effects was not indicated, nor was the functional consequences of a decrease in receptor number assessed by examination of functional parameters.

2.2.2.3 Immunological and Lymphoreticular Effects

No studies were located regarding immunological effects in humans following oral exposure to any of the 17 PAHs discussed in this profile.

A single gavage dose of 150 mg/kg fluorene to male Sprague-Dawley rats had no effect on thymus or spleen weight (Danz and Brauer 1988). Little useful information can be obtained from this study as only one dose was tested (thereby precluding assessment of the validity of the negative response) and no tests of immune function were evaluated. Male and female mice exposed to 0, 175, 350, or 700 mg/kg/day acenaphthene by gavage for 13 weeks showed no effect of treatment on splenic weight

or histopathology (EPA 1989c). Similar findings were reported after 13-week administration of 1,000 mg/kg/day anthracene, and 500 mg/kg/day fluoranthene (EPA 1988e, 1989d). After administration of 2.50 mg/kg/day fluorene for 13 weeks, however, increased absolute and relative spleen weight was seen in both sexes (EPA 1989e).

Lee and Strickland (1993) looked for antibodies specific to PAH-DNA adducts in the serum of BALB/c mice treated orally twice per week for 8 weeks with 0.5 or 5 mg/kg benz[a]anthracene, benzo[a]pyrene, benzo[b]fluoranthene, chrysene, dibenz[a,h]anthracene, or fluoranthene. Increased antibody response was noted in animals treated with the low dose of benz[a]anthracene and benzo[b]fluoranthene, but not any of the other PAHs.

2.2.2.4 Neurological Effects

No studies were located regarding neurological effects in humans following oral exposure to any of the 17 PAHs discussed in this profile.

Male and female mice exposed to 0, 175, 350, or 700 mg/kg/day acenaphthene by gavage for 13 weeks showed no effect of treatment on behavior, or histopathologic effects on nerve or brain samples (EPA 1989c). Similar findings were reported after 13-week administration of 1,000 mg/kg/day anthracene, and 500 mg/kg/day fluoranthene (EPA 1988e, 1989d). After administration of 500 mg/kg/day fluorene for 13 weeks, however, increased brain weight was observed in females, but not in males (EPA 1989e). No histopathologic changes were observed.

2.2.2.5 Reproductive Effects

No studies were located regarding reproductive effects in humans following oral exposure to the PAHs discussed in this profile. Three animal studies were located that evaluated the reproductive effects of benzo[a]pyrene in animals. The results of two oral studies in mice (Mackenzie and Angevine 1981; Rigdon and Neal 1965) and one in rats (Rigdon and Rennels 1964) indicate that benzo[a]pyrene induces reproductive toxicity in animals. The incidence and severity of these effects depends on the strain, method of administration, and dose levels used. In one study, benzo[a]pyrene administered by gavage to pregnant CD-1 mice decreased the percentage of pregnant females that reached parturition and produced a high incidence of sterility in the progeny (Mackenzie and Angevine 1981). In

contrast, benzo[a]pyrene administered in the diet caused no adverse effects on fertility of Swiss mice (Rigdon and Neal 1965) but reduced the incidence of pregnancy in female rats (Rigdon and Rennels 1964). Based on these studies, the LOAEL for benzo[a]pyrene-induced reproductive toxicity in parental mice was 160 mg/kg/day, and the LOAEL for these effects in the progeny of exposed animals was 10 mg/kg/day (Mackenzie and Angevine 1981). Because only the parental doses are quantifiable, these are the only data presented in Table 2-2.

When CD-1 mice were administered benzo[a]pyrene by gavage daily for 10 days during gestation, there was a significant reduction in the percentage of pregnant females to reach parturition at 160 mg/kg/day, the highest dose tested (Mackenzie and Angevine 1981). When F_1 progeny were bred with untreated animals, the fertility index decreased significantly in all treatment groups. At 10 mg/kg/day, the lowest dose tested, the reduced fertility noted was associated with significant alterations in gonadal morphology and germ cell development. The treatment at higher doses resulted in total sterility. Contrary to these results, no adverse effects on reproduction were observed in Swiss mice fed benzo[a]pyrene in the diet at ≤133 mg/kg/day over varying time spans during mating, gestation, and parturition (Rigdon and Neal 1965). The apparent discrepancy in the results of the two studies may be attributable to the method of benzo[a]pyrene administration and metabolic differences in the two strains of mice used.

Dietary administration of benzo[a]pyrene for 28 days revealed no treatment-related effects on the estrous cycle of female rats. These rats experienced no significant adverse effects on their fertility when bred to untreated male rats (Rigdon and Rennels 1964). In another series of experiments, when benzo[a]pyrene-fed male and female rats were bred, only two of seven females became pregnant (as compared to 3 of 6 controls); the offspring of one rat were stillborn while those of others were resorbed (Rigdon and Rennels 1964). Although the data suggest that benzo[a]pyrene may induce reproductive toxicity in rats, they are inconclusive because of the use of a single dose level, small number of animals, and inadequate reporting of data.

Male mice exposed to 0, 175, 350, or 700 mg/kg/day acenaphthene by gavage for 13 weeks showed no effect of treatment on reproductive organ weight or histology (EPA 1989c). Female mice, however, exhibited decreased ovary weights correlated with an increase of inactivity of the ovary and uterus (EPA 1989c). No adverse effects on reproductive organs were reported after 13-week

administration of 1,000 mg/kg/day anthracene, 500 mg/kg/day fluoranthene, or 500 mg/kg/day fluorene to male and female mice (EPA 1988e, 1989d, 1989e).

The available information from animal studies suggests that benzo[a]pyrene may have the potential to produce adverse reproductive effects in exposed humans. The highest NOAEL and all LOAEL values from each reliable study for reproductive effects following acute- and intermediate-duration exposures are reported in Table 2-2 and plotted in Figure 2-2.

2.2.2.6 Developmental Effects

No studies were located regarding developmental effects in humans following oral exposure to PAHs. Three animal studies were reviewed that assessed developmental effects of benzo[a]pyrene in inbred strains of rats and mice. The data from these studies indicate that prenatal exposure to benzo[a]pyrene produced reduced mean pup weight during postnatal development and caused a high incidence of sterility in the F_1 progeny of mice (Mackenzie and Angevine 1981). Using Ah-responsive and Ah-nonresponsive strains of mice, the increased incidences of stillboms, resorptions, and malformations observed correlated with the maternal and/or embryonal genotype (Legraverend et al. 1984). In another study, negative results were obtained when benzo[a]pyrene was administered to Swiss (responsive) mice (Rigdon and Neal 1965).

Benzo[a]pyrene was administered by gavage to pregnant CD-1 mice during gestation at doses of 10, 40, and 160 mg/kg/day. The viability of litters at parturition was significantly reduced in the highest dose group (Mackenzie and Angevine 1981). The mean pup weight was significantly reduced in all treatment groups by 42 days of age. The F_1 progeny that were exposed prenatally to benzo[a]pyrene (10, 40, and 160 mg/kg/day) were bred with untreated animals and further studied for postnatal development and reproductive function. The F_1 progeny from the 10-mg/kg/day group experienced decreased fertility with associated alterations in gonadal morphology and germ-cell development. Because only the parental doses are quantifiable, these are the only data presented in Table 2-2. Therefore, the LOAEL of 10 mg/kg/day noted in the F_1 progeny discussed above is not presented in Table 2-2. Higher doses produced total sterility. This study provides good evidence for the occurrence of developmental effects following *in utero* exposure to benzo[a]pyrene.

The effect of genetic differences in metabolism of orally administered benzo[a]pyrene on *in utero* toxicity and teratogenicity was evaluated in mice that either metabolize benzo[a]pyrene readily (Ah-responsive) or not (Ah-nonresponsive) (Legraverend et al. 1984). Pregnant mice, either B6AKFl (Ah-responsive) or AKR/J (Ah-nonresponsive), were fasted prior to a diet containing 120 mg/kg/day benzo[a]pyrene on days 2-10 of gestation. The mice were killed on day 18 of gestation. On day 16 of gestation, intraperitoneal injections of napthoflavone were administered to distinguish between fetuses with different Ah-genotypes (Ahb/Ahd and Ahd/Ahd). Oral administration of benzo[a]pyrene to the pregnant AKR/J mice (non-responsive) caused more stillbirths, decreased weight gain, resorptions, and birth defects among Ahd/Ahd (Ah-nonresponsive) than among Ahb/Ahd (Ah-responsive) embryos. However, no differences in *in utero* toxicity or teratogenicity were observed in Ah-genetically different embryos (Ahd/Ahd and Ahb/Ahd) of B6AKFl mothers (responsive). The authors concluded that differences in *in utero* toxicity and teratogenicity are specific to the route of administration and can be attributed to "first pass" liver metabolism occurring with oral dosing. They also concluded that *in utero* toxicity and teratogenicity are directly related to the maternal and/or embryonal genotype controlled by the Ah-locus; that is, both maternal metabolism as well as target organ metabolism (embryo/fetus) were important in determining susceptibility to developmental toxicity. Specifically, metabolism by a responsive mother reduces *in utero* toxic effects in the fetus. Similarly, responsive fetuses in the uterus of a non-responsive mother show fewer *in utero* toxic effects. Non-responsive fetuses in the uterus of a non-responsive mother show the highest incidence of *in utero* toxic effects. Although the study emphasizes the importance of administrative route in benzo[a]pyrene metabolism and resulting toxicity, it had the following limitations: 1) only one dose was evaluated; 2) no quantitative comparisons between treated groups and corresponding control animals were presented for any of the reported *in utero* toxicity or teratogenic effects; 3) small sample size; 4) purity of benzo[a]pyrene was not specified.

In another study, negative results were obtained when the potential developmental effects of benzo[a]pyrene were studied in mice (Rigdon and Neal 1965). Dietary administration of this chemical to mice at concentrations equivalent to 33.3, 66.7, or 133.3 mg/kg/day at various times before and after mating elicited no adverse effects on the developing embryos. Maternal weight gain was reduced in the mice administered the higher levels of benzo[a]pyrene, but this effect was reversed when the animals were changed to the control ration. Limitations of this study that preclude its inclusion in Table 2-2 consist of the use of an inconsistent protocol, varying number of animals, and varying time of gestation exposure.

The highest NOAEL values and all LOAEL values from each reliable study for developmental effects in mice for acute-duration exposure is recorded in Table 2-2 and plotted in Figure 2-2.

2.2.2.7 Genotoxic Effects

No studies were located regarding genotoxic effects in humans following oral exposure to any of the 17 PAHs discussed in this profile.

Pregnant *Erythrocebus patas* monkeys were treated once on gestation day (Gd) 50, 100, or 150 (term = 160 days) with 5-50 mg/kg benzo[a]pyrene (Lu et al. 1993). Fetuses were removed by Cesarean section l-50 days after treatment and fetal organs, placentae, and maternal livers were assayed for DNA adducts. Benzo[a]pyrene-DNA adducts were high in fetal organs, placentae, and maternal livers in all three trimesters of gestation. Adduct levels were higher in mid-gestation compared to early or late gestation. dG-N2-BPDE was the major adduct detected. The adduct levels in fetal tissues increased with benzo[a]pyrene dose, but at a much lower rate that placentae or maternal livers. Preference in binding to DNA of various fetal tissues was more apparent in early gestation compared to late gestation, and at lower doses compared to higher doses. During early gestation and at lower doses, benzo[a]pyrene produced a similar level of DNA binding in fetal lung, liver, maternal liver, and placenta. Individual fetal organ adduct levels correlated significantly with placental adduct levels, indicating placental and/or maternal contribution to adduct formation in fetuses. Evidence of fetal contribution to adduct formation was also found. DNA adduct levels in fetal skin were lowest of all fetal organs tested and less affected by gestational stage at time of treatment. In contrast, DNA adduct levels in fetal liver exhibited distinct gestation stage specificity with higher adduct, levels attained during mid-gestation compared to other stages of gestation. Adduct levels decreased at a much faster rate during the first 10-15 days compared to 15-50 days after treatment. However, 10% of the DNA adducts persisted 50 days after treatment in all organs studied. Together, the results suggest that placental adduction accurately indicates fetal exposure.

Male B6C3F$_1$ mice were fed 0, 0.325, 0.1825, 1.625, 3.25, or 6.5 mg/kg/day benzo[a]pyrene for 21 days (Culp and Beland 1994). Animals were killed and the liver, lung, and forestomach DNA extracted and analyzed for benzo[a]pyrene-DNA adducts. The major adduct, dG-N2-BPDE, was quantified. Adduct levels in liver and lung increased in a linear manner. Adduct levels in the forestomach appeared to plateau at the highest dose. At doses below the highest, adduct levels were in

the order of forestomach > liver > lung, with the values of average slopes being 3.0 + 0.59, 2.1 + 0.17, 1.3 + 0.37 fmol adduct/mg DNA/μg benzo[a]pyrene/day, respectively. At these doses, the lung and the forestomach were not significantly different. At the high dose, liver > forestomach > lung, and each tissue was significantly different from the other.

DNA binding of coal tar components in male mice was investigated following the ingestion of coal tar obtained from a manufactured coal plant (Weyand et al. 1991). One of four different samples (A-D) of coal tar or a mixture of four equal portions of the four samples was administered in a gel diet which contained 0.25% coal tar. The coal tar contained phenanthrene, fluoranthene, pyrene, benz[a]anthracene, chrysene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[a]pyrene, indeno[1,2,3-c,d]pyrene, and benzo[g,h,i]perylene, among other PAHs. In addition, a diet containing benzo[a]pyrene at the same level as the 0.25% diet prepared with Sample C was administered; animals consuming this diet ingested 0.01-0.02 mg benzo[a]pyrene per day. The diets were administered for 15 days. Chemical-DNA adduct formation was evaluated in animals following 14 days of treatment. Chemical-DNA adduct formation was also evaluated in animals maintained on a 0.1, 0.2, 0.5, and 1.0% coal tar diet prepared with one of the coal tar samples (C). Chemical-DNA adduct formation in animals dosed with 0.1-1.0% Sample C indicated a dose-related effect in lung DNA adduct formation, but no dose-related effect was observed for forestomach tissue. In addition, overall adduct levels in lung tissue were considerably higher than forestomach levels for animals on the 0.5 or 1% diet. In contrast, adduct levels were highest in the forestomach of animals on diets lower in coal tar content (0.1 or 0.2%). Chemical-DNA adducts of coal tar components evaluated for Samples A-D and the mixture of the four coal tar samples at 0.25% in the diet administered for 15 days indicated adducts in the lung, liver, and spleen of all animals. Adduct patterns were similar, but quantitative differences were observed between coal tar samples and tissue sites. The highest adduct levels were detected in lung DNA. Adduct formation in animals fed the benzo[a]pyrene diet, could not account for the differences in the adduct levels observed in animals given the mixtures. Also, adduct formation in animals fed the coal tar mixtures correlated with benzo[a]pyrene content in the coal tar, indicating the adducts arose from a variety of PAHs in the coal tar mixtures. The levels of 1-hydroxypyrene in the urine of these animals correlated with the pyrene content of these coal tars.

The DNA binding of manufactured gas plant residue (MGP) components in male B6C3F1 mice was investigated following oral administration (Weyand and Wu 1994). Male mice were fed a gel diet containing manufactured gas plant (MGP) residue (coal tar) at 0.3% for 28 days, or the corresponding

control diet. Two mixtures of MGP residue were used: Mix of 3 combining equal amounts of samples from three different MGP plant sites, and Mix of 7 combining equal amounts of samples from seven different MGP plant sites, including those used in the Mix of 3. The mixtures contained pyrene, benz[a]anthracene, chrysene, benzo[b]fluorene, benzo[k]fluorene, benzo[a]pyrene, indeno[1,2,3-cd] pyrene, dibenz[a,h]anthracene, benzo[g,h,i]perylene. Data was presented in terms of pyrene consumed. Animals were sacrificed on the twenty-ninth day and lung and forestomach were excised and DNA isolated. Chemical-DNA adduct formation was evaluated. Ingestion of the adulterated diets resulted in a relatively low level of DNA adducts in the forestomach in comparison with the lung (one-tenth the level). PAH-DNA adduct levels in the lung of mice maintained on the Mix of 3 (1.4 mg/kg/day pyrene) were two times greater than the level induced by the Mix of 7 (1.2 mg/kg/day pyrene) suggesting that the composition of the MGP residue may have influence PAH absorption or DNA adduct formation.

Oral exposure to a total dose of 10 mg/kg benzo[a]pyrene produced gene mutations in the mouse coat color spot test (Davidson and Dawson 1976, 1977). Dose-related increases in the frequency of micronuclei were seen in bone marrow cells harvested from MS/Ae and CD-1 male mice (four mice/strain/dose) 48 hours after administration of a single oral dose of benzo[a]pyrene ranging from 62.5 to 500 mg/kg (Awogi and Sato 1989). Although the response appeared to be stronger in the MS/Ae strain, the reduction in polychromatic erythrocytes, indicative of target cell toxicity at all levels in the CD-1 strain, limited the comparative evaluation of strain specificity.

In another study, a dose of benzo[a]pyrene (150 mg/kg) known to induce a clastogenic response was orally administered to groups of five adult males and females, pregnant females, and fetal ICR mice. An increased incidence of micronuclei in bone marrow cells harvested from the various groups of adult animals and also in the livers of the fetuses was observed (Harper et al. 1989). Genetic damage was most severe in the fetuses. The approximately 7-fold increase in micronuclei in fetal livers as compared to maternal bone marrow suggests that the transplacentally-induced genotoxicity was probably associated with the immature detoxification processes of fetal liver as compared to adult bone marrow. It would, nevertheless, appear that the fetus may be at an increased risk.

Data showing that orally administered benzo[a]pyrene induces micronuclei were confirmed in subsequent studies (Shimada et al. 1990, 1992) using rats (Sprague-Dawley) and mice (CD-1 and BDF_1), different dosing regimes (single, double, or triple doses), and different target cells (bone

marrow and peripheral blood reticulocytes). A single oral gavage dose of 63 mg/kg benzo[a]pyrene significantly ($p<0.01$) increased the yield of chromosomes with abnormal morphology in bone marrow cells collected from hybrid $lC3F_1$ male mice (Adler and Ingwersen 1989).

There is conflicting evidence that the genetic damage induced by benzo[a]pyrene is partially controlled by the expression of structural genes for benzo[a]pyrene-specific cytochromes P-450. In one study, two inbred strains of mice differing in AHH inducibility (AHH-inducible strain C57BL/6 and AHH-noninducible strain DBA/2) received two consecutive daily doses of either 10 or 100 mg/kg of the test material (Wielgosz et al. 1991). Animals were sacrificed 5 days postexposure, and bone marrow and spleen cells were examined for sister chromatid exchange and DNA adducts. Results showed a marked increase in sister chromatid exchange induction and the formation of DNA adducts in bone marrow and spleen cells recovered from the DBA/2 mice (AHH-noninducible) in both dose groups compared to the C57BL/6 (AHH-inducible) mice. However, no clear correlation between AHH inducibility and the positive clastogenic response induced by 150 mg/kg benzo[a]pyrene was found in adult male and female mice with genetically determined differences in AHH induction (Adler et al. 1989). Similarly, the transplacental exposure of 11-day-old homozygous and hybrid embryos (dams received a single oral gavage dose of 150 mg/kg and embryos were sampled 15 hours after treatment) to benzo[a]pyrene showed that the clastogenic response was independent of genetic constitution.

In contrast to the relatively uniform evidence that benzo[a]pyrene is a genotoxin in whole animals, the test material failed to induce unscheduled DNA synthesis (UDS) in the parenchymal liver cells of Brown Norway rats exposed by oral gavage to 12.5 mg/mL (Mullaart et al. 1989). There was, however, a clear increase in single-strand DNA breaks in cells from the two major centers of metabolism (the parenchymal liver and intestinal cells) of the treated animals that was not apparent in the nonparenchymal liver cells.

Significant ($p<0.05$), but marginal, increases in the frequency of abnormal sperm were found in CD-1 mice (8-12/group) exposed via oral gavage to benzo[a]pyrene doses ranging from 360 to 432 mg/kg (Salamone et al. 1988). The effect, however, was not clearly dose related, and the wide variation in the background frequency rendered the data inconclusive. Comparable doses produced no adverse effects in $B6C3F_1$ mice. Similarly, the evaluation of pyrene (241-844 mg/kg) in this study yielded uniformly negative results.

Orally administered fluoranthene (400 and 750 mg/kg) did not increase the sister chromatid exchange frequency in mice (Palitti et al. 1986). Gene mutations were not produced in bacteria or yeast in a host-mediated assay in which anthracene, benzo[a]pyrene, chrysene, or fluoranthene were administered to mice by gavage; positive results were produced in bacteria in the same test system in which mice were exposed to benz[a]anthracene and injected intraperitoneally with the bacteria (Simmon et al. 1979). Other genotoxicity studies are discussed in Section 2.4.

2.2.2.8 Cancer

No studies were located regarding cancer in humans following oral exposure to the 17 PAHs discussed in this profile. The animal studies discussed in this section are presented first by exposure duration (acute, intermediate, and chronic), and within each duration category the information on individual PAHs is discussed in alphabetical order. PAHs for which no information was available for specified exposure durations were omitted.

Acute-Duration Exposure. Mice acutely administered 1.5 mg/day benz[a]anthracene by oral gavage two times over 3 days exhibited increased incidences of hepatomas and pulmonary adenomas (80% and 85%, respectively) as compared to control incidences (10% and 30% for hepatomas and pulmonary adenomas, respectively) after 568 days of observation (Klein] 1963). No malignant tumors were observed in this study.

Mice fed benzo[a]pyrene in the diet at a concentration equivalent to 33.3 mg/kg/day exhibited forestomach neoplasms following 2 or more days of consumption. However, a lower concentration of benzo[a]pyrene (equivalent to 13.3 mg/kg/day) administered for up to 7 days did not produce forestomach tumors (Neal and Rigdon 1967) (see Table 2-2). Hamsters have also been observed to develop papillomas and carcinomas of the alimentary tract in response to gavage or dietary exposure to benzo[a]pyrene (Chu and Malmgren 1965). A 77% mammary tumor incidence was observed 90 weeks after a single oral dose of 50 mg benzo[a]pyrene (100 mg/kg) was administered to rats, as compared to a 30% incidence in untreated animals (McCormick et al. 1981).

A single dose of 0.05 mg/kg dibenz[a,h]anthracene in polyethylene glycol (PEG)-400 failed to induce tumors in male Swiss mice after 30 weeks. However, forestomach papillomas were found in 10% of mice administered a single dose of 0.05 mg/kg dibenz[a,h]anthracene followed by 30 weekly doses of

PEG alone, and in 21% of the mice when the dibenz[a,h]anthracene dose was followed by 30 weekly doses of PEG plus 3% croton oil (Berenblum and Haran 1955). Treatment with croton oil alone yielded a 14-16% tumor incidence. These results suggest that the carcinogenic activities of croton oil and dibenz[a,h]anthracene are additive in the mouse forestomach.

Intermediate-Duration Exposure. One intermediate-duration study was located that evaluated the carcinogenic potential of acenaphthene. Male and female mice exposed to 0, 175, 350, or 700 mg/kg/day acenaphthene by gavage for 13 weeks showed no evidence of tumorigenesis at necropsy (EPA 1989c).

Similarly, only one intermediate-duration study was located that evaluated the carcinogenic potential of anthracene. Male and female mice exposed to 0, 250, 500, 1,000 mg/kg/day anthracene by gavage for 13 weeks showed no evidence of tumorigenesis at necropsy (EPA 1989d).

One intermediate-duration study was located that evaluated the carcinogenic potential of benz[a]anthracene. Mice that received intermittent gavage doses of 1.5 mg/kg/day benz[a]anthracene for 5 weeks (Klein 1963). Mice were sacrificed at a median age of 437 or 547 days. The treated mice killed at 437 days exhibited a 95% incidence of pulmonary adenomas at an average of 3 per lung and a 46% incidence of hepatomas, with an average of 2.1 per tumor-bearer. Forestomach papillomas were found in 5% of the mice. Control animals killed after 441 days exhibited a 10% incidence of pulmonary adenomas. Treated mice sacrificed after 547 days exhibited a 95% pulmonary adenoma incidence, as was observed in the group sacrificed earlier, but an increased hepatoma incidence of 100%. Control animals sacrificed after 600 days had 30 and 10% incidences of pulmonary adenomas and hepatomas, respectively. This study was not adequately reported; it did not include complete histopathology, adequate treatment durations, large enough sample sizes, or statistical analysis. Although this study is inconclusive because of methodological limitations, it does provide some qualitative evidence for the potential carcinogenicity of benz[a]anthracene by the oral route.

Intragastric doses of 67-100 mg/kg benzo[a]pyrene have been shown to elicit pulmonary adenomas and forestomach papillomas in mice (Sparnins et al. 1986; Wattenberg and Leong 1970). Intermittent gavage exposure of mice to 67-100 mg/kg benzo[a]pyrene resulted in increased forestomach (100%) and pulmonary tumor incidences relative to controls at 30 weeks of age (Sparnins et al. 1986;

Wattenberg and Leong 1970). The study by Wattenberg and Leong (1970) involved gavage administration of approximately 1.0 mg of benzo[a]pyrene once a week for 8 weeks.

The incidence of forestomach tumors (papillomas and carcinomas) in mice was related to the duration of oral exposure to benzo[a]pyrene following intermediate-duration administration of dietary benzo[a]pyrene at various doses up to 250 ppm (33.3 mg/kg/day) for 30-197 days (Neal and Rigdon 1967, see Table 2-2). The tumor incidence also increased with increasing dose. In the same study, mice fed 250 ppm (33 mg/kg/day) for periods of 1-7 days exhibited increased forestomach tumor incidences following 2 or more days of benzo[a]pyrene exposure (total dose of 2 mg), while mice fed 10 ppm (13.3 mg/kg/day) for 110 days (total dose of 4.48 mg) did not develop tumors. The authors suggest that these findings provide evidence that there are no cumulative carcinogenic effects of benzo[a]pyrene or its metabolites in mice. These data suggest that differences in susceptibility may be strongly influenced by the age of the mice at the time that they were initially exposed. This study provides the best dose-response information available for the oral route of exposure despite the irregular protocol employed, although the relevance of forestomach tumors in rodents to human cancer is the subject of some controversy because humans lack a forestomach.

An association between dietary benzo[a]pyrene and the development of leukemia and tumors of the forestomach and lung has been observed in mice. Tumor incidence was related to both dose and length of exposure (except in the case of leukemia). Mice administered dietary doses of up to 1,000 ppm (up to 133 mg/kg/day) for intermediate lengths of time (23-238 days) exhibited an increased incidence of forestomach tumors (papillomas and carcinomas) (Rigdon and Neal 1966, 1969) (see Table 2-2). Mice administered 250 ppm (33.3 mg/kg/day) benzo[a]pyrene developed papillomas or carcinomas of the forestomach (64%) and all the mice in the 1,000-ppm (133 mg/kg/day) group exhibited forestomach tumors after 86 days of benzo[a]pyrene consumption. A similar relationship was observed for the incidence of lung tumors: mice fed 250 ppm (33.3 mg/kg/day) benzo[a]pyrene exhibited an increased lung adenoma incidence. The occurrence of leukemia was related to the ingestion of 250 ppm (33.3 mg/kg/day) benzo[a]pyrene; 37% of the treated mice developed leukemias (Rigdon and Neal 1969) (see Table 2-2). The lack of consistent protocol in these experiments and the short exposure duration and observation periods preclude the assessment of a dose-response relationship. Furthermore, because tumors were reported as combined papillomas and carcinomas, no distinction between these benign and malignant tumors can be made.

Mammary tumors have also been observed following intermediate-duration exposure to benzo[a]pyrene in rats. Eight weekly oral doses of 6.25 mg benzo[a]pyrene (12.5 mg/kg) administered to rats resulted in a 67% increase in the incidence of mammary tumors in female rats after 90 weeks of observation (McCormick et al. 1981). A 30% incidence of these tumors was observed in the control animals.

Two intermediate-duration studies investigated the carcinogenicity of dibenz[a,h]anthracene in animals following oral exposure. Mammary carcinomas were observed in 5% of the female BALB/c mice dosed with 0.5% dibenz[a,h]anthracene after 15 weeks of dosing; however, no control group was included (Biancifiori and Caschera 1962). In the other study, male and female rats were administered an emulsion of aqueous olive oil and dibenz[a,h]anthracene in place of their drinking water for up to 200 days (Snell and Stewart 1963). Pulmonary adenomatosis, alveologenic carcinoma, mammary carcinoma, and hemangioendotheliomas were observed in the treated rats. These tumors were not observed in the control animals. However, extensive dehydration and emaciation occurred because the animals did not tolerate the vehicle well, which lead to early death and the need to periodically remove the animals from the treatment vehicle. Neither of these studies was adequately reported: they did not perform appropriate histopathologic evaluations, treatment or study durations were inadequate, and the sample size was inadequate. Despite these methodological limitations, these studies do provide some evidence of dibenz[a,h]anthracene's carcinogenicity by the oral route.

One intermediate-duration study was located that evaluated the carcinogenic potential of fluoranthene. Male and female mice exposed to 0, 125, 250, or 500 mg/kg/day fluoranthene by gavage for 13 weeks showed no evidence of tumorigenesis at necropsy (EPA 1988e).

Similarly, only one intermediate-duration study was located that evaluated the carcinogenic potential of fluorene. Male and female mice exposed to 0, 125, 250, or 500 mg/kg/day fluorene by gavage for 13 weeks showed no evidence of tumorigenesis at necropsy (EPA 1989e).

Chronic-Duration Exposure. Benzo[a]pyrene was administered in the diet of 32 Sprague-Dawley rats/sex/group either every 9th day or 5 times/week at a dose of 0.15 mg/kg until the animals were either moribund or dead (Brune et al. 1981). An untreated control group consisted of 32 animals/sex. There was no treatment-related effect on survival and no treatment-related increase in tumors at any one site. However, a statistically significant increase in the proportion of animals with tumors of the forestomach, esophagus, and larynx combined was noted among animals receiving treatment

5 times/week (the combined incidence of animals with these tumors was 3/64, 10/64, and 3/64 in the controls, the group fed benzo[a]pyrene 5 times/week, and the group fed benzo[a]pyrene every 9th day). In the same study, groups of 32 Sprague-Dawley rats/sex were administered 0.15 mg/kg benzo[a]pyrene by gavage in a 1.5% caffeine solution either every 9th day (Group 3), every 3rd day (Group 2), or 5 times/week (Group 1) until the animals were moribund or dead, resulting in average annual doses of 6, 18, or 39 mg/kg, respectively. Survival was adversely affected only in Group 3 (mean survival.time = 87 weeks versus 102 weeks in the controls). Treatment with benzo[a]pyrene significantly increased the proportion of animals with tumors of the forestomach, esophagus, and larynx (the combined tumor incidence was 3/64, 6/64, 13/64, 2664, and 14/64 for the untreated controls, the gavage controls, and Groups 3, 2, and 1, respectively).

Summary. These results indicate that benz[a]anthracene, benzo[a]pyrene, dibenz[a,h]anthracene, and possibly other PAHs are carcinogenic to rodents following oral exposure at high doses.

All reliable CELs in mice for acute- and intermediate-duration exposure are recorded in Table 2-2 and plotted in Figure 2-2.

2.2.3 Dermal Exposure

2.2.3.1 Death

No studies were located regarding death in humans or animals after dermal exposure to the 17 PAHs discussed in this profile.

2.2.3.2 Systemic Effects

No studies were located regarding respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, or ocular effects in humans or animals after dermal exposure to any of the 17 PAHs discussed in this profile. Other systemic effects observed after dermal exposure are discussed below.

The highest NOAEL values and all LOAEL values from each reliable study for each species and duration category are recorded in Table 2-3.

TABLE 2-3. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons - Dermal

Species/ (Strain)	Exposure/ Duration/ Frequency/ (Specific Route)	System	NOAEL	LOAEL				Reference
				Less Serious		Serious		
ACUTE EXPOSURE								
Systemic								
Mouse (C57BL/6)	1-2 d 1 x/d	Dermal	0.05 M mg/cm2					Iwata et al. 1981 anthracene
Mouse (C57BL/6)	1-2 d 1 x/d	Dermal	0.001 M mg/cm2	0.005 M mg/cm2	(induction of melanocytes)	0.025 M	(substantial melanocytes)	Iwata et al. 1981 benzo[a]pyrene
Mouse (C34/HeN)	5 d 2 x/5d	Dermal		120 mg F	(contact hypersensitivity)			Klemme et al. 1987 benzo[a]pyrene
Mouse (C57BL/6)	1-2 d 1 x/d	Dermal		0.0125 M mg/cm2	(slight increase melanocytes)			Iwata et al. 1981 chrysene
Mouse (C57BL/6)	1-2 d 1 x/d	Dermal	0.05 M mg/cm2					Iwata et al. 1981 fluoranthene
Mouse (C57BL/6)	1-2 d 1 x/d	Dermal	0.05 M mg/cm2					Iwata et al. 1981 fluorene
Mouse (C57BL/6)	1-2 d 1 x/d	Dermal	0.05 M mg/cm2					Iwata et al. 1981 pyrene
Immunological/Lymphoreticular								
Mouse (C34/HeN)	5 d 2 x/5d			120 F	(contact hypersensitivity)			Klemme et al. 1987 benzo[a]pyrene

TABLE 2-3. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons - Dermal (continued)

Species/ (Strain)	Exposure/ Duration/ Frequency/ (Specific Route)	System	NOAEL	LOAEL Less Serious	LOAEL Serious	Reference
Cancer						
Mouse (CD-1)	20 d 10 x				10.1µg F [CEL: 35% (7/20) tumor incidence]	Weyand et al. 1993b benzo[b]fluoranthene
INTERMEDIATE EXPOSURE						
Immunological/Lymphoreticular						
Gn pig (Hartley)	2-3 wk 2 x			0.001% F (slight contact sensitivity)	1.0% F (contact sensitivity)	Old et al. 1963 benzo[a]pyrene
Cancer						
Mouse (C3H/HeJ)	6 mo 2 x/wk				0.05 mg M (CEL: 1/13 (8%) had a papilloma with coadministration of 0.0005 mg BaP)	Warshawshy et al. 1993 anthracene
Mouse (CD-1)	1 d 1 x/d, then 25 wk 3 d/wk (TPA)		0.09 F mg/kg		0.57 F mg/kg (CEL: 36% skin tumor incidence)	Levin et al. 1984 benz[a]anthracene
Mouse (SENCAR)	once then 23 wk 2 d/wk (TPA)				0.2 mg F (CEL: 6 papillomas/mouse)	Cavalieri et al. 1988b benzo[a]pyrene
Mouse (Swiss)	20 wk 2 x/wk 1 x/d				0.025 F mg (CEL: tumors in 90%)	Cavalieri et al. 1988b benzo[a]pyrene

TABLE 2-3. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons - Dermal (continued)

Species/ (Strain)	Exposure/ Duration/ Frequency/ (Specific Route)	System	NOAEL	LOAEL			Reference
				Less Serious	Serious		
Mouse (Crl:CD-1)	20 d every other day				0.01 mg F	(CEL: 35% developed skin tumors)	LaVole et al. 1993a benzo[b]fluoranthene
Mouse (CD-1)	20 d every other day				0.006 mg F	(CEL: 5% developed skin tumors)	LaVole et al. 1993b benzo[j]fluoranthene
Mouse (C3H/HeJ)	6 mo 2 x/wk				0.05 mg M	(CEL: 1/15 (7%) had a papilloma from chrysene alone; 3/13 (23%) having papillomas or malignancies with coadministration of 0.0005 mg BaP)	Warshawshy et al. 1993 chrysene
Mouse (C3H/HeJ)	6 mo 2 x/wk				0.05 mg M	(CEL: 1/12 (8%) had papillomas with coadministration of 0.0005 mg BaP)	Warshawsky et al. 1993 fluoranthene
Mouse (CD-1)	20 d 1 x/2d, then 22 wks (TPA)				100 mg F	(CEL: 80% incidnece of tumors)	Rice et al. 1985a indeno(1,2,3-c,d)pyr
Mouse (Swiss)	12 mo 3 x/wk		50 F		100 µg F	(CEL: 6/20 had papillomas, 3/20 had carcinomas)	indeno(1,2,3-cd)pyre

TABLE 2-3. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons - Dermal (continued)

Species/ (Strain)	Exposure/ Duration/ Frequency/ (Specific Route)	System	NOAEL	LOAEL			Reference
				Less Serious	Serious		
Mouse (C3H/HeJ)	6 mo 2 x/wk				0.05 mg M	(CEL: 3/13 (23%) had a tumor (papillomas and malignant) from the mixture alone; 8/17 (47%) with coadministration of 0.0005 mg BaP)	Warshawsky et al. 1993 mix
Mouse (C3H/HeJ)	6 mo 2 x/wk				0.05 mg M	(CEL: 1/12 (8%) had papillomas from phenanthrene alone; 1/17 (6%) had a malignant tumor with coadministration of 0.0005 mg BaP)	Warshawsky et al. 1993 phenanthrene
Mouse (C3H/HeJ)	6 mo 2 x/wk				0.05 mg M	(CEL: 1/13 (8%) had a papillomas from pyrene alone)	Warshawsky et al. 1993 pyrene
CHRONIC EXPOSURE							
Cancer							
Mouse (NMRI)	17-22 mo 2 d/wk 1 x/d				2 mg F	(CEL: 45% developed skin tumors)	Habs et al. 1984 benzo[a]pyrene
Mouse (C3H/HrJ)	99 wk 2 d/wk 1 x/d				12.5 µg M	(CEL: malignant tumors in 47/50)	Warshawsky and Barkley 1987 benzo[a]pyrene
Mouse (Swiss)	lifetime 3 d/wk 1 x/d				0.01% F	(CEL: papillomas in 5%)	Wynder and Hoffmann 1959b benzo[b]fluoranthene

TABLE 2-3. Levels of Significant Exposure to Polycyclic Aromatic Hydrocarbons - Dermal (continued)

Species/ (Strain)	Exposure/ Duration/ Frequency/ (Specific Route)	System	NOAEL	LOAEL		Reference
				Less Serious	Serious	
Mouse (NMRI)	19-20 mo 2 d/wk 1 x/d				15 µg F (CEL: skin carcinomas in 1/20)	Habs et al. 1984 mix

BaP = benzo(a)pyrene; CEL = cancer effect level; d = day(s); F = female; LOAEL = lowest-observed-adverse-effect level; M = male; mo = month(s); NOAEL = no-observed-adverse-effect level; TPA = tetradecanoyl phorbol acetate; wk = week(s); x = time(s)

Dermal Effects. Mixtures of carcinogenic PAHs cause skin disorders in human and animals; however, specific effects in humans of individual PAHs, except for benzo[a]pyrene, have not been reported. Mixtures of PAHs are also used to treat some skin disorders in humans. From these patients comes much of the data describing dermal effects of PAH exposure.

Regressive verrucae (i.e., warts) was reported following up to 120 dermal applications of 1% benzo[a]pyrene in benzene to human skin over 4 months (Cottini and Mazzone 1939). Although reversible and apparently benign, the changes were thought to represent neoplastic proliferation.

Adverse dermal effects have been noted in humans following intermediate-duration dermal exposure to benzo[a]pyrene in patients with the preexisting dermal conditions of pemphigus vulgaris (acute or chronic disease characterized by occurrence of successive crops of blisters) and xeroderma pigmentosum (a rare disease of the skin marked by disseminated pigment discolorations, ulcers, and cutaneous and muscular atrophy) (Cottini and Mazzone 1939). A 1% benzo[a]pyrene solution topically applied to patients with pemphigus resulted in local bullous eruptions characteristic of the disease. Patients with xeroderma pigmentosum exposed to 1% benzo[a]pyrene slightly longer than the pemphigus patients exhibited only pigmentary and slight verrucous effects. Similarly treated patients with preexisting active skin lesions due to squamous cell cancer showed a general improvement and/or retardation of the lesion. The severity of abnormal skin lesions appeared to be related to age; those in the lowest age range exhibited fewer and less-severe effects than those in the mid-range groups. No such age relationship of effects involving those patients with normal or preexisting skin lesions was noted.

Adverse dermal effects have also been ohserved in animals following both acute- and intermediate duration dermal exposure to various PAHs. For example, acute topical application of benzo[a]pyrene, benz[a]anthracene, or dibenz[a,h]anthracene applied to the shaved backs of Swiss mice were all reported to suppress sebaceous glands (Bock and Mund 1958). However, controls were not employed; therefore, it is not possible to determine if the effects seen were due to the solvent and/or the application procedures.

Benzo[a]pyrene was applied once weekly to the skin of female ICR/Harlan mice (43-50/group) at doses of 16, 32, or 64 μg per application for 29 weeks (Albert et al. 1991b). Cell cycle kinetics and

morphometrics were evaluated. Evidence of epidermal cytotoxicity and death followed by regeneration was seen in animals administered 64 μg benzo[a]pyrene beginning the first weeks of exposure and later in the lower dose groups. This evidence included dose-related epidermal thickening and vertical nuclei stacking, increased mitotic labeling (2-4-fold with increasing dose), increased incidence of pyknotic and dark cells, and a pronounced inflammatory response in the dermis. The increase in cell proliferation was accompanied by only a minor increase in the size of the epidermal cell population, indicating that the proliferation was a regenerative response.

An acute (96-hour) dermal application of anthracene to the backs of hairless mice followed by ultraviolet radiation exposure for 40 minutes resulted in enhanced dermal inflammation compared to mice exposed exclusively to ultraviolet radiation. However, this effect was reversed within 48 hours (Forbes et al. 1976). Anthracene thus potentiates the skin damage elicited by sunlight exposure and may be considered a photosensitizer in hairless mice.

In animals, dermal application of 1% benzo[a]pyrene to the skin of hairless mice resulted in epidermal cell growth alterations (Elgjo 1968). Increases were observed in mitotic rates, mitotic counts, and mitotic duration and the author suggested that these were indicative of a regenerative reaction. However, concurrent controls were not utilized. The authors concluded that the alterations in the kinetics of epidermal cell growth produced by benzo[a]pyrene were more sustained than after application of croton oil. The study is limited for drawing conclusions concerning the dermal toxicity of benzo[a]pyrene because experimental data were compared with historical controls only, no acetone control was evaluated, and the statistical significance of the increased values was not determined.

2.2.3.3 Immunological and Lymphoreticular Effects

No studies were located regarding immunological effects in humans following dermal exposure to the 17 PAHs discussed in this profile.

Benzo[a]pyrene can elicit an immune response when applied dermally to the skin of animals. In mice, acute application of 120 μg benzo[a]pyrene elicited an allergic contact hypersensitivity in C3H mice that was antigen specific (Klemme et al. 1987). Slight contact hypersensitivity was also observed in guinea pigs following two dermal applications of 0.001% benzo[a]pyrene given over a period of 2-3 weeks. This response was more severe at a dose of 1.0% benzo[a]pyrene (Old et al. 1963).

In addition to eliciting a contact hypersensitivity response, benzo[a]pyrene has been shown to suppress this response to other sensitizers. The effects of dermally applied benzo[a]pyrene (alone or following dermal pretreatment with the prostaglandin synthetase inhibitor, indomethacin) on contact hypersensitivity (cell-mediated immunity), and production of antibodies to dinitrophenol (DNP) (humoral immunity) were studied in male BALB/c mice treated for 6 weeks to 6 months (Andrews et al. 1991a). A group of mice treated with acetone served as controls. Benzo[a]pyrene alone caused a significant reduction ($p<0.01$) in the contact hypersensitivity response to dinitrofluorobenzene (DNFB) as measured by increases in ear thickness when compared to the vehicle controls. However, indomethacin pretreatment prevented the benzo[a]pyrene-induced contact hypersensitivity response. Benzo[a]pyrene also reduced antibody titres to DNP in treated mice. This suppressive effect on humoral immune function was not restored by pretreatment with indomethacin. These findings led the authors to conclude that the mechanism of benzo[a]pyrene-induced suppression of cell-mediated immunity involved prostaglandins, whereas benzo[a]pyrene-induced suppression of humoral immunity operated via a mechanism independent of prostaglandins. In a subsequent experiment, the effects of dermally applied benzo[a]pyrene (alone or following subcutaneous implantation of the prostaglandin synthetase inhibitor, indomethacin) on Langerhans cells and on skin prostaglandin (PGE_2) levels were studied in male BALB/c mice treated for 3 weeks (Andrews et al. 1991b). Langerhans cells are antigen-presenting cells involved in cell-mediated immunity in skin. A group of mice treated with indomethacin served as controls. Benzo[a]pyrene alone caused a significant increase in the number of skin Langerhans cells, but reduced the percentage of Langerhans cells with dendritic morphology. Skin PGE_2 levels were also significantly increased by benzo[a]pyrene. Indomethacin attenuated the increase in Langerhans cell number and the changes in their morphology, and increased PGE_2 levels, such that all of these parameters were similar to those measured in the control animals. Based on these results, the authors suggested that benzo[a]pyrene induces increases in skin PGE_2 that in turn alter Langerhans cell number and morphology such that the cell-mediated immune response to skin antigens is suppressed.

An earlier study also demonstrated that benzo[a]pyrene affects epidermal Langerhans cells and dermal immunological responses. Female BALB/c mice were administered dermal applications on the dorsal skin of 0.5% benzo[a]pyrene in acetone twice weekly for up to 6 months (Ruby et al. 1989). Animals treated with acetone served as controls. The density, area, perimeter, and morphology of epidermal Langerhans cells were evaluated, along with the contact hypersensitivity response to DNFB. Benzo[a]pyrene treatment caused an increase in the number of epidermal Langerhans cells (as

determined by Ia antigens and -glucuronidase) from week 2 to week 5 of treatment and after weeks 10 and 18. The area and perimeter of these cells were unaffected by benzo[a]pyrene treatment, but the morphology was altered in that the dendrites appeared shortened. The contact hypersensitivity response to DNFB was significantly reduced in the benzo[a]pyrene-treated mice from 4 to 24 weeks of treatment. The authors propose that benzo[a]pyrene alters Langerhans cell number and morphology such that the cell-mediated immune response to skin antigens is suppressed. Skin tumors appeared in 20% of the benzo[a]pyrene-treated mice after 18 weeks of treatment, and 35% of the mice had 1-3 tumors after 24 weeks of treatment. The tumors were squamous papillomas (58%) and squamous cell carcinomas (42%). The changes in Langerhans cell number, distribution, and morphology coincided with the onset of tumors and other nonneoplastic skin lesions that were observed (epidermal hyperplasia and cellular atypia).

All reliable LOAELs from each reliable study for immunological effects for each species and duration category are recorded in Table 2-3.

No studies were located regarding the following health effects in humans or animals following dermal exposure to the 17 PAHs discussed in this profile:

2.2.3.4 Neurological Effects

2.2.3.5 Reproductive Effects

2.2.3.6 Developmental Effects

2.2.3.7 Genotoxic Effects

No studies were located regarding genotoxic effects in humans following dermal exposure to the 17 PAHs discussed in this profile. A single topical application of benzo[a]pyrene (0.5-500 μg/mouse) or chrysene (50-1,000 μg/mouse) to groups of HRA/Skh hairless mice (four mice/dose/group) resulted in significantly increased frequencies of micronucleated keratinocytes (He and Baker 1991). In the same study, micronuclei were not induced in the mouse skin cells following application of 2.5-2,500 μg/pyrene per mouse. Male SENCAR mice receiving two topical applications of 20 μg benzo[a]pyrene at 72-hour intervals exhibited increased DNA adduct formation in both epidermal and

lung tissue (Mukhtar et al. 1986). Following a single topical application, 100 μg benzo[b]fluoranthene, benzo[j]fluoranthene, benzo[k]fluoranthene, and indeno[1,2,3-c,d]pyrene were reported to bind to DNA in CD-l mouse skin (Weyand et al. 1987). The relative extent of binding was benzo[b]fluoranthene > benzo[j]fluoranthene > benzo[k]fluoranthene > indeno[1,2,3-c,d]pyrene. Covalent binding of chemicals to DNA can result in strand breaks and DNA damage, ultimately leading to mutations.

Benzo[a]pyrene (62.5 or 500 μg) was applied once to the shaved backs of male C57BL/6 mice (Bjelogrlic et al. 1994). Mice were killed at different time intervals after the treatment. DNA was isolated from the skin, purified, and analyzed for benzo[a]pyrene-7,8-diol-9,10-epoxide-DNA adducts. Skin was also evaluated for monoclonal antibody binding to mouse p53 protein, which has been shown to increase in response to DNA damage. Alterations in p53 are the most frequently observed mutations in human cancer. Benzo[a]pyrene-7,8-diol-9,10-epoxide-DNA adducts reached their maximum concentration 24 hours after the treatment, and decreased sharply within 1 week, regardless of the dose. An increase in p53 protein was seen only after treatment with 500 μg benzo[a]pyrene.

Benzo[j]fluoranthene, benzo[j]fluoranthene-4,5-diol, and benzo[j]fluoranthene-9,10-diol were applied to the shaved backs of CD-l mice and the DNA adducts were isolated and separated using multidimensional thin-layer chromatography (TLC) and reverse-phase high performance liquid chromatography (HPLC) (Weyand et al. 1993a). The highest level of adducts was observed with benzohlfluoranthene-4,5-diol, which resulted in the formation of 383 mol of DNA adducts/mg DNA. This level of DNA modification was more than 2 orders of magnitude greater than that observed with benzo[j]fluoranthene. In contrast, the major DNA adducts detected with benzo[j]fluoranthene-9,10-diol had chromatographic properties distinctly different than the adducts formed from either benzo[j]fluoranthene or B[j]F-4,5-diol. The adducts of the diols corresponded to DNA adducts produced *in vitro* from the respective diolepoxides. In a companion study, benzo[b]fluoranthene, benzo[b]fluoranthene-9,10 diol, 6-hydroxy-benzo[b]fluoranthene-9,10-diol, or 5-hydroxybenzo[b]fluoranthene-9,10-diol were applied to the shaved backs of CD-1 mice and the DNA adducts were isolated and separated using multidimensional TLC and reverse-phase HPLC (Weyand et al. 1993b). Benzo[b]fluoranthene formed one major adduct and 4 minor adducts. The DNA adducts formed from 5-hydroxybenzo[b]fluoranthene-9, l0 diol had identical retention to the major and one of the minor adducts of benzo[b]fluoranthene. These two adducts accounted for 58% of the modified nucleotides produced by benzo[b]fluoranthene application to mouse skin.

The DNA binding of manufactured gas plant residue (MGP) components in male B6C3F1 mice was investigated following topical administration (Weyand and Wu 1994). For topical exposure, male mice were treated with 10 mg MGP residue in 200 μL acetone, and sacrificed 24 hours later. Two mixtures of MGP residue were used: Mix of 3 combining equal amounts of samples from three different MGP plant sites, and Mix of 7 combining equal amounts of samples from seven different MGP plant sites, including those used in the Mix of 3. The mixtures contained pyrene, benz[a]anthracene, chrysene, benzo[b]fluorene, benzo[k]fluorene, benzo[a]pyrene, indeno[1,2,3-cd]pyrene, dibenz[a,h]anthracene, benzo[g,h,i]perylene. Data were presented in terms of pyrene. Animals were sacrificed 24 hours after treatment, and skin and lung were excised and DNA isolated. Chemical-DNA adduct formation was evaluated. Topical application MGP residue in acetone resulted in similar levels of DNA adduct in the skin for both the Mix of 3 and the Mix of 7. The total level of adducts detected in the lung after topical administration was identical to the response after dietary exposure, i.e., the Mix of 3 (1.4 mg/kg/day pyrene) produced adduct levels that were two times greater than the levels induced by the Mix of 7 (1.2 mg/kg/day pyrene). Other genotoxicity studies are discussed in Section 2.4.

2.2.3.8 Cancer

No studies were located that gave evidence of a direct association between human dermal exposure to individual PAHs and cancer induction. However, reports of skin tumors among individuals exposed to mixtures containing PAHs lend some qualitative support to their potential for carcinogenicity in humans. The earliest of these is the report by Pott (1775) of scrotal cancer among chimney sweeps. More recently, skin cancer among those dermally exposed to shale oils has been reported (Purde and Etlin 1980). However, these reports provide only qualitative suggestions pertaining to the human carcinogenic potential of all of the 17 PAHs discussed in this profile, or at least the compounds found in chimneys and shale oils, such as benzo[a]pyrene, chrysene, dibenz[a,h]anthracene, benz[a]anthracene, and benzo[b]fluoranthene. Limitations in these reports include no quantification of exposure to individual PAHs and concurrent exposure to other putative carcinogens in the mixtures.

It has been suggested that an increase in the number of skin melanocytes correlates with the sebaceous gland suppression index, and that the short-term melanocyte-activation test is useful for the detection of skin carcinogens and promoters. Some chemical carcinogens have been shown to induce melanogenesis in melanoblasts in the skin. Anthracene, benzo[a]pyrene, chrysene, fluoranthene,

fluorene, and pyrene were examined for their ability to induce melanocyte activation by topical application to the backs of mice for 1 or 2 consecutive days. Benzo[a]pyrene, an animal skin carcinogen, was a potent melanocyte inducer at doses of 20-100 μg/mouse (0.005-0.025 mg/cm^2) as demonstrated by an increase of up to 19 times over controls in the number of dopa-positive cells, whereas no effects were seen at 4 μg/mouse (0.001 mg/cm^2). Chrysene, a weak skin carcinogen (in animals), increased the number of dopa-positive cells to four times that of controls following an application of 50 μg/mouse (0.0125 mg/cm^2), while larger doses did not cause further increases in the numbers of these cells. Other PAHs such as anthracene, fluoranthene, fluorene, and pyrene (PAHs that are considered to be noncarcinogenic) produced no increases in the number of active melanocytes when applied at a dose of 200 μg/mouse (0.05 mg/cm^2) (Iwata et al. 1981).

Complete Carcinogenesis Studies. Studies in laboratory animals have demonstrated the ability of benz[a]anthracene, benzo[b]fluoranthene, benzo[j]fluoranthene, benzo[a]pyrene, chrysene, dibenz[a,h]anthracene, and indeno[1,2,3-c,d]pyrene to induce skin tumors (i.e., they are complete carcinogens) following intermediate dermal exposure. Anthracene, fluoranthene, fluorene, phenanthrene, and pyrene do not act as complete carcinogens. The data supporting these conclusions are discussed below by chemical. Only those studies considered adequate and reliable with respect to study design and adequacy of reporting are presented in Table 2-3.

Anthracene. Skin painting experiments were conducted on groups of 20 male C3H/HeJ mice (Warshawsky et al. 1993). Anthracene dissolved in toluene was applied to shaved skin twice weekly for six months at a dose of 0.05 mg. Tumor incidence was determined at the end of the study. For anthracene, administration alone produced tumors in 0 of 14 animals. With coadministration of 0.05 mg benzo[a]pyrene, 1 of 13 (8%) had a papilloma, with a mean latency period of 85 weeks. Anthracene was negative as a complete carcinogen following chronic dermal exposure (Habs et al. 1980). Swiss mice receiving 10% anthracene in acetone topically applied to their backs three times a week throughout their lifetime did not develop any skin tumors after 20 months (Wynder and Hoffmann 1959a).

Benz[a]anthracene. Benz[a]anthracene has been shown to cause skin tumors in mice following intermediate-duration dermal application. Graded concentrations of benz[a]anthracene in toluene or *n*-dodecane applied to the backs of mice for 50 weeks resulted in dose-related increases in tumor incidence (Bingham and Falk 1969). This response was enhanced when *n*-dodecane was the solvent

compared with toluene. Malignant tumors were observed at dose levels of about 0.02% benz[a]anthracene (0.15 mg/kg/day) and above when toluene was the solvent; however, when n-dodecane was the solvent, tumors were observed.at much lower concentrations of 0.0002% benz[a]anthracene (0.0015 mg/kg/day). The dose-response relationship reported in this study is extremely shallow (sublinear) over two orders of magnitude. A possible explanation for this is that the tumorigenic potency of certain PAHs is tempered by their cytotoxicity. Thus, the cytotoxic effects to epithelial cells may self-limit their potency as tumorigens. No solvent controls were included for comparison (Bingham and Falk 1969).

Intermediate-duration topical application of benz[a]anthracene to the backs of mice for 30 weeks resulted in a slightly elevated (2.6%) (but not statistically significant) skin tumor incidence. No definitive conclusions can be drawn from this study since only one dose was employed and no statistical analysis was performed.

Benzo[b]fluoranthene. A dose-response relationship for the dermal carcinogenicity of benzo[b]fluoranthene has been demonstrated over a one order-of-magnitude dose range in Swiss mice receiving (0.0l-0.5%) benzo[b]fluoranthene throughout their lifetime. Survival was also dose related. Although this study was designed as a long-term (chronic) bioassay, malignant tumors (90% carcinomas) appeared as early as 4 months in the high-dose group. Papillomas and carcinomas (65% and 85%, respectively) also appeared after 5 months in the mid-dose group. As a result, this study provides evidence that benzo[b]fluoranthene is carcinogenic following intermediate-duration exposure. The lowest dose at which benzo[b]fluoranthene elicited malignant tumors was 0.l%, which is approximately equal to a dose of 2.9 mg/kg received three times weekly, or an average daily dose of 1.2 mg/kg (Wynder and Hoffmann 1959b, see Table 2-3). In another chronic dermal study, benzo[b]fluoranthene produced a significant carcinogenic response of approximately one-third the potency of benzo[a]pyrene. The lowest dose at which tumors appeared was 3.4 μg benzo[b]fluoranthene; however, no distinction was made between papillomas and carcinomas (Habs et al. 1980).

Benzo[j]fluoranthene. Benzofilfluoranthene (0.1% or 0.5%) applied to the skin of female Swiss mice thrice weekly for life induced skin papillomas in 70% and 95% of the animals, respectively, and skin carcinomas in 105% and 95% of the animals, respectively, after 9 months of treatment (Wynder and Hoffmann 1959b).

No statistically significant increase in the incidence of skin tumors was noted in female NMRI mice dermally administered 3.4, 5.6, or 9.2 µg benzo[j]fluoranthene in acetone twice weekly for life (Habs et al. 1980). A total of 4 benzo[j]fluoranthene-treated mice developed skin tumors (application site sarcoma, papillomas, and a carcinoma).

Benzo[k]fluoranthene. Chronic dermal application of benzo[k]fluoranthene to Swiss mice resulted in no tumors, but skin papillomas were observed in 10% of animals when the concentration of benzo[k]fluoranthene was increased. Statistical analyses were not performed (Wynder and Hoffmann 1959b). In another study, no significant increase in tumor incidence was observed in NMRI mice painted with up to 9.2 µg of benzo[k]fluoranthene twice a week for a lifetime; no effect on mortality was noted (Habs et al. 1980).

Benzo[a]pyrene. Benzo[a]pyrene is a potent experimental skin carcinogen, and it is often used as a positive control in bioassays of other agents. Mixtures of PAHs that include benzo[a]pyrene such as coal tar were shown to be dermal carcinogens in animals as early as 1918 (Yamagiwa and Ichikawa 1918). In its role as a positive control, benzo[a]pyrene is usually administered at a single dose level, and thus quantitative evaluation of dose-response relationships is not possible.

Intermediate (19-20 weeks) topical application of a benzo[a]pyrene solution to the backs of mice resulted in a dose-related development of skin papillomas and squamous cell carcinomas (Cavalieri et al. 1988b, see Table 2-3; Shubik and Porta 1957). Benzo[a]pyrene was applied once weekly to the skin of female ICR/Harlan mice (43-50/group) at doses of 16, 32, or 64 µg for 29 weeks (Albert et al. 1991ba). Cell kinetics, morphometrics, and tumor formation were evaluated. Skin tumors were first apparent 12-14 weeks after the start of exposure in the 32- and 64-µg groups and after 18 weeks in the 16-µg group. The overwhelming majority of these tumors were benign. The average time of progression from benign papillomas to malignant carcinomas was 8.1 ± 4.5 weeks. Because there was good correspondence between the dose-response patterns for epidermal damage and the occurrence of skin tumors, and because tumors that initially appear as benign can be the result of tumor promoting agents that increase cell proliferation rates, the authors proposed that the tumors seen after benzo[a]pyrene treatment were the result of promotion related to benzo[a]pyrene-induced tissue damage. However, benign tumors can be formed as a result of genetic damage as well. Because benzo[a]pyrene causes genetic damage in addition to increased rates of cell proliferation, it is likely that genetic damage also played a role. Following a similar protocol in mice (once weekly dermal

applications of benzo[a]pyrene in acetone at doses of 16, 32, and 64 μg/mouse for 34 weeks), tumor development was reported to be best described by a dose-squared response. Quantitative data for tumor incidence were not presented (Albert et al. 1991b).

Carcinogenicity experiments on mouse skin were conducted with groups of 20 female CD-1 mice. Benzo[a]pyrene (0.05 mg) dissolved in 50 mL toluene was applied to shaved skin of mice twice weekly for 6 months (Warshawsky et al. 1993). Tumor incidence was determined at the end of the study. Benzo[a]pyrene produced no tumors.

In mice, the tumorigenic dose of benzo[a]pyrene is influenced by the solvent used for delivery. Graded concentrations of benzo[a]pyrene dissolved in decalin or a solution of n-dodecane and decalin were topically administered to the backs of mice for 50 weeks (Bingham and Falk 1969). Use of the n-dodecane and decalin solvent mixture significantly enhanced the potency of benzo[a]pyrene at lower doses in comparison with decalin alone. Malignant tumors appeared in 21% of the animals at 0.00002% (0.0054 mg/kg/day) benzo[a]pyrene in dodecane and decalin solvent. In contrast, a 42% skin tumor incidence was not observed until 0.02% (4.8 mg/kg/day) benzo[a]pyrene in decalin alone was applied. The method of application was not specified, sample sizes were small and no decalin solvent controls were included; however, decalin is not considered to be carcinogenic. In this same study, intermediate (50 weeks) dermal application of benzo[a]pyrene dissolved in the co-carcinogens 1-dodecanol or 1-phenyldodecane produced skin tumors in animals exposed to 0.05% benzo[a]pyrene in either solvent. The tumor incidence varied depending on the solvent concentration; however, the latency period was reduced only when 1-dodecanol was the solvent (Bingham and Falk 1969).

Mice receiving 0.001-0.01% of benzo[a]pyrene dermally applied to their backs throughout their lifetimes exhibited a dose-response relationship for skin tumors (Wynder and Hoffmann 1959a). A dose of 0.001% benzo[a]pyrene produced skin carcinoma and papilloma incidences of 4% and 45%, respectively. In another study conducted by Wynder and Hoffmann (1959b), higher concentrations of benzo[a]pyrene produced an 85% incidence of combined papillomas and carcinomas. These studies had a number of weaknesses, including no statistical treatment and no solvent control group. Dose quantification is difficult because of the method of application (Wynder and Hoffmann 1959a, 1959b). NMRI mice topically administered 2 μg benzo[a]pyrene throughout their lifetime also developed skin papillomas and carcinomas (45%) (Habs et al. 1984, see Table 2-3). CH3 mice administered a higher dose of 12.5 μg benzo[a]pyrene for 99 weeks exhibited malignant skin tumors (94%) (Warshawsky

and Barkley 1987, see Table 2-3). Increasing malignant carcinoma incidences in these dermal application studies can be correlated to increasing benzo[a]pyrene concentrations.

In mice, the tumorigenic dose of benzo[a]pyrene is dependent on the strain. For example, Habs et al. (1980) tested 1.7-4.6 μg benzo[a]pyrene (0.016-0.04 mg/kg/day) in order to determine its dose-response relationship as a carcinogen when topically applied to the backs of NMRI mice throughout their lifetimes. A clear-cut dose-response relationship was seen for benzo[a]pyrene and the induction of tumors. The lowest dose at which skin tumors appeared was 1.7 μg (0.016 mg/kg/day). This strain of NMRI mice also has a high (70%) background incidence rate of systemic tumors, so an evaluation of the effects of benzo[a]pyrene on any organ other than the site of administration was not possible:

Chrysene. Skin painting experiments with intermediate (6 months) dermal exposure with chrysene were conducted on groups of 20 male C3H/HeJ mice (Warshawsky et al. 1993). Chrysene (0.05 mg) dissolved in toluene was applied to shaved skin twice weekly for 6 months. Tumor incidence was determined at the end of the study. For chrysene, administration alone produced papillomas in 1 of 15 animals (7%), with a mean latency period of 81 weeks. With coadministration of 0.0005 mg benzo[a]pyrene, 3 of 13 (23%) had tumors (papillomas and malignant), with a mean latency period of 70 weeks.

Chrysene has elicited skin tumors in mice following chronic (68-82 weeks) dermal exposure. Topical application of a chrysene solution in *n*-dodecane/decalin to the skin of mice produced a significant increase in the carcinogenic potency of chrysene compared with the use of decalin alone; 26% and 63% of mice exhibited papillomas and carcinomas, respectively, at 49 weeks (Horton and Christian 1974). Because only one dose level was employed, no dose-response relationship can be inferred, and no solvent control was included. However, in other experiments decalin and *n*-dodecane have been shown to be noncarcinogenic in mice (Bingham and Falk 1969). An average dose of 1.2 mg/kg/day is the lowest dose of chrysene that has been found to elicit malignant tumors in laboratory animals.

In another chronic study, a higher concentration of chrysene applied dermally to the backs of Swiss mice for a lifetime also resulted in increased papilloma and carcinoma incidences (48% and 42%, respectively) compared to controls (Wynder and Hoffmann 1959a). Since only one dose was employed, no dose-response information can be inferred from this study.

Dibenz[a,h]anthracene: Dibenz[a,h]anthracene has also demonstrated a dose-response relationship for skin tumors over a two-orders-of-magnitude dose range following chronic exposure. Swiss mice received concentrations of 0.001-0.1% dibenz[a,h]anthracene applied to their backs throughout their lifetimes and exhibited dose-related papilloma and carcinoma incidences at the site of application at the two lowest doses. A decreased tumor rate at the highest dose tested probably reflects dibenz[a,h]anthracene's toxicity and the resulting decreased survival observed. The lowest concentration at which dibenz[a,h]anthracene elicited tumors was 0.001% (40% incidence of papillomas and 40% incidence of carcinomas), which is approximately equal to a dose of 0.029 mg/kg (0.012 mg/kg/day) (Wynder and Hoffmann 1959a). In another chronic derrnal study of dibenz[a,h]anthracene, a dose-related increase in skin carcinoma formation was observed, as well as decreased survival time and tumor latency period (Van Duuren et al. 1967).

Groups of 50 female NMRI mice received dermal applications of dibenz[a,h]anthracene in acetone (total doses = 0, 136, 448, or 1,358 nmol) three times a week for a total of 112 weeks (Platt et al. 1990). Papillomas were observed in 6%, 8%, and 32% of the treated animals, respectively.

Fluoranthene. Skin painting experiments with intermediate-duration (6 months) dermal exposure were conducted on groups of 20 male C3H/HeJ mice (Warshawsky et al. 1993). Fluoranthene was dissolved in toluene and applied to shaved skin twice weekly for 6 months. Tumor incidence was determined at the end of the study. For fluoranthene, administration alone produced tumors in 0 of 15 animals. With coadministration of 0.0005 mg benzo[a]pyrene, 1 of 12 (8%) had papillomas, with a mean latency period of 95 weeks.

Chronic dermal application of up to 1% fluoranthene to the backs of mice did not induce skin tumors following a lifetime of application (Hoffmann et al. 1972; Horton and Christian 1974; Wynder and Hoffmann 1959a).

Fluorene. Fluorene has been reported to be negative as a complete carcinogen (dose not specified) (Kennaway 1924). This information was obtained from an old, secondary source and therefore, its reliability is not known.

Indeno[1,2,3-c,d]pyrene. Indeno[1,2,3-c,d]pyrene was applied to the skin of female Swiss mice three times weekly for 12 months in concentrations of 0.5% (500 μg/application), 0.1%, 0.05%, and 0.01%

(20 mice per group) using acetone as the solvent. A tumor dose-response with 7 papilloma-bearing mice and 5 carcinoma-bearing mice for 0.5%, 6 papilloma-bearing and 3 carcinoma-bearing mice for 0.1%, and no skin tumors for 0.05% and 0.01% solutions was observed (Hoffmann and Wynder 1966). Chronic dermal application of indeno[1,2,3-c,d]pyrene in dioxane to mice did not produce an increased incidence of skin tumors. Similarly, chronic topical application of up to 9.2 µg of indeno[1,2,3-c,d]pyrene in acetone to the backs of mice for a lifetime resulted in no tumor induction (Habs et al. 1980).

Phenanthrene. Phenanthrene tested negative as a complete carcinogen in a mouse study inadequately reported in an old secondary source (Kennaway 1924). Skin painting experiments with intermediate-duration (6 months) dermal exposure were conducted on groups of 20 male C3H/HeJ mice (Warshawsky et al. 1993). Phenanthrene dissolved in toluene was applied to shaved skin twice weekly for 6 months. Tumor incidence was determined at the end of the study. For phenanthrene, administration alone produced papillomas in 1 of 12 animals (8%), with a mean latency period of 100 weeks. With coadministration of 0.0005 mg benzo[a]pyrene, 1 of 17 (6%) had malignant tumors, with a mean latency period of 53 weeks.

Pyrene. Skin painting experiments with intermediate-duration (6 months) exposure were conducted on groups of 20 male C3H/HeJ mice. Pyrene dissolved in toluene was applied to shaved skin twice weekly for 6 months. Tumor incidence was determined at the end of the study. For pyrene, administration alone produced papillomas in 1 of 13 animals (8%), with a mean latency period of 96 weeks. With coadministration of 0.0005 mg benzo[a]pyrene, 0 of 13 animals had tumors.

Mice chronically administered a 10% pyrene solution throughout their lifetimes did not develop skin tumors (Wynder and Hoffmann 1959a). However, prolonged dermal exposure of mice to 0.5% pyrene in decalin/n-dodecane solvent produced a slightly elevated (15%) skin carcinoma incidence; the level of statistical significance was not provided (Horton and Christian 1974).

Mixtures. Chronic dermal exposure of NMRI mice to a tar condensate that contained several PAHs (pyrene, fluoranthene, chrysene, benz[a]anthracene, benzo[a]pyrene, indeno[1,2,3-c,d]pyrene, benzo[g,h,i]perylene) in addition to other compounds produced a carcinogenic effect as evidenced by an increase in the incidence of skin papillomas and carcinomas (Habs et al. 1984). Because of the

presence of other compounds in the tar condensate, the carcinogenic effect cannot be definitely attributed to the PAHs present in the mixture.

Skin painting experiments of a mixture of anthracene, chrysene, fluoranthene, phenanthrene, and pyrene were conducted on groups of 20 male C3H/HeJ mice (Warshawsky et al. 1993). Compounds dissolved in toluene were applied to shaved skin twice weekly for 6 months. Tumor incidence was determined at the end of the study. Treatment included solutions of a mixture of the five noncarcinogenic PAHs at 0.05 mg, or the same compounds in solution with 0.0005 mg benzo[a]pyrene, a dose known to be noncarcinogenic in a similar study design. For the mixture of the 5 PAHs at 0.05 mg each, administration alone produced papillomas and malignant tumors in 3 of 13 animals (23%), with a mean latency period of 73 weeks. With coadministration of benzo[a]pyrene, 8 of 17 (47%) had tumors (papillomas and malignant), with a mean latency period of 66 weeks.

Initiation-Promotion Studies. Carcinogenesis has been demonstrated to be a multistage process in the cells of certain animal tissues, including skin, lung, liver, and bladder. This process is believed to occur in human tumorigenesis as well. The PAHs have been studied extensively for their ability to act as tumor initiators and/or promoters. Following is a brief discussion, by chemical, of the results of the initiation-promotion studies performed with 13 of the 17 PAHs discussed in this profile. Only those studies considered adequate and reliable are presented in Table 2-3.

The difficulty inherent in extrapolating initiation-promotion experiments to human exposure precludes their being used as the basis for human cancer effect levels. Since PAHs occur in complex mixtures of chemicals that may include tumor promoters, their activity as initiating agents is noteworthy. Thus, it is possible that humans dermally exposed to PAHs that are initiating agents, concomitantly with other chemicals that may be active as tumor promoters (including other PAHs) found at nearby hazardous waste sites, may have an increased risk of skin cancer.

Anthracene. Anthracene has been found to be inactive as an initiating agent under a dermal initiation/promotion protocol using tetradecanoyl phorbol acetate (TPA) as the promoter (LaVoie et al. 1983a).

Benz[a]anthracene. Benz[a]anthracene has been observed to be a tumor initiator in an intermediate-duration dermal study. CD-1 mice topically administered 2.5 µmol (0.57 mg) benz[a]anthracene

followed by promotion with TPA (for 25 weeks) exhibited an increased skin tumor incidence (36%) as compared to controls (Levin et al. 1984, see Table 2-3).

Benzo[a]pyrene. Benzo[a]pyrene is active as a tumor initiator using initiation/promotion protocols. Topical application of a single initiating dose of benzo[a]pyrene to the backs of mice followed by promotion with TPA or croton oil resulted in an 80-92% incidence of skin papillomas (Cavalieri et al. 1988b, see Table 2-3). Ten doses of benzo[a]pyrene (0.1 mg/dose) topically applied to the backs of Swiss mice followed by promotion with croton oil (for 20 weeks) also resulted in the development of skin tumors (Hoffmann et al. 1972).

In a dermal initiation/promotion assay, groups of 24 female SENCAR mice were administered a single dermal application of benzo[a]pyrene at doses ranging from 4 to 300 nmol (initiating dose), followed 7 days later by twice weekly applications of the promoter TPA, for a total of 24 weeks. Benzo[a]pyrene was active as a skin tumor initiator; the number of tumors per tumor bearing mouse, the percentage of tumor bearing mice, and the number of tumors per mouse were all significantly greater than in acetone controls and increased in a dose-related manner at doses ≥20 nmol (Cavalieri et al. 1991).

In a similar experiment, 24 8-week-old female SENCAR mice were treated dermally with 0.0002 mg (1 nmol) of benzo[a]pyrene in acetone on a shaved portion of dorsal skin (Higginbotham et al. 1993). One week later, tumor promotion was begun with TPA twice weekly for 27 weeks. The number of skin tumors was charted weekly and the mice were killed after experimental weeks. Complete necropsies were performed and tissues were fixed in formalin. Benzo[a]pyrene-treated mice had no skin tumors.

Benzo[e]pyrene. Benzo[e]pyrene is inactive as a skin tumor initiator in mouse skin (Slaga et al. 1980a).

Benzo[b]fluoranthene. The ability of benzo[b]fluoranthene to initiate skin tumor formation has been demonstrated using a standard initiation/promotion protocol with either croton oil or phorbol myristate acetate as a tumor promoter (Amin et al. 1985a; LaVoie et al. 1982). In another study, dermal applications of initiation doses of benzo[b]fluoranthene (10-100 μg) followed by TPA (for 20 weeks)

to the backs of CD-1 mice elicited a dose-related skin tumor incidence, predominantly consisting of squamous cell papillomas (LaVoie et al. 1982).

In a dermal initiation/promotion assay, groups of 20 female CD-1 mice were administered 10 dermal applications of benzo[b]fluoranthene at total doses of 0, 1, and 4 umol (initiating dose), followed 10 days later by thrice weekly applications of the promoter TPA for a total of 20 weeks (Weyand et al. 1991). Benzo[b]fluoranthene was active as a skin tumor initiator; the number of tumors per tumor-bearing mouse (8.5) and the percentage of tumor-bearing mice (100%) were significantly greater than in acetone controls and were increased in a dose-related manner.

Tumor initiation experiments were conducted with groups of 20 female CD-1 mice. Benzo[b]fluoranthene was applied to the shaved backs of the mice every other day using a total of 10 subdoses (Weyand et al. 1993b). Total doses were 10.1, 30.3, and 100.9 μg in acetone. Negative control mice were treated with acetone. Ten days after the last dose, promotion was begun by applying 2.5 μg TPA thrice weekly for 20 weeks. Tumors were counted weekly. Benzo[b]fluoranthene produced a 35%, 90%, and 95% incidence of tumor-bearing mice with 0.45, 3.70, and 8.65 tumors per mouse for the low, mid and high doses, respectively. No distinction was made between papillomas and carcinomas (Weyand et al. 1993b). Groups of 20 female Crl:CD-1 mice were dermally exposed to a total of 0, 0.01, 0.03, or 0.1 mg of benzo[b]fluoranthene in acetone applied every other day for 20 days in 10 subdoses (LaVoie et al. 1993a). Negative control mice were treated with acetone only. Ten days after the last application of acetone or hydrocarbon, tumor promotion was begun by applying 2.5 μg TPA in acetone three times weekly for 20 weeks. Tumor incidence was recorded after 20 weeks of promotion. The study was repeated for the 0.03 and 0.1 mg doses. Of the mice receiving 0.01 mg benzo[b]fluoranthene, 35% had developed tumors, with an average of 0.45 tumors/mouse. For the 0.03 mg dose, 70-90% of the mice developed tumors with an average of 1.4-3.7 tumors per mouse, whereas the 0.1 mg dose caused 95% of the mice to develop and average of 7.1-8.6 tumors. Of the animals treated with acetone only, 5-15% developed skin tumors. In this study, tumors were not identified as papillomas or carcinomas.

Benzo[j]fluoranthene. Benzo[j]fluoranthene has also been demonstrated to be a tumor initiator in mice, although it is not as potent as benzo[b]fluoranthene. Benzo[j]fluoranthene, however, is more potent than benzo[k]fluoranthene. Mice receiving initiating doses of benzo[j]fluoranthene (30-1,000 μg) followed by TPA promotion exhibited a dose-related increase in tumor incidence

(LaVoie et al. 1982, 1993a; Weyand et al. 1992). Groups of 20 female Crl:CD-1 mice were dermally exposed to a total of 0, 0.006, 0.012, 0.025, or 0.25 mg of benzojjlfluoranthene in acetone applied every other day for 20 days in 10 subdoses (LaVoie et al. 1993b). Negative control mice were treated with acetone only. Ten days after the last application of acetone or hydrocarbon, tumor promotion was begun by applying 2.5 μg TPA in acetone three times weekly for 20 weeks. Tumor incidence was recorded after 20 weeks of promotion. Five percent of the mice receiving 0.006 mg benzo[j]fluoranthene had developed tumors, with an average of 0.4 tumors per mouse. For the 0.012 mg dose, 10% of the mice developed tumors with an average of 0.4 tumors per mouse; 0.025 mg PAH caused 45% of the mice to develop tumors at an average of 0.65 tumors per mouse, whereas the 0.25 mg dose caused 95% of the mice to develop an average of 8.7 tumors. The control animals developed no tumors.

Benzo[k]fluoranthene. Benzo[k]fluoranthene has also been demonstrated to be a tumor initiator in mice, although it too, is not as potent as benzo[b]fluoranthene. Mice receiving initiating doses of benzo[k]fluoranthene (30-1,000 μg) followed by TPA promotion exhibited a dose-related increase in 'tumor incidence (LaVoie et al. 1982).

Benzo[g,h,i]perylene. Benzo[g,h,i]perylene has been shown to be inactive as an initiating agent when applied at a total dose of 0.25 mg/animal and negative as a complete carcinogen when a 1% solution was applied thrice weekly for 12 months (IARC 1983).

Chrysene. Chrysene is a tumor initiator in classic initiation/promotion bioassays on mouse skin using croton oil or phorbol myristate acetate as promoting agents (Slaga et al. 1980a; Wood et al. 1979a). Initiating doses of chrysene followed by promotion with TPA or croton resin induced a dose-related papilloma incidence in mice (Slaga et al. 1980a; Wood et al. 1979a).

Dibenz[a,h]anthracene. Dibenz[a,h]anthracene has also demonstrated tumor-initiating activity using a standard initiation/promotion protocol (Slaga et al. 1980a). Dibenz[a,h]anthracene has been reported to initiate skin development in a dose-response relationship at doses as low as 0.028 μg followed by promotion with TPA (for 25 weeks) (Buening et al. 1979a).

In a dermal initiation/promotion assay, groups of 50 female NMRI mice were administered a single dermal application of dibenz[a,h]anthracene at doses of 0, 300, or 600 nmol (initiating dose) followed

7 days later by twice weekly applications of the promoter, TPA, for a total of 24 weeks (Platt et al. 1990). Dibenz[a,h]anthracene was active as a skin tumor initiator only at the highest dose tested; 93% of the animals administered 600 nmol dibenz[a,h]anthracene developed skin tumors by 24 weeks.

Fluoranthene. Fluoranthene did not exhibit initiating activity in Swiss mice topically administered 10 doses followed by promotion with croton oil (for 20 weeks) (Hoffmann et al. 1972).

Indeno[1,2,3-c,d]pyrene. A pronounced dose-response relationship has been exhibited by indeno[1,2,3-c,d]pyrene in an initiation-promotion bioassay when TPA was employed as the promoting agent, although it was not as potent an initiator as benzo[b]fluoranthene (Rice et al. 1985a). In another study, 2.83 tumors/mouse were noted after a total initiating dose of 1.0 mg indeno[1,2,3-c,d]pyrene and promotion with TPA for 20 weeks (Rice et al. 1986).

The skin tumor initiating activity of indeno[1,2,3-c,d]pyrene and several of its metabolites generated *in* viva in mouse skin was tested in female Crl:CD/l mice (Rice et al. 1986). Initiating doses of indeno[1,2,3-c,d]pyrene or the metabolites were applied every other day to the shaved skin of groups of 25 mice for a total of 10 doses, which was followed 10 days later by thrice weekly applications of the tumor promotor, TPA, for 20 weeks. None of the metabolites were as active in inducing skin tumors as the parent compound (2.83 tumors/mouse as compared to 0.48-1.68 tumors/mouse at 20 weeks). These findings led the authors to conclude that the principal ultimate mutagenic metabolite, indeno[1,2,3-c,d]pyrene-1,2-oxide, is not the ultimate carcinogenic metabolite of indeno[1,2,3-c,d]pyrene.

Phenanthrene. Phenanthrene was ineffective as an initiator in various mouse strains (LaVoie et al. 1981b; Salaman and Roe 1956; Wood et al. 1979a). CD-1 mice topically administered a single dose of 10 μmol phenanthrene followed by a promoter were observed to have a papilloma incidence 2-4 times that of background; however, the incidences were not statistically significant in comparison to controls because of the small number of animals tested and the high spontaneous tumor incidence (Wood et al. 1979a).

Pyrene. Pyrene has been shown to be inactive as an initiating agent (Salaman and Roe 1956; Van Duuren and Goldschmidt 1976).

Mixtures. Co-administration of pyrene and benzo[a]pyrene to the backs of ICR/Ha mice has produced an enhancement of benzo[a]pyrene tumorigenicity (Van Duuren and Goldschmidt 1976). There is evidence that benzo[g,h,i]perylene is a co-carcinogen with benzo[a]pyrene when both are applied simultaneously to the skin of Swiss mice (Van Duuren et al. 1973). Dermal pretreatment with 100 μg pyrene substantially enhanced benzo[a]pyrene tumor initiation in CD-1 mice, while 100 μg fluoranthene produced a marginal enhancement (Slaga et al. 1979).

2.3 TOXICOKINETICS

Occupational studies provide evidence that inhaled PAHs are absorbed by humans. Animal studies also show that pulmonary absorption of benzo[a]pyrene occurs and may be influenced by carrier particles and solubility of the vehicle; however, the extent of absorption is not known. Absorption of benzo[a]pyrene following ingestion is low in humans, while oral absorption in animals varies among the PAH compounds depending on the lipophilicity. Oral absorption increases with more lipophilic compounds or in the presence of oils in the gastrointestinal tract. Percutaneous absorption of PAHs appears to be rapid for both humans and animals, but the extent of absorption is variable among these compounds and may be affected by the vehicle used for administration. Therefore, absorption of PAHs following inhalation, oral, or dermal exposure may be affected by vehicle of administration.

There was no information available on the distribution of PAHs in humans. PAHs appear to be widely distributed in tissues of animals following oral and inhalation exposure; peak tissue concentrations occurred earlier with higher exposure levels. Placental transfer of PAHs appears to be limited, and therefore, fetal levels are not as high as maternal levels.

Metabolism of PAHs occurs in all tissues and involves several possible pathways. Metabolism of PAHs has been studied extensively *in vitro* and *in vivo*. The metabolism products include epoxide intermediates, dihydrodiols, phenols, quinones, and their various combinations. The phenols, quinones, and dihydrodiols can all be conjugated to glucuronides and sulfate esters; the quinones also form glutathione conjugates.

Quantitative data on the excretion of PAHs in humans are lacking. In general, feces is the major elimination route of PAHs in animals following inhalation exposure. Excretion of benzo[a]pyrene appears to be high following low-level exposure in rats but low in dogs and monkeys. PAHs are

eliminated to a large extent within 2 days following low- and high-level oral exposure in rats. Following dermal exposure, elimination of PAHs occurs rapidly in the urine and feces of guinea pigs and rats.

Absorption of inhaled PAHs appears to occur through the mucous lining of bronchi, while ingested PAHs are taken up by the gastrointestinal tract in fat-soluble compounds. Percutaneous absorption is through passive diffusion. The mechanism of action of most PAHs involves covalent binding to DNA by PAH metabolites. The bay region diol epoxide intermediates of PAHs are currently considered to be the ultimate carcinogen for alternant PAHs. Once the reactive bay region epoxide is formed, it may covalently bind to DNA and other cellular macromolecules and presumably initiate mutagenesis and carcinogenesis.

2.3.1 Absorption

2.3.1.1 Inhalation Exposure

Absorption of PAHs in humans following inhalation exposure can be inferred from the presence of urinary metabolites of PAHs in workers exposed to these compounds in an aluminum plant (Becher and Bjorseth 1983). The high concentration of PAHs in the occupational setting did not correspond to the amount of PAHs deposited, metabolized, and excreted in the urine in this study. The authors suggested that PAHs adsorbed to airborne particulate matter may not be bioavailable and that the dose-uptake relationship may not be linear over the entire PAH concentration range.

Twelve workers from a coke plant participated in an intensive skin monitoring program combined with personal air sampling and biological monitoring during 5 consecutive 8-hour shifts (Van Rooij et al. 1993b). The mean concentration of total pyrene in the breathing zone air of the 12 workers ranged from 0.1 to 5.4 $\mu g/m^3$. The mean respiratory uptake of pyrene varied between 0.5 and 32.2 μg/day. Based on the estimates of the dermal and respiratory pyrene uptake, it is concluded that an average of 75% of the total absorbed amount of pyrene enters the body through the skin. The total excreted amount of urinary 1-hydroxypyrene as a result of exposure to PAHs during the five consecutive work shifts varied between 36 and 239 nmol. Analysis indicated that dermal absorption was most important in contributing to 1-hydroxypyrene excretion. Of the total dose absorbed by both routes combined,

13-49% is excreted as 1-hydroxypyrene. Variation in excretion is influenced by smoking habits, and consumption of alcohol (see Section 2.3.1.3).

Eleven healthy male smokers and 11 male smokers with lung cancer between the ages of 30-60 years, with a smoking history of 15-25 cigarettes per day for over 10 years were involved in a study (Likhachev et al. 1993). Urinary excretion of benzo[a]pyrene-7,8-diol and 3-hydroxybenzo[a]pyrene was determined. Both benzo[a]pyrene metabolites were detected in the urine, but quantities of 3-hydroxybenzo[a]pyrene were very low. The level of benzo[a]pyrene-7,8-diol in the urine varied considerably both in healthy smokers and smokers with lung cancer. However, the average value of this metabolite in the urine of healthy smokers was significantly higher than in the urine of lung cancer patients who smoked (1.06 mg/kg/day versus 0.56 mg/kg/day).

Animal studies on inhalation absorption of PAHs are limited to benzo[a]pyrene exposure. Rapid absorption was evident following inhalation exposure of low and high levels of benzo[a]pyrene to rats. Acute and intermediate-duration exposure to 4.8 mg/m^3 [^{14}C]-benzo[a]pyrene by nose-only inhalation in rats resulted in elevated levels of radioactivity in tissues and excreta within 3 hours of exposure (Wolff et al. 1989c). High levels of radioactivity were detected in the gastrointestinal tract, which may be due to biliary excretion or mucocilliary clearance of benzo[a]pyrene from the upper respiratory tract. Intratracheal administration of 0.001 mg/kg [^{3}H]-benzo[a]pyrene to rats also resulted in rapid absorption through the lungs. Radioactivity in the liver reached a maximum of 21% of the administered dose within 10 minutes of instillation (Weyand and Bevan 1986, 1988). Presence of radioactivity in other tissues and the bile was also indicative of its absorption in rats. Similar results were also seen in guinea pigs and hamsters following intratracheal exposure to benzo[a]pyrene (Weyand and Bevan 1986, 1987b, 1988).

Pregnant Wistar rats were exposed head-only to 200, 350, 500, 650, or 800 mg/m^3 of [^{14}C]-benzo[a]pyrene aerosol for 95 minutes on gestational day 17 (Withey et al. 1993a). Animals were killed immediately or 6 hours postexposure. Concentration of benzo[a]pyrene and metabolites in maternal blood sampled immediately after exposure were elevated 10-fold over the 4-fold increase in dose. At 6 hours postdosing, the increase was still approximately 10-fold, although the actual concentrations were 2-7-fold less than at 0 hours. Concentrations of benzo[a]pyrene and metabolites in fetal blood sampled immediately after exposure were elevated 5-fold over the 4-fold increase in exposure concentrations. Fetal tissues sampled 6 hours post-dosing had a 9-fold increase in

benzo[a]pyrene and metabolite concentration over the dose range, due to lower concentration in the 200-650 mg/m^3 dose groups at 6 hours compared to 0 hours. Fetal concentrations were 2-10-fold less than maternal concentrations. Benzo[a]pyrene concentrations in blood, lung, liver, and fetal tissues were significantly decreased from 0 to 6 hours postexposure while levels in fat tissue increased. For benzo[a]pyrene sampled immediately postdosing, lung > blood > liver > kidney > fat > fetus. For total metabolites sampled immediately postdosing, lung > blood > liver > kidney > fetus > fat. For benzo[a]pyrene sampled 6 hours postdosing, fat > lung > kidney > liver > blood > fetus. For total metabolites sampled 6 hours postdosing, lung = fat > kidney > liver = blood > fetus.

Twenty male Fisher 344 DuCrj rats were divided into two groups and exposed to diesel exhaust containing 0.151 mg/m^3 pyrene or HEPA-filtered air for 8 weeks, 5 days/week, 7 hours/day (Kanoh et al. 1993). At 2, 4, and 8 weeks during the exposure, the rats from each group were put into a metabolic cage and their urine was collected for 24 hours. Urinary levels of 1-hydroxypyrene in the rats of the exposure group increased remarkably over those of the control group, reaching 2.4 times as much by the end of the 2nd week, and 5.6 times by the 4th and 8th weeks.

Inhalation absorption of benzo[a]pyrene may be affected by the size of particles on which benzo[a]pyrene is adsorbed. The elimination of benzo[a]pyrene from the lungs was studied following intratracheal administration of pure benzo[a]pyrene crystals or benzo[a]pyrene coated on carbon particles in two size ranges (0.5-1.0 μm and 15-30 μm) (Creasia et al. 1976). Fifty percent of the pure benzo[a]pyrene crystals was cleared from the lungs within 1.5 hours and >95% cleared within 24 hours, while only 50% of the benzo[a]pyrene adsorbed to the small carbon particles cleared within 36 hours. Elution of benzo[a]pyrene was even slower with the larger particle size (approximately 4-5 days). These results indicate that the bioavailability of benzo[a]pyrene is altered by the particle size of the carrier. The initial lung deposition of [^{3}H]-benzo[a]pyrene adsorbed onto gallium oxide (Ga_2O_3) particles was 4.9 μg of which 3.1% remained after 30 minutes (Sun et al. 1982). A control study, conducted without the Ga_2O_3 particles at a concentration of 1 mg/m^3, found that 8.2 μg was inhaled, of which 0.9% remained in lungs after 30 minutes. The excretion of hydrocarbon was monitored for over 2 weeks at which time nearly all the initial lung burden was recovered in the excreta, indicating complete absorption of the instilled hydrocarbon. Significant differences in the clearance of benzo[a]pyrene coated with Ga_2O_3 and pure benzo[a]pyrene suggested that a substantial amount of benzo[a]pyrene/Ga_2O_3 particles was removed from the lungs by mucocilliary clearance and subsequent ingestion.

The above results corroborate findings in an *in vitro* experiment by Gerde and Scholander (1989) who developed a model of the bronchial lining layer. These investigators concluded that the release rate of PAHs from carrier particles is the rate-determining step in the transport of PAHs from these particles to the bronchial epithelium.

The absorption of benzo[a]pyrene may also be affected by the solubility of the vehicle used in administration. Approximately 70% of benzo[a]pyrene administered with triethylene glycol was excreted 6 hours following intratracheal instillation (Bevan and Ulman 1991). Excretion rates of benzo[a]pyrene were only 58.4% and 56.2% with ethyl laurate and tricaprylin, respectively, within a 6-hour period. The small volume of benzo[a]pyrene instilled is probably deposited in the bronchial region which allows more water-soluble materials (triethylene glycol) to pass the mucous layer lining than water-insoluble compounds (ethyl laurate and tricaprylin) (Bevan and Ulman 1991).

Nasal instillation of [^{3}H]-benzo[a]pyrene (0.13 mg/kg) to hamsters resulted in the metabolism of [^{3}H]-benzo[a]pyrene in the nasal cavity (Dahl et al. 1985). A large fraction of the metabolites was recovered from the epithelial surface, indicating that benzo[a]pyrene was first absorbed in the mucosa, metabolized, and returned to the mucus. Monkeys and dogs received nasal instillation of [^{14}C]-benzo[a]pyrene at doses of 0.16-0.21 mg/kg (Petridou-Fischer et al. 1988). Radiolabeled metabolites were detected in the nasal cavity, but little or no activity was detected in the blood and excreta of either species during the 48 hours after exposure. These results indicate that absorption of benzo[a]pyrene and/or its metabolites was poor or very slow following nasal instillation in monkeys and dogs.

2.3.1.2 Oral Exposure

There is evidence suggesting that benzopyrene is orally absorbed in humans (Buckley and Lioy 1992; Hecht et al. 1979). Following ingestion of diets containing very low levels of benzo[a]pyrene, the metabolite, 1-hydroxypyrene, was detected in the urine (Buckley and Lioy 1992). No quantitative data on the excretion of the benzo[a]pyrene were provided. The concentration of benzo[a]pyrene in human feces was examined in eight volunteers who ingested broiled meat that contained approximately 9 µg of benzo[a]pyrene (Hecht et al. 1979). The feces of these individuals did not contain detectable levels of benzo[a]pyrene (<0.1 µg/person), which is similar to what was seen following consumption of

control meat that contained undetectable amounts of benzo[a]pyrene by these same volunteers, suggesting that most of the ingested benzo[a]pyrene was absorbed.

Oral absorption of benzo[a]pyrene in rats is incomplete and may be influenced by the presence of oils and fat in the gastrointestinal tract. Oral absorption of benzo[a]pyrene was estimated to be 40%, with a bioavailability of 7.8-11.5%, in Sprague-Dawley rats infused intraduodenally to a total dose of approximately 0.0005 mg/kg for 90 minutes (Foth et al. 1988a). Nearly 80% of a gavage dose of 0.0527 mg/kg [^{14}C]benzo[a]pyrene in peanut oil was detected in the excreta of rats 48 hours after exposure; however, some of the recovered radioactivity may never have been absorbed by the alimentary tract of the rats, but may have passed into the excreta in the peanut oil (Hecht et al. 1979). Radioactivity found in the liver, lungs, kidneys, and testis following a low dose of [^{3}H]-benzo[a]pyrene to Sprague-Dawley rats provides supporting evidence of oral absorption (Yamazaki and Kakiuchi 1989; Yamazaki et al. 1987). The extent of oral absorption in rats is enhanced when benzo[a]pyrene is solubilized in a vehicle (triolein, soybean oils, high-fat diet) that is readily absorbed following low- and high-dose levels (Kawamura et al. 1988; O'Neill et al. 1991).

Oral absorption of benzo[a]pyrene was estimated to be 38-58% following dietary or gavage exposure to high levels in rats (Chang 1943). Anthracene was absorbed to a slightly higher extent (53-74%) than benzo[a]pyrene in rats while phenanthracene was poorly absorbed (4-7%) (Chang 1943). However, the data were limited because an inadequate number of rats was used and study details were lacking.

In general, the oral absorption of chrysene, dibenzanthracene, and pyrene was high following exposure to high doses in rats (Chang 1943; Grimmer et al. 1988; Withey et al. 1991). Following dietary or gavage administration of chrysene in rats, 64-87% of the dose was excreted in the feces (Chang 1943). Recovery of chrysene in excreta of Wistar rats was 74% four days after a single gavage dose of 22 mg/kg chrysene in corn oil (Grimmer et al. 1988). Administration of dibenz[a,h]anthracene in the diet (250 mg) or by stomach tube (200 mg) resulted in more than 90% of the dose being excreted in the feces of white rats (Chang 1943). As with chrysene, absorption of dibenz[a,h]anthracene could not be quantified. Male Wistar rats administered 2-15 mg/kg of [^{14}C]-pyrene recovered 68-92% of the dose in the excreta by 6 days postexposure (Withey et al. 1991). Bioavailability of pyrene and its metabolites was 65-84% over a period of 8 hours following administration.

Blood levels of fluoranthene, pyrene, and benz[a]anthracene after oral administration were examined in rats (Lipniak and Brandys 1993). Fluoranthene, pyrene, or benz[a]anthracene in Tween 80/isotonic saline, was administered orally to rats at a dose of 20 mg/kg. Blood levels after administration indicated that peak concentrations of the three compounds were reached at 1-2 hours after administration. The peak concentration of fluoranthene (≈30 mg/cm^3) was twice as high as that of pyrene, and 5 times higher than benz[a]anthracene.

The effect of diet matrix (gel or powder) on urinary excretion of 1-hydroxypyrene and hydrocarbon binding to DNA was investigated in mice (Wu et al. 1994). Female mice were fed a gel or powder diet containing manufactured gas plant (MGP) residue (coal tar) at 0.1% or 0.3% for 15 days, or the corresponding control diet. Two mixtures of MGP residue were used: Mix of 3 combining equal amounts of samples from three different MGP plant sites, and Mix of 7 combining equal amounts of samples from seven different MGP plant sites, including those used in the Mix of 3. The mixtures contained pyrene, benz[a]anthracene, chrysene, benzo[b]fluorene, benzo[k]fluorene, benzo[a]pyrene, indeno[1,2,3-cd]pyrene, dibenz[a,h]anthracene, benzo[g,h,i]perylene. Data were presented in terms of pyrene consumed and 1-hydroxypyrene excreted. Urine was collected on the first, seventh, and fourteenth day of diet administration. 1-Hydroxypyrene levels in the urine were determined using HPLC and fluorescence. Diet matrix had little effect on the bioavailability of the PAHs.

The intestinal absorption of PAHs is highly dependent on the presence of bile (Rahman et al. 1986). To study the role of bile in the intestinal absorption of PAHs, conscious rats with bile duct and duodenal catheters were given [^{3}H]-benzo[a]pyrene, phenanthrene, anthracene, 2,6-dimethylnaphthalene (DMN), and 7,12-dimethylbenz[a]anthracene (DMBA) with or without exogenous bile. The efficiency of PAH absorption was estimated from the cumulative recovery of radioactivity in the bile and urine over 24 hours. The efficiencies of absorption without bile (as a percentage of absorption with bile) were benzo[a]pyrene, 22.9%; phenanthrene, 96.7%; anthracene, 70.8%; DMN, 91.6%; DMBA, 43.4%. Absorption of the four- or five-membered rings (DMBA and benzo[a]pyrene) was strongly dependent on the presence of bile in the intestinal lumen. The absorption of the tricyclic PAHs (phenanthrene and anthracene) differed with respect to their dependency on bile for efficient absorption. This difference correlated with a difference in water solubility, with anthracene being 18 times less water-soluble than phenanthrene. Those products with low water solubility are dependent on the creation of an intermediate phase of the products of lipolysis and bile salts (Rahman et al. 1986). These reactions occur during the normal process of lipid digestion and absorption in the intestine.

2.3.1.3 Dermal Exposure

Application of 2% crude coal tar to the skin of humans for 8-hour periods on 2 consecutive days yielded evidence of PAH absorption (Storer et al. 1984). Phenanthrene, anthracene, pyrene, and fluoranthene were detected in the blood, but benzo[a]pyrene (which is present in coal tar) was not detected. This difference was attributed to differences in percutaneous absorption, rapid tissue deposition after absorption, or metabolic conjugation with rapid urine excretion. In another study, coal tar ointment was applied to skin of volunteers at various sites (Van Rooij et al. 1993a). The surface disappearance of PAH and the excretion of urinary 1-hydroxy-pyrene were used as parameters for dermal absorption. Surface disappearance measurements showed low but significant differences in dermal PAH absorption between anatomical sites: shoulder > forehead, forearm, groin > ankle, hand (palmar site). An *in vitro* study using human skin revealed that the extent of permeation across viable human skin after 24 hours was estimated to be 3% of the total applied radioactivity from [^{14}C]-benzo[a]pyrene (10 μg/cm^2) (Kao et al. 1985). Using human cadaver skin, it was shown that 23.7±9.7% of the applied benzo[a]pyrene penetrated into the skin (Wester et al. 1990). These results suggest that substantial metabolism and/or binding of benzo[a]pyrene takes place in viable human skin which limits the amount of PAH available to penetrate the skin into the systemic circulation.

Twelve workers from a coke plant participated in an intensive skin monitoring program combined with personal air sampling and biological monitoring during 5 consecutive 8-hour shifts (Van Rooij et al. 1993b). Measurements on exposure pads at six skin sites (jaw/neck, shoulder, upper arm, wrist, groin, ankle) showed that mean total skin contamination of the 12 workers ranged between 21 and 166 μg pyrene per day. The dermal uptake of pyrene ranged between 4 and 34 μg/day, which was about 20% of the pyrene contamination on the skin. The mean concentration of total pyrene in the breathing zone air of the 12 workers ranged from 0.1 to 5.4 μg/m^3. The mean respiratory uptake of pyrene varied between 0.5 and 32.2 μg/day. Based on the estimates of the dermal and respiratory pyrene uptake, it is concluded that an average of 75% of the total absorbed amount of pyrene enters the body through the skin. The total excreted amount of urinary 1-hydroxy-pyrene as a result of exposure to PAHs during the 5 consecutive work shifts varied between 36 and 239 nmol. Analysis indicated that dermal absorption was most important in contributing to 1-hydroxy-pyrene excretion. Of the total dose absorbed by both routes combined, 13-49% is excreted as 1-hydroxy-pyrene. Variation in excretion is influenced by smoking habits, and consumption of alcohol.

Percutaneous absorption of [^{14}C]-benzo[a]pyrene in mice, rats, monkeys, and guinea pigs is rapid and high (Ng et al. 1992; Sanders et al. 1986; Wester et al. 1990; Yang et al. 1989). A single dose of 7 μg/cm^2 [^{14}C]-benzo[a]pyrene in acetone was applied to a 4-cm^2 area of the dorsal skin of female hairless guinea pigs for 24 hours (Ng et al. 1992). Approximately 73% of the administered dose was absorbed dermally by 7 days postexposure; most of the dose was absorbed by day 3. The skin wash at 24 hours of exposure contained about 10.6% of dose (Ng et al. 1992). *In vitro* absorption of benzo[a]pyrene through guinea pig skin demonstrated similar results; 67% absorption in a 24-hour exposure (Ng et al. 1992). Seven days after exposure to 125 μg/cm^2 benzo[a]pyrene, 80% of the total recovered radioactivity was eliminated in the feces of mice (Sanders et al. 1986). The site of application still retained 7% of the recovered radioactivity after 7 days. However, the area of application was not covered to prevent animals from licking the test material which may have lead to ingestion of benzo[a]pyrene.

Groups of 12 male Wistar rats were dosed with 2, 6, or 15 mg/kg of [^{14}C]-pyrene applied to 4 cm^2 of a shaved area of the mid-back (Withey et al. 1993b). Three animals in each dose group were killed at 1,2,4, and 6 days postdosing, and the brain, lungs, heart, liver, spleen, kidneys, testes, muscle, and perirenal fat were removed and analyzed for pyrene and [^{14}C]-pyrene equivalents. Blood, urine, and feces, as well as the skin from the application site were also analyzed. The rate of uptake from the skin was rapid (t1/2 = 0.5-0.8 d) relative to rate processes for the other organs, and about 50% of the applied dose was excreted over the 6 days of the study. Levels of pyrene were highest in the liver, kidneys, and fat. Levels of metabolites were also high in the lung.

Dermal absorption of benzo[a]pyrene in rats and monkeys may be affected by the vehicle of administration (Wester et al. 1990; Yang et al. 1989). Following application of 10 ppm benzo[a]pyrene on the skin of rhesus monkeys, an average absorption of 51 ± 22% was reported with acetone vehicle and 13.2 ± .4% with soil; however, absorption data were based on radioactivity recovered in urine only, and not in feces (Wester et al. 1990). The great variation in the absorption with the acetone vehicle limits these results. This may be related, in part, to the dependence on monitoring radioactivity recovered in urine only as opposed to monitoring radioactivity recovered in urine and feces. Disappearance of the applied dose from the application site was 40% at 24 hours following administration (Wester et al. 1990). Sprague-Dawley rats absorbed 4-5 times more of a 1 ppm dose of benzo[a]pyrene when it was applied dermally alone, compared to a soil-sorbed crude oil mixture (Yang et al. 1989). The greater lipophilicity of the crude oil alone probably increased the

rate of dermal uptake of the test material, since the authors determined that absorption was dependent on the monolayer of soil in contact with the skin, which is comparable to the contact between the skin and oil. Therefore, the soil binding of the PAHs may have slowed absorption. However, no quantitative data were available.

Female Sprague-Dawley rats were exposed dermally to [^{3}H]-benzo[a]pyrene (1 ppm) containing petroleum crude oil alone or in fortified soil matrix for 4 days (Yang et al. 1989). Recovery of radioactivity was 35.3% of the dose applied in oil, as follows: urine (5.3% of dose), feces (27.5%), and tissues (2.5%) 96 hours after beginning of exposure. Recovery was 9.2% of applied dose with benzo[a]pyrene from petroleum crude-fortified soil; recoveries in urine, feces, and tissues were 1.9%, 5.8%, and 1.5%, respectively, at 96 hours. Benzo[a]pyrene (10 ppm) with acetone vehicle or in soil was applied to a 12 cm^2 area of abdominal skin of female rhesus monkeys for 24 hours (Wester et al. 1990). Urine contained 51 ± 22% of the dose with acetone vehicle and 13.2 ± 3.4% with soil.

The percutaneous absorption of [^{14}C]-anthracene (9.3 µg/cm^2) was 52.3% in rats, estimated from radioactivity in urine, feces, and tissues over a 6-day period (Yang et al. 1986). Over time, the permeation of anthracene significantly decreased suggesting that anthracene was dermally absorbed in a dose-dependent manner. Diffusion of anthracene through the skin (stratum corneum) depended on the amount of anthracene on the skin's surface.

When 6.25 µg/cm^2 [^{14}C]-phenanthrene and pyrene was applied to guinea pigs, dermal absorption was 80% and 94%, respectively (Ng et al. 1991, 1992). *In vitro* absorption of phenanthrene and pyrene in guinea pig skin was about 79-89% and 70%, respectively (Ng et al. 1991, 1992).

Monitoring the removal of compounds from the epidermis is indicative of measuring the compound's dermal absorption. The disappearance of radiolabeled benzo[a]pyrene and its metabolites from the epidermis was monophasic, following first order kinetics with a half-life of approximately 2 hours (Melikian et al. 1987). Recovery of the radiolabel was 99-100% throughout the period of the experiment (8 hours), indicating that volatilization of benzo[a]pyrene from the skin was not a confounding factor (Melikan et al. 1987). In contrast, removal of one of its metabolites, 7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydrobenzo[a]pyrene (anti-BPDE), from the epidermis was biphasic. The second, slower phase of removal suggested that the stratum comeum, the outermost layer of skin which consists of several layers of inactive, keratinized cells surrounded by extracellular

lipids, may act as a reservoir that can retain and slowly release topically applied lipophilic substances such as benzo[a]pyrene but is penetrated rapidly by more polar compounds such as anti-BPDE.

2.3.2 Distribution

2.3.2.1 Inhalation Exposure

No studies were located regarding the distribution of PAHs in humans following inhalation exposure. In general, tissue distribution of benzo[a]pyrene following inhalation exposure is qualitatively similar for different species (Bevan and Weyand 1988; Weyand and Bevan 1986, 1987a, 1988; Wolff et al. 1989c). Highest radioactivity was distributed to the cecum, small intestine, trachea, kidneys, and stomach in rats following a 3-hour or 4-week inhalation exposure to 4.8 mg/m^3 [^{14}C]-benzo[a]pyrene (Wolff et al. 1989c). The lungs and liver of rats contained 2.7% and 4.6% of the recovered dose 6 hours after intratracheal administration of 0.001 mg/kg [^3H]-benzo[a]pyrene (Bevan and Weyand 1988). [^3H]-Benzo[a]pyrene intratracheally administered to rats demonstrated that the highest fractions were distributed to the lung, liver, kidney, gastrointestinal tract, and carcass (Weyand and Bevan 1986, 1987a, 1988). The concentration of benzo[a]pyrene and its metabolites in the intestine increased with time, suggesting the occurrence of biliary excretion and enterohepatic recirculation. Tissue distribution of radioactivity was qualitatively similar in guinea pigs and hamsters (Weyand and Bevan 1987b). Mice that received 2.5 mg/kg benzo[a]pyrene intratracheally also experienced a similar tissue distribution, but Schnizlein et al. (1987) noted that as the lung burden of benzo[a]pyrene diminished, radioactivity continued to increase in the lung-associated lymph nodes for 6 days. This accumulation may eventually affect humoral immunity.

The distribution pattern of benzo[a]pyrene was not significantly affected following aerosol exposure with or without Ga_2O_3 particles (Sun et al. 1982). However, significant differences in the levels of benzo[a]pyrene delivered to the different tissues did exist. Maximum levels were achieved in the liver, esophagus, small intestine, and blood at 30 minutes following exposure. At 12 hours, maximum levels were seen in the lower gastrointestinal tract. Higher tissue levels of hydrocarbon resulted from absorption of benzo[a]pyrene-Ga_2O_3 particles. Inhaled benzo[a]pyrene adsorbed on insoluble Ga_2O_3 particles was cleared predominantly by mucocilliary transport and ingestion. This latter mechanism of

absorption led to the increased levels and longer retention times of benzo[a]pyrene in the stomach, liver, and kidneys (Sun et al. 1982).

Pregnant Wistar rats inhaled head-only high levels of [^{14}C]-pyrene aerosol on gestational day 17 (Withey et al. 1992). Concentrations of pyrene and metabolites in maternal and fetal blood were elevated 8-fold with a fourfold increase in exposure concentrations. However, pyrene levels in fetal blood were about 10 times lower than maternal blood immediately after exposure. In general, radioactivity increased in fat but decreased in blood, lungs, and liver tissues from 0 to 6 hours postexposure. There was only a small increase in the concentration of radioactivity in fetuses over the whole exposure range compared to maternal levels, suggesting placental transfer of pyrene and its metabolites are limited or that metabolism in fetal tissues is limited.

In a similar study, pregnant Wistar rats were exposed head-only to 200, 350, 500, 650, or 800 mg/m^3 of [^{14}C]-benzo[a]pyrene aerosol for 95 minutes on gestational day 17 (Withey et al. 1993a). Animals were killed immediately or 6 hours postexposure. Concentration of benzo[a]pyrene and metabolites in maternal blood sampled immediately after exposure were elevated 10-fold over the 4-fold increase in dose. At 6 hours postdosing, the increase was still approximately 10-fold, although the actual concentrations were 2-7-fold less than at 0 hours. Concentrations of benzo[a]pyrene and metabolites in fetal blood sampled immediately after exposure were elevated 5-fold over the 4-fold increase in exposure concentrations. Fetal tissues sampled 6 hours post-dosing had a 9-fold increase in benzo[a]pyrene and metabolite concentration over the dose range, due to lower concentration in the 200-650 mg/m^3 dose groups at 6 hours compared to 0 hours. Fetal concentrations were 2-10-fold less than maternal concentrations. Benzo[a]pyrene concentrations in blood, lung, liver, and fetal tissues were significantly decreased from 0 to 6 hours postexposure while levels in fat tissue increased. For benzo[a]pyrene sampled immediately postdosing, lung > blood > liver > kidney > fat > fetus. For total metabolites sampled immediately postdosing, lung > blood > liver > kidney > fetus > fat. For benzo[a]pyrene sampled 6 hours postdosing, fat > lung > kidney > liver > blood > fetus. For total metabolites sampled 6 hours postdosing, lung = fat > kidney > liver = blood > fetus.

2.3.2.2 Oral Exposure

No studies were located regarding the distribution of PAHs in humans following oral exposure.

Tissue levels of benzo[a]pyrene in Sprague-Dawley rats were highest 2-8 days after initial exposure to multiple doses of 0.0005 mg [^{3}H]-benzo[a]pyrene (Yamazaki and Kakiuchi 1989). The highest radioactivities were found in the kidney and testis. [^{3}H]-Benzo[a]pyrene distributed to the protein fractions of the liver, lung, and kidney (Yamazaki et al. 1987). The radioactivity in the protein fractions of these tissues increased gradually over time. In contrast, the radioactivity in the lipid fractions of these tissues accounted for 70% of the administered dose at 3 hours but decreased rapidly with time. The nucleic acid fraction maintained approximately 10% of the total radioactivity throughout the experiment. The increase in protein binding of radioactivity associated with benzo[a]pyrene and its metabolites, and the persistence of the radioactivity associated with the protein fractions, suggests that protein binding may allow benzo[a]pyrene and its metabolites to accumulate in certain tissues, thus increasing the likelihood of cytotoxicity, mutagenicity, or carcinogenicity of benzo[a]pyrene and its metabolites in these organs. In addition, these organs have low metabolic activity while the liver has a high detoxification potential and can facilitate the excretion of these toxic products (Yamazaki et al. 1987).

Single oral doses of 12 mg/kg [^{14}C]-benzo[a]pyrene were administered by gavage to pregnant NMRI:Han mice on gestational days 11, 12, 13, or 18 (Neubert and Tapken 1988). Distribution of radioactivity was measured at 6, 24, and 48 hours after exposure. Maternal and embryo levels were highest with exposure on gestational day 11. The difference in radioactivity between maternal and embryo liver tissues increased when exposure occurred at later gestation. In another experiment, mice were exposed to 24 mg/kg benzo[a]pyrene for 3 consecutive days during early (gestational days 9-11) or late gestation (days 15-17) (Neubert and Tapken 1988). Maternal tissue levels were not much different from those observed following the administration of single doses. After multiple dose administration, elimination appeared to be faster in maternal tissues, but slower in embryonic tissues. Placental levels were always higher than those in embryonic tissue. Results suggest that benzo[a]pyrene does not cross the placental barrier readily and, therefore, that levels in embryonic tissues of mice never reach levels found in maternal tissues.

In general, orally absorbed benz[a]anthracene, chrysene, and pyrene were rapidly and widely distributed in the rat (Bartosek et al. 1984; Withey et al. 1991). Maximum concentrations of benz[a]anthracene and chrysene in perfused tissues, like the liver, blood, and brain, were achieved within 1-2 hours after administration of high doses (76 and 152 mg/kg) (Bartosek et al. 1984). Maximum levels in lesser perfused tissues, like adipose and mammary tissue, were reached in

3-4 hours. In male Wistar rats receiving a gavage dose of 2-15 mg/kg of [^{14}C]-pyrene, the fat had the highest tissue levels of radioactivity, followed by kidney, liver, and lungs (Withey et al. 1991).

Orally absorbed dibenz[a,h]anthracene in rats was also widely distributed to several tissues (Daniel et al. 1967). However, maximum tissue concentrations were not reached until 10 hours after administration. Highest tissue concentrations were in the liver and kidneys, followed by adrenal glands, ovaries, blood, and fat. Soon after administration, large quantities of dibenz[a,h]anthracene were found in the liver and kidneys. The elimination rate from these organs was rapid. At 3-4 days after administration, dibenz[a,h]anthracene was distributed only in the adrenal glands, ovaries, and fat.

The permeability of the placenta to dimethylbenz[a]anthracene, benzo[a]pyrene, and 3-methylcholanthrene (MC) was compared by Shendrikova and Aleksandrov (1974). Pregnant rats received the PAH orally in sunflower oil at a dose of 200 mg/kg on the 21st day of pregnancy. Within 30 minutes after administration of dimethylbenz[a]anthracene, trace amount of the compound could be detected in the fetus. Maximum levels (1.53-1.6 μg/g) were reached 2-3 hours after administration. Only trace amounts were detected in the fetus at 5 hours after administration. Concentration profiles in the liver and placenta were similar to those seen in the fetus. Benzo[a]pyrene was detected in the fetus at 2.77 μg/g. MC was only present in trace amounts. Concentration differences in the fetus among the various PAHs appeared to be highly dependent on the gastrointestinal absorption of the compound. The difference in fetal concentration of the PAHs did not reflect their ability to permeate the placenta.

2.3.2.3 Dermal Exposure

No studies were located regarding the distribution of PAHs in humans following dermal exposure. Evidence regarding the distribution of PAHs in animals following dermal exposure is limited. Although PAHs can readily penetrate the skin, there are few data on distribution to tissues. In one published study on this subject, only 1.3% of an applied dose of [^{14}C]-anthracene (9.3 μg/cm^2) was detected in tissues, primarily liver and kidneys, of rats 6 days after administration (Yang et al. 1986). Groups of 12 male Wistar rats were dosed with 2, 6, or 15 mg/kg of [^{14}C]-pyrene applied to 4 cm^2 of a shaved area of the mid back (Withey et al. 1993b). Three animals in each dose group were killed at

1, 2, 4, and 6 days postdosing, and the brain, lungs, heart, liver, spleen, kidneys, testes, muscle, and perirenal fat were removed and analyzed for pyrene and [^{14}C]-pyrene equivalents. Blood, urine, feces, as well as the skin from the application site were also analyzed. The rate of uptake from the skin was rapid (t1/2 = 0.5-0.8 d) relative to rate processes for the other organs, and about 50% of the applied dose was excreted over the 6 days of the study. Levels of pyrene were highest in the liver, kidneys, and fat. Levels of metabolites were also high in the lung.

2.3.3 Metabolism

The lipophilicity of PAHs enables them to readily penetrate cellular membranes and remain in the body indefinitely. However, the metabolism of PAHs renders them more water-soluble and more excretable. Metabolism of PAHs occurs in all tissues. The metabolic process involves several possible pathways with varying degrees of enzyme activities. The activities and affinities of the enzymes in a given tissue determine which metabolic route will prevail.

The metabolism of PAHs has been studied extensively *in vitro* and *in vivo.* The most commonly used system is the rat liver microsomal fraction, although other species are also used. Cells and cultured tissues from human and other animals have also significantly contributed to the elucidation of the PAH metabolic scheme.

The structural similarity of PAHs contributes to the similarities that exist in their biotransformation. Benzo[a]pyrene metabolism has been extensively reviewed and will be used as a model for PAH metabolism. In the many microsomal, cell, and cultured tissue preparations that have been examined, the metabolic profiles are qualitatively similar. However, there are differences in the relative levels and rates of formation of specific metabolites among tissues and cell preparations used from various animal species and strains. These differences are susceptible to change as a result of pretreatment of the animals with either inducers or inhibitors of particular enzymes. Furthermore, it is known that the metabolism of alternant PAHs (such as benzo[a]pyrene, benz[a]anthracene, chrysene, and dibenz[a,h]anthracene) differs from nonalternant PAHs (such as benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[j]fluoranthene, and indeno[1,2,3-c,d]pyrene) (see Section 2.2). Therefore, the metabolism of benzo[b]fluoranthene will also be discussed as a model for nonalternant PAH metabolism.

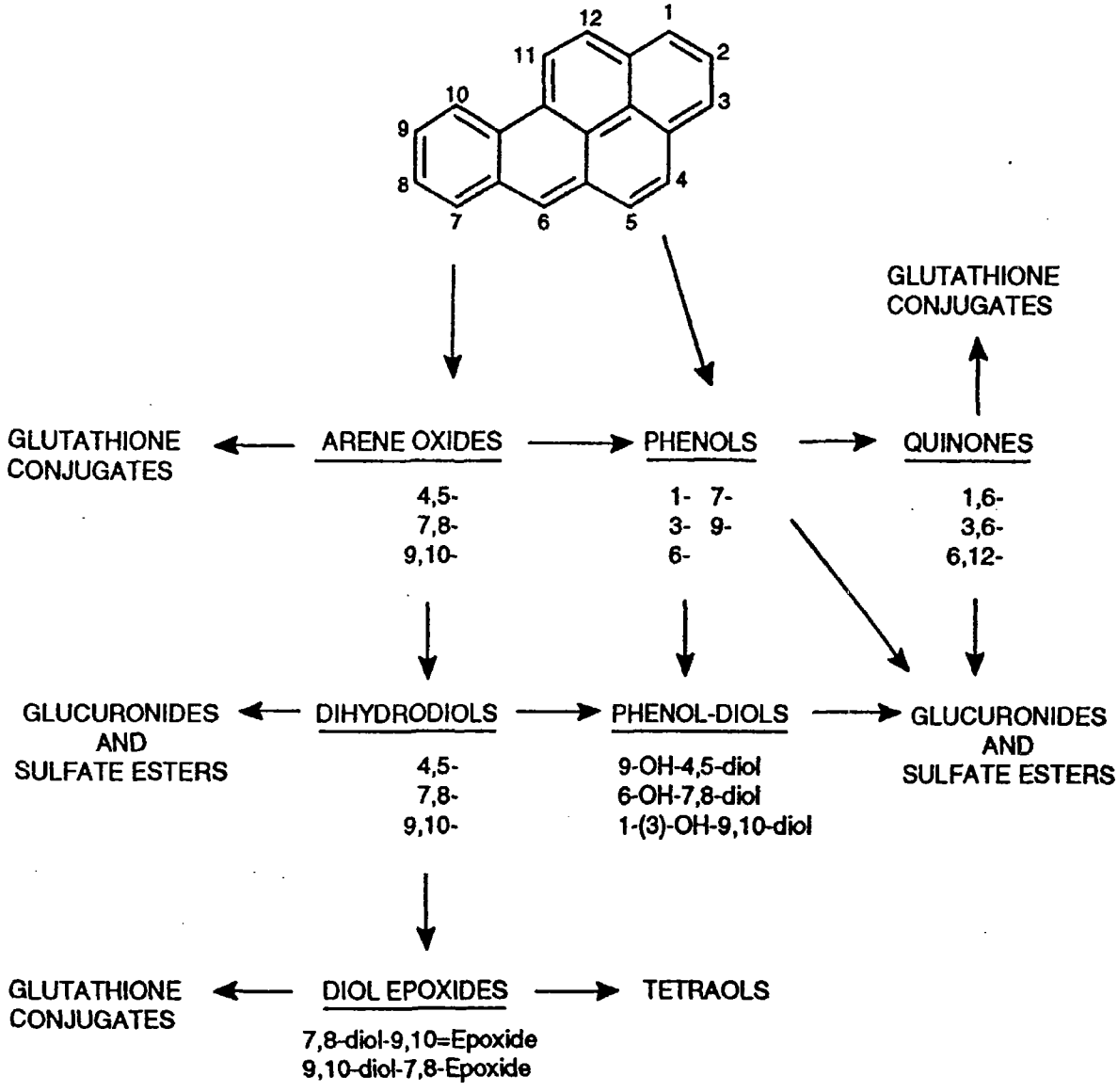
The metabolism of benzo[a]pyrene is summarized in Figure 2-3. Benzo[a]pyrene is metabolized initially by the microsomal cytochrome P-450 systems to several arene oxides. Once formed, these arene oxides may rearrange spontaneously to phenols, undergo hydration to the corresponding trans-dihydrodiols in a reaction catalyzed by microsomal epoxide hydrolase, or react covalently with glutathione, either spontaneously or in a reaction catalyzed by cytosolic glutathione-S-transferases (IARC 1983). Phenols may also be formed by the P-450 system by direct oxygen insertion, although unequivocal proof for this mechanism is lacking. 6-Hydroxybenzo[a]pyrene is further oxidized either spontaneously or metabolically to the 1,6-, 3,6-, or 6,12-quinones. This phenol is also a presumed intermediate in the oxidation of benzo[a]pyrene to the three quinones catalyzed by prostaglandin endoperoxide synthetase (Panthanickal and Marnett 1981). Evidence exists for the further oxidative metabolism to two additional phenols. 3-Hydroxybenzopyrene is metabolized to the 3,6-quinone and 9-hydroxy-benzo[a]pyrene is further oxidized to the K-region 4,5-oxide, which is hydrated to the corresponding 4,5-dihydrodiol (4,5,9-triol). The phenols, quinones, and dihydrodiols can all be conjugated to glucuronides and sulfate esters; the quinones also form glutathione conjugates (Agarwal et al. 1991; IARC 1983).

In addition to being conjugated, the dihydrodiols undergo further oxidative metabolism. The cytochrome P-450 system metabolizes benzo[a]pyrene-4,5-dihydrodiol to a number of uncharacterized metabolites, while the 9,10-dihydrodiol is metabolized predominantly to its l- and/or 3-phenol derivative with only minor quantities of a 9,10-diol-7,8-epoxide being formed. In contrast to the 9,10-diol, benzopyrene-7,8-diol is metabolized to a 7,8-dihydrodiol-9,10-epoxide, and phenol-diol formation is a relatively minor pathway. The diol epoxides can be conjugated with glutathione either spontaneously or by a glutathione-S-transferase catalyzed reaction. They may also hydrolyze spontaneously to tetrols (Hall and Grover 1988).

The route by which PAHs and other xenobiotics enter the body may determine their fate and organ specificity. For example, an inhaled compound may bypass the first-pass effect of the liver and reach peripheral tissues in concentrations higher than one would see after oral exposures. Enzyme activities among tissues are variable.

Benzo[a]pyrene was metabolized *in vitro* by human bronchial epithelial and lung tissue to the 9,10-dihydrodiol, 7,8-dihydrodiol, and small quantities of the 4,5-dihydrodiol and 3-hydroxybenzo[a]pyrene, all of which are extractable into ethyl acetate (Autrup et al. 1978; Cohen et

FIGURE 2-3. Proposed Metabolic Scheme for Benzo(a)pyrene.



al. 1976; Kiefer et al. 1988). These metabolites also conjugated with glutathione and sulfates, but none conjugated with glucuronide. The rate of formation of the dihydrodiols was greater in the bronchial epithelium than in the lung (Autrup et al. 1978; Cohen et al. 1976). This may render some areas of the respiratory tract more sensitive to the effects of carcinogens. One principal difference seen in human lung was the generation of a major ethyl acetate-soluble metabolite that was identified as the sulfate conjugate of 3-hydroxybenzo[a]pyrene, benzo[a]pyrene-3-yl-hydrogen sulfate. This sulfate is very lipid soluble and, thus, would not be readily excreted in the urine (Cohen et al. 1976). Activation of benzo[a]pyrene has also been detected in human fetal esophageal cell culture (Chakradeo et al. 1993).

Intratracheal instillation of benzo[a]pyrene to rats resulted in quinones constituting the highest concentration of metabolites in the lung and the liver within 5 minutes after instillation (Weyand and Bevan 1986, 1988). An *in vitro* study with rat lung demonstrated that the lung tissue has a high capacity to form quinones originating from oxidation at the six position of benzo[a]pyrene to form quinones and subsequently to water-soluble products. Ozone exposure resulted in an increase in the metabolism of benzo[a]pyrene metabolites with the greatest increase observed in the formation of metabolites generated by oxidation at the six position. The proposed retention of quinones following ozone exposure might lead to cytotoxicity associated with superoxide-anion generation by quinone-quinol redox-cycling. However, the high levels of benzo[a]pyrene used in this *in vitro* study may not relate to what occurs *in vivo*. Metabolism of benzo[a]pyrene at carbon six was higher at a lower dose than at the higher dose. Therefore, quinone production and detoxification may represent a major pathway of lung PAH detoxification *in vivo* (Basett et al. 1988).

Approximately 50% of the benzo[a]pyrene that was intratracheally instilled in hamsters was metabolized in the nose (Dahl et al. 1985). The metabolite produced in the hamster nose included tetrols, the 4,5-, 7,8-, and 9,10-dihydrodiol, quinones, and 3-and 9-hydroxybenzo[a]pyrene. Similar metabolites were detected in nasal and lung tissues of rats inhaling benzo[a]pyrene (Wolff et al. 1989b). The prevalence of quinone production was not seen in hamsters as it was in rats (Dahl et al. 1985; Weyand and Bevan 1987a, 1988). In monkeys and dogs, dihydrodiols, phenols, quinones, and tetrols were identified in the nasal mucus following nasal instillation of benzo[a]pyrene (Petridou-Fischer et al. 1988). *In vitro* metabolism of benzo[a]pyrene in the ethmoid turbinates of dogs resulted in a prevalence of phenols (Bond et al. 1988). However, small quantities of .quinones and dihydrodiols were also identified.

Rat lung microsomes facilitated the dissociation of small amounts of benzo[a]pyrene from diesel particles, but only a small fraction of the amount dissociated was metabolized (Leung et al. 1988). The ability to dissociate benzo[a]pyrene was related to the lipid content of the microsomal fraction. Microsomes are able to enhance the slow dissociation of a small amount of benzo[a]pyrene from diesel particles in a form that can be metabolized. Free benzo[a]pyrene was principally and extensively metabolized to the 9,10-dihydrodiol.

A human hepatoma cell line (HepG2) has high benzo[a]pyrene-metabolizing activity and converts benzo[a]pyrene to metabolites (Diamond et al. 1980). When [^{3}H]-benzo[a]pyrene was added to the incubate, a large fraction of the radioactivity was not extractable into chloroform. The extractable fraction contained 9,10-dihydrodiols, 7,8-dihydrodiols, quinones, 3-hydroxybenzo[a]pyrene, and the unchanged parent compound. The cell lysate also consisted of the same metabolites, but the proportions of 3-hydroxybenzo[a]pyrene and the parent compound were much higher than in the medium. Conversely, the proportion of water-soluble metabolites in the cell lysate was lower than in the medium. Treatment of the medium and cell lysate with β-glucuronidase converted only 5-7% of the water-soluble metabolites to chloroform-extractable material. Aryl sulfatase had no effect on radioactivity. These results suggested that this human liver tumor cell line does not extensively utilize the phenol detoxification pathway (Diamond et al. 1980).

Metabolism of benzo[a]pyrene in the primary culture of human hepatocytes primarily resulted in the formation of 3-hydroxybenzo[a]pyrene, 4,5-dihydrodiol, 9,10-dihydrodiol, and 7,8-dihydrodiol (Monteith et al. 1987). As the dose of benzo[a]pyrene increased, the amount of metabolites increased linearly. Binding to DNA was associated with the amount of unconjugated 7,8-dihydrodiol. DNA binding was linear up to a benzo[a]pyrene concentration of 100 μmol. At this concentration, binding increased 64-844 times over the extent of binding at 10 umol. As the concentration of benzo[a]pyrene increased, the ratio of dihydrodiol/phenolic metabolites also increased. Although the capacity to form dihydrodiols was not saturated at 100 umol benzo[a]pyrene, there was a change in the relative proportion of the dihydrodiol metabolites formed as the dose of benzo[a]pyrene increased. As benzo[a]pyrene concentration increased, the 9,10-dihydrodiol was the more prevalent metabolite, but levels of 7,8-dihydrodiol also increased (Monteith et al. 1987).

Epoxide hydrolase is a microsomal enzyme that converts alkene and arene oxides to dihydrodiols. Appreciable enzyme activity was observed in human livers. Comparison of epoxide hydrolase

activities with various substrates revealed that the human liver has a single epoxide hydrolase with broad substrate specificity (Kapitulnik et al. 1977). Epoxide hydrolase activity is also present in other tissues and increases the likelihood for carcinogenic effects in these organs. Ethyl acetate extracts of human and rat bladder cultures contained 9,10-dihydrodiol, 7,8-dihydrodiol, and 3-hydroxybenzo[a]pyrene. Covalent binding of [^{3}H]-benzo[a]pyrene with DNA occurring in both human and rat bladder cultures suggested that benzo[a]pyrene-7,8-diol-9, 10-epoxide is generated. The urothelium of the bladder clearly has the ability to generate the ultimate carcinogen (Moore et al. 1982).

Hepatic microsomes from rats induced with 3-methylcholanthrene convert benzo[a]pyrene to benzo[a]pyrene-7,8-diol-9,10-epoxide (BPDE) 10 times faster than untreated microsomes. The rate-limiting step in BPDE formation is the competition for P-450 between benzo[a]pyrene and the 7,8-dihydrodiol. Formation of BPDE is directly correlated with the 3-methylcholanthrene inducible form(s) of P-450 (Keller et al. 1987). Formation of the proximate carcinogen, 7,8-dihydrodiol, is stereoselective. Rabbit hepatic microsomes generated more of the 7R,8R enantiomer with an optical purity of >90% (Hall and Grover 1987). The major stereoisomer formed by rat liver microsomes is (+)-diol-epoxide-2 (R,S,S,R absolute conformation) (Jerina et al. 1976, 1980). This metabolite is highly tumorigenic (Levin et al. 1982) and gives rise to the major adduct formed upon reaction with DNA. The adduct is a diol epoxide-deoxyguanosine formed by alkylation at the exocyclic nitrogen (N-2) of deoxyguanosine. This diol epoxide-deoxyguanosine has been isolated from several animal species (Autrup and Seremet 1986; Horton et al. 1985) and human tissue preparations (Harris et al. 1979).

Studies using rat liver microsomes have shown that hydroxy metabolites of benzo[a]pyrene undergo glucuronidation (Mackenzie et al. 1993). Assays with three different DNA-expressed glucuronidases from human liver indicate preferential glucuronidation for the 2- and 5-hydroxy, 4- and 11-hydroxy, or l-, 2-, and 8-hydroxy derivatives of benzo[a]pyrene. There are differences in preferential activities for the glucuronidation of various benzo[a]pyrene metaboiites among the various DNA-expressed glucuronidases from human liver, with some glucuronidases being relatively or totally inactive toward this class of compounds (Jin et al. 1993). The results of this study suggest that the relative content of particular types of glucuronidases in a cell or tissue may be important for determining the extent to which a particular carcinogen is deactivated.

Several xenobiotics can induce enzymes to influence the rat liver microsomal metabolite profiles of various PAHs. For example, AHH, the cytochrome P-450 isoenzyme believed to be primarily responsible for the metabolism of benzo[a]pyrene and other PAHs, is subject to induction by PAHs. Treatment of pregnant and lactating rats with a single intraperitoneal dose of Aroclor 1245 increased the metabolism of benzo[a]pyrene by liver microsomes from pregnant and fetal rats 9-fold and 2-fold, respectively, and 2-fold in lactating rats (Borlakoglu et al. 1993). The pretreatment enhanced the formation of all metabolites, but the ratio of the 7,8-diol (the proximate carcinogen) was increased 3-fold in lactating rats and 5-fold in pregnant rats. Similar results were observed in rabbit lung microsomes (Ueng and Alvares 1993). Cigarette smoke exposure has been shown to increase PAH metabolism in human placental tissue (Sanyal et al. 1993), and in rat liver microsomes (Kawamoto et al. 1993). In studying benz[a]anthracene metabolism, some xenobiotics were found to be weak or moderate inducers, but even less efficient ones altered the benz[a]anthracene profile significantly. Thiophenes equally enhanced oxidation at the 5,6- and the 8,9-positions. Benzacridines favored K-region oxidation (5,6-oxidation) (Jacob et al. 1983b). Indeno[1,2,3-c,d]pyrene stimulated the bay region oxidation (3,4-oxidation) of benz[a]anthracene (Jacob et al. 1985). Similar xenobiotic effects were observed with chrysene as a substrate (Jacob et al. 1987). While some enzyme activities are being enhanced, alternate enzymatic pathways may be suppressed (Jacob et al. 1983a).

Rat liver microsomes also catalyzed benzo[a]pyrene metabolism in cumene hydroperoxide (CHP)-dependent reactions which ultimately produced 3-hydroxybenzo[a]pyrene and benzo[a]pyrene-quinones (Cavalieri et al. 1987). At low CHP concentrations, 3-hydroxybenzo[a]pyrene was the major metabolite. As CHP concentrations increased, levels of quinones increased and levels of 3-hydroxybenzo[a]pyrene decreased. This effect of varying CHP levels was reversed by preincubating with pyrene. Pyrene inhibited quinone production and increased 3-hydroxybenzo[a]pyrene production. Pretreatment with other PAHs like naphthalene, phenanthrene, and benz[a]anthracene nonspecifically inhibited the overall metabolism. The binding of benzo[a]pyrene to microsomal proteins correlated with quinone formation. This suggested that a reactive intermediate was a common precursor. The effects of pyrene on benzo[a]pyrene metabolism indicated that two distinct microsomal binding sites were responsible for the formation of 3-hydroxybenzo[a]pyrene and benzo[a]pyrene-quinone (Cavalieri et al. 1987).

Rat mammary epithelial cells (RMEC) have been shown to activate PAHs (Christou et al. 1987). Cytochrome-P-450 in RMEC is responsible for the monooxygenation of DMBA. Prior exposure'of

cultured cells to benz[a]anthracene induced DMBA metabolism. The metabolite profile following benz[a]anthracene-induction was significantly different from the profile obtained with purified P-450c, the predominant PAH-inducible enzyme in rat liver. The bay region 3,4-dihydrodiol, which was not formed with P-450c, was clearly detectable in RMEC. Low epoxide hydrolase activity in the benz[a]anthracene-induced RMEC limited the formation of all other DMBA dihydrodiols. The DMBA monooxygenase activity of benz[a]anfhracene-induced RMEC was inhibited by a-naphthaflavone. The study concluded that DMBA metabolism by RMEC depended on the induction of P-450c and at least one additional form of P-450 that is sensitive to α-naphthaflavone (Christou et al. 1987).

As expected from results of other studies, the perfused rat lung can release high quantities of benzo[a]pyrene metabolites and conjugates into the perfusate (Molliere et al. 1987). Addition of a liver to this perfusion system up gradient from the lungs reduces the concentration of parent compound and free metabolites to less than 20% of that seen in the liver's absence. The liver provides a protective effect on the lung to inhibit covalent binding of benzo[a]pyrene metabolites to pulmonary macromolecules.

The effects of various factors that can modify the hepatic clearance of PAHs, specifically benz[a]anthracene and chrysene, were studied by Fiume et al. (1983). The hepatic clearance and rate constants of these PAHs were significantly reduced in the perfused livers of fasted rats relative to those of fed rats. This reduction was attributed to a decrease in aryl hydrocarbon hydroxylase activity. Fasting also accelerated the depletion of cytochrome P-450 and other microsomal enzymes. In contrast, pretreatment of the rats with these PAHs resulted in increased clearance of both hydrocarbons from the perfusion medium when compared to control rats.

It was also noted by Fiume et al. (1983) that the livers of male rats demonstrated a significantly higher hepatic clearance of benz[a]anthracene than female rats, perhaps suggesting a sexual difference with aryl hydrocarbon hydroxylase activity. Similar findings regarding sexual differences in the metabolism of chrysene by rat livers were also reported by Jacob et al. (1985, 1987). Furthermore, Fiume et al. (1983) demonstrated that age can play a role in PAH metabolism. The hepatic clearance of PAHs in older rats (2 years) was significantly less than the hepatic clearance in younger rats (8 weeks). However, activation of benzo[a]pyrene to mutagenic derivatives, as measured by the *Salmonella typhimurium* test, with hepatic microsomes from male rats from 3 weeks to 18 months of age showed no age-dependent changes (Hilali et al. 1993).

A proposed metabolic scheme for the metabolism of the nonaltemant PAH, benzo[b]fluoranthene is presented in Figure 2-4. Nonalternant PAHs, in contrast to several alternant PAHs, do not appear to exert their genotoxic effect primarily through the metabolic formation of simple dihydrodiol epoxides. In the case of benzo[b]fluoranthene, there is evidence to suggest that metabolism to the dihydrodiol precursor to its bay-region dihydrodiol does occur. Rather than this metabolite being converted to its dihydrodiol epoxide; however, it appears to be extensively converted to its 5-hydroxy derivative. It is the further metabolism of this phenolic dihydrodiol to 5, 9, 10-trihydroxy- 11,12-epoxy-9,10,11,12-tetra-hydrobenzo[b]fluoranthene that has been linked to the genotoxic activity of benzo[b]fluoranthene in mouse skin (Weyand et al. 1993b). In the case of benzo[j]fluoranthene, two potentially genotoxic metabolites have been identified. These are the trans-4,5- and 9,10-dihydrodiols of benzo[j]fluoranthene. It is the conversion of trans-4,5-dihydro-4,5-dihydroxybenzo[j]fluoranthene to anti-4,5-dihydroxy-5,6a-epoxy-4,5,6,6a-tetrahydrobenzo[j]fluoranthene that is principally associated with DNA adduct formation in mouse skin (LaVoie et al. 1993b; Weyand et al. 1993a). Benzo[k]fluoranthene in rat microsomes was shown to result in the formation of 8,9-dihydrodiol. This dihydrodiol can form a dihydrodiol epoxide that is not within a bay region. This may represent an activation pathway of benzo[k]fluoranthene that may be associated, in part, with its genotoxic activity. In the case of nonalternant PAHs, reactive metabolites, that deviate from classical bay region dihydrodiol epoxides, have been linked to their tumorigenic activity.

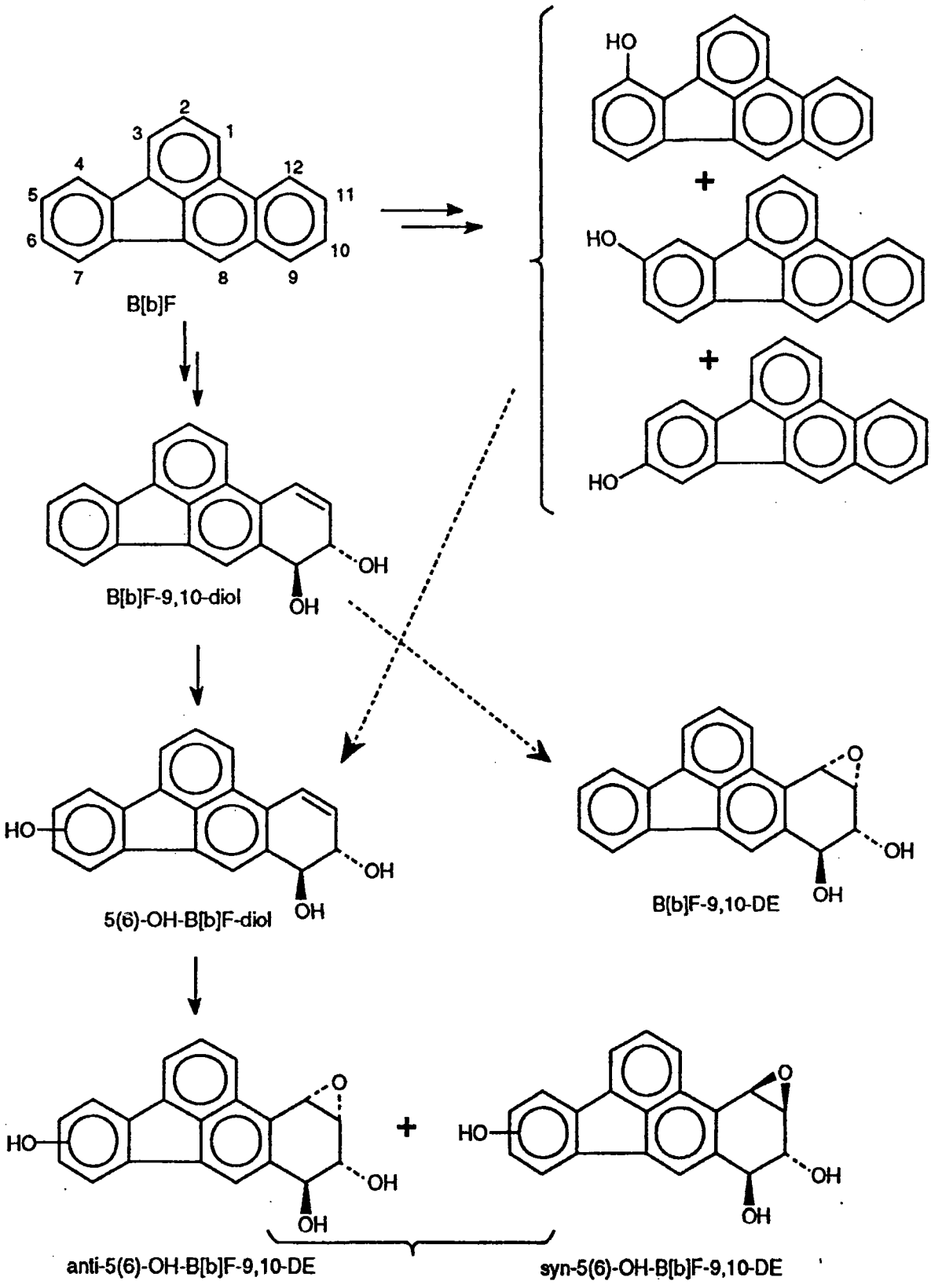
2.3.4 Excretion

2.3.4.1 Inhalation Exposure

Urinary metabolites of PAHs were detected in workers exposed to these compounds in an aluminum plant (Becher and Bjorseth 1983). The ambient levels of PAHs in the workplace (indicated by the authors to exceed 95 mg/m^3, although these data were not presented) did not correspond to the amount of PAHs deposited, metabolized, and excreted in the urine in this study. No quantitative inhalation data were available in humans regarding the excretion of PAHs.

Thirty-four workers in an electrode paste plant were monitored for response to exposure (Ovrebo et al. 1994). Exposure to benzo[a]pyrene was 0.9 $\mu g/m^3$; exposure to pyrene was 3.5 $\mu g/m^3$. 1-Hydroxypyrene was measured in the urine. Results from these workers were compared to two reference control groups, research and development workers and nickel refinery workers.

FIGURE 2-4. Proposed Metabolic Scheme for Benzo(b)fluoranthene.



Measurements of PAH levels were collected by personal sampling and at two stationary sites. PAH aerosols were collected on filters during the mixing of hot coal tar with carbon. The value of PAHs on the filters varied from 4.3 to 84.6 $\mu g/m^3$, with a mean of 14.4 $\mu g/m^3$. The PAH particulates were assayed for 8 of 11 PAHs classified as carcinogenic, including benz[a]anthracene, benz[g,h,i]perylene, benzo[a]pyrene, benzo[e]pyrene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[j]fluoranthene, chrysene, fluoranthene, and indeno[1,2,3-c,d]pyrene, and presented relative to the marker compound, pyrene. Content of these compounds ranged from 30 to 150% of the pyrene content on the filters, which was 1.6 $\mu g/m^3$. For example, the benzo[a]pyrene level was 0.8 $\mu g/m^3$. Urine analysis indicated a mean urinary value of 1-hydroxypyrene among electrode paste plant workers of 6.98 umol/mol creatinine, compared to 0.08 µmol/mol creatinine for the R&D workers, and 0.14 µmol/mol creatinine for the industrial worker group. Smokers had higher levels of 1-hydroxypyrene compared to non-smokers in all groups. The urinary 1-hydroxypyrene level in the electrode plant workers correlated inversely with age. No correlation was found between frequency of use of a protective mask and the urinary 1-hydroxypyrene concentration.

In an ongoing comprehensive evaluation of biological markers, workers in or near an iron foundry with varying exposures to PAHs were analyzed for response to exposure (Santella et al. 1993). Exposure to benzo[a]pyrene, determined by personal monitors, was 2-60 ng/m^3. 1-Hydroxypyrene was measured in the urine. Cigarette smoking, but not age or charbroiled food, influenced the level of 1-hydroxypyrene. When workers were classified into three categories (low, <.0005 mg/m^3; medium, 0.0005-0.0012 mg/m^3; high, >0.0012 mg/m^3), mean 1-hydroxypyrene levels were 2.7, 1.8, and 3.6 µmol/mol creatinine, respectively. There was a significant difference between the groups after controlling for smoking exposure, but there was no consistent trend. The authors indicate that this study evaluates biological markers of exposure at PAH levels that are very low, compared to other studies.

Workers employed in a graphite electrode producing plant (n=16) and a coke oven (n=33) were compared to a control population of maintenance workers in a blast furnace (n=54) (Van Hummelen et al. 1993). The concentration of PAHs in the environment was measured by personal air samplers, the concentration of hydroxypyrene in urine was measured, and smoking habits were evaluated. The mean age of the workers was 40, and did not differ significantly between the three plants. The proportion of smokers was not different among the three groups. The mean exposure for workers in the graphite electrode producing plant was 11.33 $\mu g/m^3$ (0.011 mg/m^3) and was correlated with a urinary

hydroxypyrene concentration of 3.18 μg/g creatinine prior to the shift and 6.25 μg/g creatinine after the shift. For the coke oven workers, airborne PAHs were measured at 23.7 $\mu g/m^3$ but this was not illustrative of true exposure, since there were a few very high exposures in the sample: 90.10 $\mu g/m^3$ for 7 workers compared to 5.57 $\mu g/m^3$ for 26 workers. In accordance with the predominantly low exposure, the urinary hydroxypyrene levels were 0.51 μg/g creatinine before the shift and 0.75 μg/g creatinine after the shift.

The excretion of benzo[a]pyrene following low-level inhalation exposure is rapid and high in rats (Bevan and Weyand 1988; Weyand and Bevan 1986; Wolff et al. 1989c); however, elimination is low in dogs and monkeys (Petridou-Fischer et al. 1988). After nose-only inhalation of 4.8 mg/m^3 [^{14}C]-benzo[a]pyrene for a single exposure or daily for 4 weeks, excretion of radioactivity in the feces of Fischer-344 rats was approximately 96% of the administered concentration (Wolff et al. 1989c). The excretion half-lives in feces and urine were 22 and 28 hours, respectively.

2.3.4.2 Oral Exposure

Five volunteers (21-41 years of age) ingested specially prepared diets high in PAHs, specifically benzo[a]pyrene (from grilled beef), for 2-3 days for an intake of approximately 0.007-0.02 mg/day (Buckley and Lioy 1992). A 100-250-fold increase in ingested benzo[a]pyrene in the high-PAH diet corresponded to a 6-12-fold increase in the elimination of 1-hydroxypyrene. However, benzo[a]pyrene and its other metabolites (not specified) were not measured in excreta, which prevented determination of the total excretion (and an estimate of oral absorption).

Male Sprague-Dawley rats received a low dose of [^{3}H]-benzo[a]pyrene (suspended in 10% ethanolsoybean oil) daily for 3, 5, or 7 days (Yamazaki and Kakiuchi 1989). Highest radioactivity was excreted 2-8 days after first exposure. Polar and phenol metabolites represented approximately 60% and 20% of the radioactivity detected in urine, respectively. The conjugated form accounted for 80% of these urinary metabolites. Only small amounts of unmetabolized benzo[a]pyrene were detected in the urine. Excretion into the feces was not studied.

Male Wistar rats eliminated a large amount of a single gavage dose of 0.22 mg/kg chrysene by 2 days postexposure (Grimmer et al. 1988). The unchanged parent compound represented 0.17% and 13.09% in the urine and feces, respectively. The recovery of the dose in excreta was 74% of dose after 4 days

of which about 61% was represented by hydroxychrysene compounds. The metabolite pattern was similar for urine and feces. The major metabolites identified were 1- and 3-hydroxychrysene, with about 100 times higher amounts in the feces (33.1% and 17.87%, respectively, of administered dose) than urine (0.79% and 0.35%, respectively). Approximately 79% of a large chrysene dose (1,217-2,717 mg/kg in the diet) was eliminated in the feces of rats; however, levels in the urine were not measured (Chang 1943). As the dose of chrysene in the diet increased, the percentage of excreted hydrocarbon also increased.

Male Wistar rats were given single oral doses of 2, 4, 6, 9, or 1.5 mg/kg of [^{14}C]-pyrene (Withey et al. 1991). Recovery of the dose in excreta was 82% for the two low-dose groups and 50-63% for the other groups 2 days postexposure. The urine and feces contained 34-45% and 21-50% of the dose, respectively, at 4 days postexposure. Recovery of radioactivity in the bile was approximately 10% of the dose after 6 hours.

2.3.4.3 Dermal Exposure

No studies were located regarding the excretion of PAHs in humans following dermal exposure to single PAHs. Excretion patterns of 1-hydroxypyrene in urine were studied in two psoriatic patients, each treated daily with coal tar pitch covering over 50% of their skin for 3 weeks (Hansen et al. 1993). The coal tar contained 1.43 mg/g pyrene. After 1 week of treatment, the urinary concentration of 1-hydroxypyrene increased approximately 100 times. However, the concentration after 3 weeks of treatment was decreased to that observed before treatment was initiated. The authors speculate that the healing of the psoriatic lesions may have rendered the skin less permeable to the PAHs after 3 weeks of treatment and healing.

The urinary excretion of 1-hydroxypyrene was evaluated in 65 automotive repair workers (automobile or diesel truck repair) whose skin was exposed to used mineral oils, and compared to values from non-professionally exposed control males on control diets (Granella and Clonfero 1993). Smoking exposure was equivalent in both groups. Pyrene concentrations were determined in the oily material taken from cloths used to clean various types of engines. Values of urinary 1-hydroxypyrene were determined on Friday at the end of the working week, and again on Monday morning prior to work. Smoking and PAH-rich diets were considered confounding factors. At both the beginning and the end of the working week, the values of urinary 1-hydroxypyrene were slightly higher in exposed subjects

(0.178 + 0.150 and 0.194 + 0.135 µmol creatinine on Monday and Friday, respectively) than in controls ((0.124 + 0.090 µmol/mol creatinine on Monday and Friday, respectively). The urinary 1-hydroxypyrene values were higher in both smoking and non-smoking subjects than controls. The highest values were found in urinary samples of smokers exposed to used mineral oils (0.259 + 0.090 µmol/mol creatinine). In non-smoking workers, post-shift 1-hydroxypyrene values were 0.154 + 0.105 µmol/mol creatinine, compared to 0.083 + 0.042 µmol/mol creatinine for the non-smoking controls. In automobile repair workers, there was no significant difference in the levels of 1-hydroxypyrene at the beginning and end of the work week. Tobacco smoking had more influence on the levels of 1-hydroxypyrene than did occupational exposure in this group. The influence of PAHs in the diet was only detectable when the subjects returned to work after the weekend. No explanation was given for this finding. This data suggests that exposure to PAHs through dermal contact with used engine oil is low.

The elimination of benzo[a]pyrene was rapid and high in mice and guinea pigs following low- and high-level dermal exposure (Ng et al. 1992; Sanders et al. 1986). The percentages of recovered radioactivity in urine and feces were 24.5%, 46.9%, and 25% for Swiss Webster mice dermally exposed to benzo[a]pyrene at 1.25, 12.5, and 125 µg/cm^2, respectively, for 7 days (Sanders et al. 1986). The feces in the high-dose animals had 35%, 58%, and 80% of the total recovered radioactivity after 24 hours, 48 hours, and 7 days, respectively. The amount of radioactivity excreted in urine was about 10% of amount excreted in feces. A elimination half-life of about 30 hours was estimated for benzo[a]pyrene. The data are limited because the exposed area of skin was not reportedly covered or collars were not employed to prevent ingestion of test compound by the animal. In guinea pigs, 73% of the dose was excreted 7 days after low-level (0.28 mg) exposure to benzo[a]pyrene (Ng et al. 1992).

The excretion of dermally absorbed phenanthrene and pyrene was rapid in guinea pigs (Ng et al. 1991, 1992). The presence of [^{14}C]-activity in the urine and feces of rats that received [^{14}C]-anthracene applied to the skin provides evidence of its absorption (Yang et al. 1986). Six days after administration of 9.3 µg/cm^2, the amounts detected in the urine and feces were 29.1% and 21.9% of the dose, respectively.

2.3.4.4 Other Routes of Exposure

No studies were located regarding excretion of PAHs in humans following other routes of exposure.

Three female Beagle dogs were given a bolus of aerosolized crystals of 7.7 mg/kg benzo[a]pyrene or 2.8 mg/kg phenanthrene in a single breath by intratracheal instillation (Gerde et al. 1993a). The blood borne clearance of the PAHs was monitored by repeatedly sampling blood through catheters in the ascending aorta and the right atrium of the dog. Half of the benzo[a]pyrene cleared within 2.4 minutes. Half of the phenanthrene cleared in 1.0 minute. Compared to clearance of phenanthrene, a less lipophilic PAH, the data indicate that the clearance of benzo[a]pyrene was limited by diffusion through the alveolar septa, while clearance of the moderately lipophilic phenanthrene was limited mostly by the rate of perfusion of the blood. The results indicate that inhaled PAHs of sufficient lipophilicity to limit diffusion through cells have a greater potential for toxicity to the lung than less lipophilic PAHs. Because of the thicker epithelia, bronchi should be at greater risk than the alveoli for PAH-induced toxicity exerted at the port of entry. Clearance of PAHs from the respiratory tract follows a biphasic pattern, with a rapid clearance of most of the PAH followed by a slow clearance of a small fraction. Previously published models predict that the rapid phase represents clearance through the thin epithelial barriers in the alveoli, the slow clearance is through the thicker epithelium of the airways, and the rate of clearance from either region will be slowed if the PAH has a high degree of lipophilicity. This study sought to validate model predictions for rates of alveolar clearance of PAHs of different lipophilicities. In a companion study, 3 female Beagle dogs were given doses of 0.00091 g/kg benzo[a]pyrene instilled on the surface of the conducting airways (Gerde et al. 1993b). Sequential lavage of the mucous-retained materials followed the instillations. Benzo[a]pyrene was retained within the mucous lining layer sufficiently to be transported with the mucocilliary escalator. Fractions of benzo[a]pyrene penetrating to the bronchial epithelium had a clearance half-time in the range of 1.4 hours. This long retention indicates a diffusion-limited uptake of benzo[a]pyrene by the airways. Physiological models have predicted that the lipophilicity of solutes such as PAHs will delay clearance from the respiratory tract. This clearance consists of a delayed penetration of the mucous lining layer, allowing mucocilliary clearance, followed by a slow penetration of PAHs through walls of the conducting airways.

Excretion of radioactivity in the urine of rats following intratracheal instillation only accounted for 2.2% of the administered benzo[a]pyrene at 6 hours (Bevan and Weyand 1988; Weyand and Bevan

1986). Amounts of radiolabel in the blood were also very small. However, levels could still be determined in order to derive toxicokinetic parameters. The data obtained by Weyand and Bevan (1986) fit best to a three-compartment model whereby the half-lives for the three phases were 4.3, 31.5, and 277 minutes.

Results obtained by Weyand and Bevan (1986, 1988) revealed that a large fraction of the administered dose was excreted in the bile of rats, therefore suggesting that fecal elimination is the major excretion route. After 6 hours, 53% of the 0.001 mg/kg dose was excreted into the intestine and intestinal contents of rats that were without a bile duct cannula, while cannulated rats excreted 74% in the bile over the same period (Weyand and Bevan 1986). These results indicate the occurrence of enterohepatic recirculation. Metabolites excreted in the bile included thioether conjugates (62.5%), glucuronide conjugates (22.8%), sulfate conjugates (7.4%), and free benzo[a]pyrene (9.8%) (Weyand and Bevan 1988). Radioactivity detected in the gastrointestinal tract of rats following pulmonary exposure to benzo[a]pyrene also suggests that biliary excretion occurs (Weyand and Bevan 1987a; Wolff et al. 1989c). The percentage of benzo[a]pyrene excretion into bile declined as intratracheal doses increased from 0.00016 to 0.35 mg in rats and guinea pigs (Weyand and Bevan 1987b). However, the biliary excretion of benzo[a]pyrene in hamsters remained the same after administration of either dose.

Female Wistar rats received low doses of chrysene (0.002 and 0.004 mg/kg) intratracheally (Grimmer et al. 1988). The major metabolite in the excreta was 1-hydroxychrysene. Hydroxychrysene compounds represented 31.26-48.9% of dose in the feces and about 3% in the urine. The unmetabolized parent compound was 17-19% of the administered dose in feces and only 1-2% in urine.

Less than 10% of instilled radioactivity was excreted in the urine and feces of dogs and monkeys 48 hours after intratracheal administration of [^{3}H]-benzo[a]pyrene into the nostril (Petridou-Fischer et al. 1988).

Nineteen outbred male rats were dosed intraperitoneally once with 200 mg/kg benzo[a]pyrene in sunflower oil (Likhachev et al. 1993). Concentrations of benzo[a]pyrene-7,8-diol, a marker metabolite of bioactivation of benzo[a]pyrene, and 3-hydroxy-benzo[a]pyrene, a marker metabolite of deactivation, were measured daily in the urine and feces for 15 days. Levels of these metabolites were

correlated with tumor latency. Another group of- 10 rats was dosed intraperitoneally once with 15 mg/kg benzo[a]pyrene in sunflower oil and urine was collected for 3 days. Five rats were killed on day 3 and the other 5 were killed on day 8. Liver DNA concentrations of benzo[a]pyrene-7,8,9,10-tetrols were determined in animals killed on day 8. Considerable individual variation was observed in the levels of daily and total excretion of benzo[a]pyrene-7,8-diol and 3-hydroxy-benzo[a]pyrene in rats receiving 200 mg/kg benzo[a]pyrene. Both metabolites were excreted primarily in the feces. More than half of the total metabolites excreted were detected during the first five days, and peak concentrations were observed on the second day after benzo[a]pyrene administration. Peritoneal malignant fibrous histiocytomas developed in 10 of the 16 survivors at 15 days. Levels of urinary benzo[a]pyrene-7,8-diol correlated positively with tumor latency. In the animals exposed to 15 mg/kg benzo[a]pyrene, a high correlation was found between excretion of benzo[a]pyrene-7,8-diol and benzo[a]pyrene-DNA adducts in the liver.

[^{14}C]-Benzo[a]pyrene was administered to male germfree rats (Yang et al. 1994). Urine was collected 24 hours before and every 24 hours for 7 days after administration. Urinary metabolites, consisting of 9% of the administered radioactivity, were fractionated by lipophilic ion exchange chromatography, and characterized by reversed-phase HPLC, ultraviolet spectrometry, and gas chromatography/mass spectrometry. About 90% of the administered dose was excreted within 7 days; 80% in the feces and 9% in the urine. About 90% of the radioactivity in the urine was recovered in the methanol eluate. In this eluate, more than 80% of the urinary metabolites were conjugated, while neutral metabolites constituted 13-18%. The neutral metabolites consisted of 7,8,9,10-tetrols (trace), trans-11,12-dihydrodiol (major), trans-7,8-dihydrodiol (trace), three isomer trihydroxy-benzo[a]pyrenes (major), carboxylic methyl ester derivatives of benzo[a]pyrene quinones, and trioxo-benzo[a]pyrenes (major). Most of the urinary radioactivity was excreted within 72 hours of dosing, with a peak excretion of 24-48 hours. A similar time course was observed for excretion in feces (data not shown).

Six hours after intravenous administration of 0.08 mg/kg [^{14}C]-benzo[a]pyrene to rabbits, 30% and 12% of the dose was excreted in the bile and urine, respectively (Chipman et al. 1982). Excretion of activity into the bile was biphasic over a period of 30 hours with apparent half-lives of 0.27 and 4.623 hours for the rapid and slow phases, respectively. Treatment of the bile and urine with β-glucuronidase and aryl sulfatase increased the amount of activity in the bile and urine that was extractable into ethyl acetate indicating the presence of glucuronide and sulfate conjugates.

Intraduodenal administration of the bile resulted in 21% and 14% of the intraduodenal dose being excreted into the bile and urine, respectively. Since biliary metabolites undergo enterohepatic recirculation, the half-life for ^{14}C-activity is expected to be longer in animals without biliary fistulae (Chipman et al. 1982).

The overall elimination of [^{3}H]-benzo[a]pyrene following intravenous administration (0.001 mg/kg) best fits a triexponential model, as after inhalation exposure (Weyand and Bevan 1986). The half-lives for the three phases were 1.5, 22.4, and 178 minutes. These parameters were very similar to those derived from intratracheal instillation.

2.3.5 Mechanisms of Action

PAHs are absorbed through the lungs by transport across the mucus layer lining the bronchi (Bevan and Ulman 1991). In general, PAHs are lipophilic compounds that can cross the lungs through passive diffusion and partitioning into lipids and water of cells (Gerde et al. 1991, 1993a, 1993b). The rapid, blood-bound redistribution of hydrocarbons at low blood concentrations from lungs to other organs indicates that diffusion is the rate-determining step (Gerde et al. 1991). The absorption rates vary among the PAHs, probably depending on the octanol/water partition coefficient. Essentially all of gastrically instilled benzo[a]pyrene is absorbed via uptake of fat-soluble compounds (Busbee et al. 1990). Oral absorption of benzo[a]pyrene is enhanced by some oils (such as corn oil) in the gastrointestinal tract (Kawamura et al. 1988). The mechanism of dermal absorption of PAHs is most likely passive diffusion through the stratum comeum (Yang et al. 1986).

PAHs and their metabolites are distributed to tissues by transport through the blood. Therefore, PAHs reach more-perfused tissues rapidly following exposure and are eliminated more slowly from less-perfused tissues (Bartosek et al. 1984). A large fraction of orally absorbed benzo[a]pyrene is believedto be transported by lipoproteins from the gastrointestinal tract to the blood via the thoracic duct lymph flow (Busbee et al. 1990).

The carcinogenic mechanism of action of altemant PAHs is fairly well elucidated, but it is not as well described for nonaltemant PAHs. Furthermore, it is not known exactly how PAHs affect rapidly proliferating tissues. PAHs express their carcinogenic activity through biotransformation to chemically reactive intermediates that then covalently bind to cellular macromolecules (i.e., DNA) leading to

mutation and tumor initiation. The products of PAH metabolism include epoxide intermediates, dihydrodiols, phenols, quinones, and their various combinations. The bay region (e.g., the sterically hindered, cup-shaped area between carbons 10 and 11 of benzo[a]pyrene or 1 and 12 of benz[a]anthracene) diol epoxide intermediates of PAHs are considered to be the ultimate carcinogen for alternant PAHs (Jerina et al. 1980). These diol epoxides are easily converted into carbonium ions (carbocations) which are alkylating agents and thus mutagens and initiators of carcinogenesis. Therefore, the carcinogenic and toxic potential of PAHs relies on their metabolites. However, several of the tumorigenic PAHs (i.e., the nonaltemant PAHs) discussed in this profile do not have a bay region, or have been shown not to be similarly activated via a simple bay region epoxide (e.g., Amin et al. 1985a, 1985b). This observation has important implications regarding the expression of carcinogenicity for the nonalternant PAHs. If these chemicals are activated to carcinogens via a mechanism that differs from alternant PAHs, then they may also differ with respect to tumor site and species specificity.

A prerequisite for conversion of PAHs into these active bay region diol epoxides is the presence of cytochrome P-450 and associated enzymes.responsible for this conversion. These enzymes can be found primarily in the liver, but they are also present in the lung, intestinal mucosa, and other tissues. Thus, factors such as distribution to the target tissue(s), solubility, and intracellular localization proximate to these enzymes figure prominently in the expression of a PAH's carcinogenicity. In fact, in order to assess whether there was any correlation between carcinogenic potency and the ability to induce P-450 isoenzymes, several indices of P-450 isoenzyme activity (*O*-demethylation of ethoxyresorufin, metabolic activation of 2-amino-6-methyldipyrido [1,2-α:3',2'd]imadazol [Glu-P-I] to mutagens, and immunological detection of polyclonal antibodies against purified rat P-450 I) were measured in microsomal preparations incubated with benzo[a]pyrene and benzo[e]pyrene (Ayrton et al. 1990). While both PAHs increased several parameters of P-450-I activity, benzo[a]pyrene was markedly more potent than benzo[e]pyrene. Based on these results, the authors concluded that the carcinogenic potency of the PAHs tested could be predicted by the degree to which they induced these enzymes.

Changes in the cytochrome P-450 system can affect the carcinogenicity of the PAHs. This system is susceptible to induction by the PAHs themselves as well as other chemicals commonly found in the environment. The degree and specificity (i.e., which enzymes are affected) of induction depend on the tissue and species and strain. The induction of one enzyme particularly important to the metabolism

of PAHs, AHH, is also known to be under genetic control (see discussions in Section 2.2.2 on responsive versus nonresponsive mouse strains). Given the heterogeneity of human genotypes, it is likely that certain human subpopulations exist that are more susceptible to AHH induction and thus more susceptible to the induction of cancer (see Section 2.7).

Once the reactive bay region epoxide is formed, it may covalently bind to DNA and other cellular macromolecules and presumably initiate mutagenesis and carcinogenesis. Indeed, the level of DNA-adduct formation has been found to correlate with tumor induction activity for a number of PAHs in newborn rat liver and lung (Weyand and LaVoie 1988) and in mouse skin (Albert et al. 1991b; Alexandrov and Rojas-Moreno 1990). Furthermore, no benzo[a]pyrene-DNA-adducts were found in rat skin, which is known to be resistant to PAH-induced skin tumor formation (Alexandrov and Rojas-Moreno 1990). The types of adducts formed in various tissues may dictate target organ susceptibility to PAH-induced carcinogenicity. Various metabolites of benzo[a]pyrene were administered to rats intraperitoneally and DNA adducts from lung, liver, and lymphocytes were measured (Ross et al. 1991). The only metabolites that led to DNA binding were 2-, 9-, and 12-hydroxybenzo[a]pyrene and the truns-7,8-dihydrodiol of benzo[a]pyrene. The authors suggested that different DNA adducts resulting from the *in vivo* metabolism of benzo[a]pyrene in different tissues may be related to tissue specificity of benzo[a]pyrene-induced carcinogenicity.

Although the bulk of this work on PAH-induced carcinogenicity has been done in animal models and animal *in vitro* systems, work in human *in vitro* systems indicates that these same mechanisms of activation may be involved in humans. For example, induction of AHH and formation of the reactive intermediate, benzo[a]pyrene 7,8-dihydrodiol, has been observed in the epithelial tissue from human hair follicles (Merk et al. 1987). All the steps necessary for cellular transformation and cancer induction were demonstrated in cultured human skin fibroblasts: inducible AHH activity, altered cellular proliferation kinetics, and DNA damage (Milo et al. 1978). Thus, humans are likely to be susceptible to tumor induction by PAHs by these mechanisms.

Carcinogenic PAHs have been suggested to have an effect on immune function (Luster and Rosenthal 1993; Saboori and Newcombe 1992), thereby allowing the induction of carcinogenesis, while noncarcinogenic PAHs do not affect immune function (see Section 2.4). The effects of dermally applied benzo[a]pyrene alone or following dermal pretreatment with the prostaglandin synthetase inhibitor, indomethacin, on contact hypersensitivity (cell-mediated immunity), production of antibodies

to DNP (humoral immunity), and the induction of skin tumors was studied in male BALBc mice treated for 6 weeks to 6 months (Andrews et al. 1991b). A group of mice treated with acetone served as controls. Skin tumors were observed in the mice treated with benzo[a]pyrene beginning at week 18 of treatment. Pretreatment with indomethacin significantly increased (by 21%) the latency of tumor induction by benzo[a]pyrene and significantly reduced (by 46%) the weight of benzo[a]pyrene-induced skin tumors. Based on these findings, the authors suggested that benzo[a]pyrene-induced skin carcinogenesis may be mediated by a mechanism that involves prostaglandin suppression of cellular immunity. Undoubtedly, several other factors yet to be determined are involved in the ultimate expression of PAH-induced toxicity and carcinogenicity.

2.4 RELEVANCE TO PUBLIC HEALTH

PAHs occur ubiquitously in the environment from both synthetic and natural sources. PAHs occur in the atmosphere most commonly in the products of incomplete combustion. These products include fossil fuels; cigarette smoke; industrial processes (such as coke production and refinement of crude oil); and exhaust emissions from gasoline engines, oil-fired heating, and burnt coals. PAHs are present in groundwater, surface water, drinking water, waste water, and sludge. They are found in foods, particularly charbroiled, broiled, or pickled food items, and refined fats and oils. Individuals living in the vicinity of hazardous waste sites where PAHs have been detected at levels above background may experience exposure to these chemicals via inhalation of contaminated air or ingestion of contaminated food, soil, or water.

Evidence exists to indicate that certain PAHs are carcinogenic in humans and animals. The evidence in humans comes primarily from occupational studies of workers who were exposed to mixtures containing PAHs as a result of their involvement in such processes as coke production, roofing, oil refining, or coal gasification (e.g., coal tar, coke oven emissions, soot, shale, and crude oil). Cancer associated with exposure to PAH-containing mixtures in humans occurs predominantly in the lungs and skin following inhalation and dermal exposure, respectively. Some ingestion of PAHs is probably due to swallowing of particulates containing PAHs subsequent to mucocilliary clearance from the lung. Certain PAHs have also been shown to induce cancer in animals. The site of tumor induction is influenced by route of administration: stomach tumors are observed following ingestion, lung tumors following inhalation, and skin tumors following dermal exposure, although tumors can form at other locations (e.g., lung tumors after dermal exposure).

Noncancer adverse health effects associated with PAH exposure have been observed in animals but generally not in humans (with the exception of adverse hematological and dermal effects). Animal studies demonstrate that PAHs tend to affect proliferating tissues such as bone marrow, lymphoid organs, gonads, and intestinal epithelium.

Minimal Risk Levels (MRLs) for Polycyclic Aromatic Hydrocarbons

Inhalation MRLS

No inhalation MRLs have been derived for PAHs because no adequate dose-response data that identify threshold levels for noncancer health effects are available in humans or animals for any duration of exposure.

Oral MRL.s

No acute, or chronic oral MRLs were derived for PAHs because there are no adequate human or animal dose-response data available that identify threshold levels for appropriate noncancer health effects. Serious reproductive and developmental effects in animals associated with acute oral exposure to PAHs have been reported. These are not appropriate end points for the derivation of an MRL. Noncancer effects noted in longer term oral toxicity studies in animals include increased liver weight (generally not considered to be adverse) and aplastic anemia (a serious effect), neither of which is an appropriate end point for the derivation of an MRL. Intermediate-duration oral MRLs were derived for acenaphthene, anthracene, fluoranthene, and fluorene.

Acenaphthene

- An MRL of 0.6 mg/kg/day has been derived for intermediate-duration oral exposure (15-364 days) to acenaphthene.

The MRL was based on a minimal LOAEL of 175 mg/kg/day for liver weight (EPA 1989c). Four groups of CD-l mice (20/sex/group) were gavaged daily with 0, 175, 350, or 700 mg/kg/day acenaphthene for 90 days. The toxicological evaluations of this study included body weight changes, food consumption, mortality, clinical pathological evaluations (including hematology and clinical

chemistry), organ weights and histopathological evaluations of target organs. The results of this study indicated no treatment-related effects on survival, clinical signs, body weight changes, total food intake, and ophthalmological alterations. Liver weight changes accompanied by microscopic alterations (cellular hypertrophy) were noted in both the mid- and high-dose groups, and seemed to be dose-dependent. Additionally, high-dose males and mid- and high-dose females showed significant increases in cholesterol levels. Increased relative liver weights in males, and increased absolute and relative liver weight in females, without accompanying microscopic alterations or increased cholesterol levels were also observed at the low dose; in light of the effects seen at higher doses, this change was considered to be a minimum LOAEL. There was no NOAEL. The MRL was obtained by dividing the LOAEL value by 300 (3 for a minimum LOAEL, 10 for extrapolation from animals to humans, and 10 for human variability) and rounding to one significant figure.

MRLs for acute-duration and chronic-duration have not been derived because suitable NOAEL and LOAEL values have not been identified in the available literature.

Fluoranthene.

- An MRL of 0.4 mg/kg/day has been derived for intermediate-duration oral exposure (15-364 days) to fluoranthene.

The MRL was based on a minimal LOAEL of 125 mg/kg/day for increased relative liver weight in male mice (EPA 1988e). Four groups of CD-1 mice (20/sex/group) were gavaged daily with 0, 125, 250, or 500 mg/kg/day fluoranthene for 90 days. The toxicological evaluations of this study included body weight changes, food consumption, mortality, clinical pathological evaluations (including hematology and clinical chemistry), organ weights, and histopathological evaluations of target organs. The results of this study indicated no treatment-related effects on survival, clinical signs, body weight changes, total food intake, or ophthalmological alterations. All treated mice exhibited nephropathy, increased salivation, and increased liver enzyme levels in a dose-dependent manner. However, these effects were either not significant, not dose-related, or not considered adverse at 125 mg/kg/day. Mice exposed to 500 mg/kg/day had increased food consumption throughout the study. Mice exposed to 250 mg/kg/day had statistically increased SGPT values and increased liver weight. Compound-related microscopic liver lesions (indicated by pigmentation) were observed in 65 and 87% of the mid- and high-dose mice, respectively. Male mice exposed to 125 mg/kg/day had increased relative liver

weight. The LOAEL is 125 mg/kg/day, based on-relative liver weight in males. There was no NOAEL. The MRL was obtained by dividing the LOAEL value by 300 (3 for a minimal LOAEL, 10 for extrapolation from animals to humans, and 10 for human variability) and rounding to one significant figure.

Fluorene.

- An MRL of 0.4 mg/kg/day has been derived for intermediate-duration oral exposure (15-364 days) to fluorene.

The MRL was based on a minimal LOAEL of 125 mg/kg/day for relative liver weight (EPA 1989e). Four groups of CD-1 mice (20/sex/group) were gavaged daily with 0, 125, 250, or 500 mg/kg/day fluorene for 90 days. The toxicological evaluations of this study included body weight changes, food consumption, mortality, clinical pathological evaluations (including hematology and clinical chemistry), organ weights and histopathological evaluations of target organs. The results of this study indicated no treatment-related effects on survival, body weight changes, total food intake, or ophthalmological alterations. All treated male mice exhibited increased salivation, hypoactivity, and urine-wet abdomens. A significant decrease in red blood cell count and packed cell volume was observed in females treated with 250 mg/kg/day and in males and females at 500 me/kg/day. Decreased hemoglobin concentration was also observed in the high-dose group. A dose-related increase in relative liver weight was observed in all treated mice, and in absolute liver weight at >250 mg/kg/day. A significant increase in absolute and relative spleen and kidney weight was observed at 250 mg/kg/day.. Increases in absolute and relative liver and spleen weights at the high dose were accompanied by histopathological increases in hemosiderin in the spleen and in the Kupffer cells of the liver. The LOAEL is 125 mg/kg/day based on increased relative liver weight. There was no NOAEL. The MRL was obtained by dividing the LOAEL value by 300 (3 for a minimal LOAEL, 10 for extrapolation from animals to humans, and 10 for human variability) and rounding to one significant figure.

Anthracene.

- An MRL of 10 mg/kg/day has been derived for intermediate-duration oral exposure (15-364 days) to anthracene.

The MRL was based on a NOAEL of 1,000 mg/kg/day for liver effects (EPA 1989d). The objective of this study was to evaluate the toxicity of anthracene in a subchronic toxicity study. Four groups of male and female CD-1 mice (20/sex/group) were placed on study, and were dosed with 0, 250, 500, and 1,000 mg/kg/day fluorene in corn oil by gavage for 13 weeks. The mice were observed twice daily for clinical signs. Body weights and food consumption were reported weekly. Hematologic and serum chemistry evaluations were completed at final sacrifice. At final sacrifice, gross post-mortem examinations were completed, organ weights were taken, and histological examinations were subsequently done on the tissues collected from all organ systems. No treatment-related finding were noted in survival, clinical signs, mean body weights, food consumption, and ophthalmological examinations, hematology, clinical chemistry, organ weights , gross pathology, and histopathology. In summary, anthracene produced no discemable effects. This study was conducted under the same laboratory conditions as the 90-day study of acenaphthene (EPA 1989c), and under similar laboratory conditions as the 90-day studies of fluoranthene (EPA 1988e) and fluorene (EPA 1989e), from which intermediate-duration MRLs were derived, based on liver effects. In these studies (EPA 1988e, 1989c, 1989e), many other treatment-related and dose-related effects were observed, including renal, hematological, and splenic, that lent support to the derivation of the MRL for each compound. Thus, although no toxic effects were noted even at the highest dose tested in the study cited for anthracene (EPA 1989d), this free-standing NOAEL has considerable credibility, based on the assumption that toxic effects would have been observed if present, as was seen for the other compounds using the same study design. The NOAEL is 1,000 mg/kg/day based on the absence of liver effects, and any other effects in the organ systems studied. The NOAEL was the highest dose used in the study. The MRL was obtained by dividing the NOAEL value by 100 (10 for extrapolation from animals to humans, and 10 for human variability).

Dermal MRLs

No acute-, intermediate-, or chronic-duration MRLs were derived for the 17 PAHs because of the lack of appropriate methodology for the development of dermal MRLs.

Death. There have been no reports of death in humans following exposure to any of the PAHs. However, benzo[a]pyrene is fatal to mice following ingestion, and aeath in animals has been reported following parenteral exposure to a number of PAHs. The intraperitoneal LD_{50} values in mice for pyrene, anthracene, and benzo[a]pyrene are 514, >430, and 232 mg/kg, respectively (Salamone 1981).

Reduced survival time in "Ah-responsive" mice (those capable of producing increased levels of cytochrome P-450 enzymes) was observed following a single intraperitoneal dose of 500 mg/kg benzo[a]pyrene (Robinson et al. 1975). In contrast, oral exposure to 120 mg/kg/day benzo[a]pyrene results in reduced survival of "Ah-nonresponsive" mice (those whose P-450 enzymes are not induced by PAHs).

While the results in animal studies indicate that exposure to high doses of PAHs is lethal, the majority of the data are from parenteral exposure. This route is not applicable to exposure routes humans may expect to encounter, so the relevance of these findings to public health is not known. Parenteral administration bypasses the first-pass effect in the liver that occurs following oral exposure (PAHs may be expected to be ultimately biotransformed to inactive metabolites more quickly in the liver than in other tissues). However, because death has been observed in animals following oral exposure as well, it can be assumed that acute exposure to high enough doses of the PAHs can be lethal.

Systemic Effects.

Respiratory Effects. Adverse noncancer respiratory effects, including bloody vomit, breathing problems, chest pains, chest and throat irritation, and abnormalities in chest X-rays have been reported in humans exposed to PAHs and respirable particles in a rubber factory (Gupta et al. 1993). Inhalation is a significant route of exposure to PAHs in humans. *In vitro* studies using human lung tumor cells demonstrate that the benzo[a]pyrene-induced cytotoxicity (as measured by protein incorporation or cloning efficiency) observed was most likely due to formation of such reactive products as the 7,8-diol 9,10-epoxide metabolite of benzo[a]pyrene (Kiefer et al. 1988). Thus, human lung cells are capable of metabolizing PAHs to reactive intermediates. This implies that inhalation exposure to PAHs could result in toxicity in the respiratory tract.

Adverse effects on the respiratory tissue of laboratory animals have also been observed. The effects of benzo[e]pyrene, pyrene, anthracene, benz[a]anthracene, and benzo[a]pyrene on respiratory mucosa were studied in tracheal explants in rats (Topping et al. 1978). The PAHs were incorporated into beeswax pellets that were placed into tracheal grafts that had been transplanted subcutaneously into the subscapular region of isogenic host rats and the pellets remained in place for 4 weeks. Approximately 50-60% of the test substance was delivered to the tracheal tissue by the end of 4 weeks, in most instances. Benzo[e]pyrene induced only mild changes that included slight hyperplasia of the tracheal

epithelium. A more long-lasting epithelial hyperplasia was observed with pyrene, anthracene, and benz[a]anthracene, and tracheas implanted with pyrene also exhibited a more severe mucocilliary hyperplasia. In addition, undifferentiated epithelium and small areas of squamous metaplasia were also seen with these PAHs, effects that persisted at least 8 weeks after exposure. Severe and long-lasting hyperplasia and transitional hyperplasia as well as metaplasia were seen in tracheas exposed to benzo[a]pyrene, and after 8 weeks, 75% of the epithelium was still abnormal. Acute inflammation (edema and/or granulocyte infiltration), subacute inflammation (mononuclear infiltration and an increase in fibroblasts), and fibrosis and hyalinization in the second half of the experiment were seen with all PAHs. The authors concluded that all of the PAHs tested induced pathological changes in the respiratory mucosa of the transplanted tracheas. The effects were different for the noncarcinogenic PAHs (benzo[e]pyrene, pyrene, anthracene, benz[a]anthracene), as compared to the carcinogenic PAH (benzo[a]pyrene); the former induced changes that were short-lived while the latter produced more severe, long-lasting (metaplastic) changes.

Cultured fetal hamster tracheal explants were exposed to two concentrations each of benz[a]anthracene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[e]pyrene, and pyrene *in vitro* for 4 days, and the effects of these PAHs on the respiratory epithelium were evaluated by scanning electron microscopy (Richter-Reichhelm and Althoff 1986). Exposure to benzo[e]pyrene and pyrene, as well as the lower concentrations of benz[a]anthracene and benzo[b]fluoranthene, resulted in effects similar to those seen in the DMSO controls: up to a 10% incidence of focally slight inhibition of epithelial differentiation and/or metaplasia. When the concentrations of all of the PAHs except benzo[e]pyrene and pyrene were doubled, the frequency of these lesions increased to 50-100%, and the incidence of dysplasia (including hyperplasia) 1 was also observed to occur in a dose-related manner in explants exposed to benz[a]anthracene, benzo[b]fluoranthene, and benzo[k]fluoranthene. These lesions were not seen in the cultures exposed to benzo[e]pyrene, pyrene, or DMSO. The authors note that these effects on respiratory epithelium seen *in vitro* are similar to the preneoplastic changes seen *in vivo* following exposure to PAHs, and thus, this system may serve as a good screen for assessing risk to the respiratory tract.

These observations, coupled with the fact that the respiratory system appears to be a target for PAH-induced cancer in humans, suggest that the respiratory system may be a target organ for PAH-induced noncancer adverse effects in humans as well.

Cardiovascular Effects. PAHs are contained in cigarette smoke, and smoking is a well-established risk factor in the development of atherosclerosis. Arterial smooth muscle cell proliferation, collagen synthesis, lipid accumulation, and cellular necrosis are all involved in the pathogenesis of the atherosclerotic plaque. *In vitro* studies conducted using bovine, rabbit, and human smooth muscle cells from arteries demonstrated that benzopyrene affects some of the aforementioned processes. Cell proliferation was not affected by benzo[a]pyrene, but a decrease in collagen secretion and an increase in cellular toxicity were noted in both the animal and human cell cultures (Stavenow and Pessah-Rasmussen 1988).

Male White Leghorn chickens (six/group) were given weekly intramuscular injections of benzo[a]pyrene, benzo[e]pyrene, anthracene, and dibenz[a,h]anthracene for 16 weeks prior to removal of the abdominal aorta to investigate the effects of benzo[a]pyrene on the development of arteriosclerotic plaques (Penn and Snyder 1988). Animals injected with DMSO (the vehicle) served as controls. Microscopic plaques were found in the aortas of all treated and control animals. However, the plaque volume index (PVI), which is a measure of both plaque cross-sectional area and plaque length, was nine times larger in the benzo[a]pyrene animals than the controls. Benzo[e]pyrene and dibenz[a,h]anthracene also caused an increase in plaque volume as compared to controls. However, the plaque sizes in the animals treated with anthracene were no different than controls. Therefore, the authors concluded that benzo[a]pyrene, benzo[e]pyrene, and dibenz[a,h]anthracene "promoted" the development of preexisting atherosclerotic plaques in male chickens as opposed to initiating the development of new plaques. The ability to promote plaque development was not correlated with the mutagenicity or carcinogenicity of the PAH tested. Similarly, administration of benzo[a]pyrene or benzo[e]pyrene into atherosclerosis-susceptible or atherosclerosis-resistant pigeons for 3-5 months of treatment indicated that benzo[a]pyrene, but not benzo[e]pyrene, enhanced the formation of arterial lesions in female, but not male, birds (Hough et al. 1993). Female pigeons were also infertile, and showed ovarian abnormalities.

These results, therefore, suggest that PAHs may contribute to the pathogenesis of atherosclerosis in humans. This is a particularly relevant health risk for those individuals who are exposed to high levels of PAHs in the environment and who also smoke cigarettes.

Gastrointestinal Effects. Anthracene has been associated with gastrointestinal toxicity in humans. Humans that consumed laxatives that contained anthracene (anthracene concentration not specified) for

prolonged periods were found to have an increased incidence (73.4%) of melanosis of the colon and rectum as compared to those who did not consume anthracene-containing laxatives (26.6%) (Badiali et al. 1985). The authors suggested that the melanosis observed may be attributed to the consumption of anthracene laxatives and not to intestinal stasis. This study is severely limited because of confounding factors such as the existence of other predisposing factors for melanosis and lack of follow-up.

Several PAHs discussed in this profile have been shown to alter enzyme activity in the intestinal mucosa of animals following oral administration, which could conceivably lead to increased production of reactive intermediates and tissue injury. Given the selectivity of PAHs for rapidly proliferating tissues such as gastrointestinal mucosa and the results discussed above, exposure to PAHs (particularly oral) by humans could lead to adverse gastrointestinal effects.

Hematological Effects. Adverse hematological effects have been observed in animals following exposure to PAHs. For example, administration of a single intraperitoneal dose of benzo[a]pyrene to mice resulted in a small spleen, marked cellular depletion, prominent hemosiderosis, and follicles with large lymphocytes. These pathological lesions were associated with death (Shubik and Porta 1957). Death due to adverse hematological effects (e.g., aplastic anemia and pancytopenia resulting in hemorrhage) has also been observed in mice following intermediate-duration oral exposure to benzo[a]pyrene (Robinson et al. 1975). Fluoranthene and fluorene administered by gavage to male and female mice for 13 weeks caused hematological effects including decreased packed cell volume and decreased hemoglobin content (EPA 1988e, 1989e). In addition, it has been shown that benzo[a]pyrene is toxic to cultured bone marrow cells when applied directly (Legraverend et al. 1983)

PAHs appear to affect other blood elements, as well. The influence of several PAHs on calcium ionophore-induced activation of isolated rabbit platelets was studied (Yamazaki et al. 1990). The activation of the platelets was assessed by measuring thromboxane B_2 synthesis in response to stimulation by the calcium ionophore, A-23 187. The authors reported that thromboxane B_2 synthesis was inhibited by incubation of the stimulated platelets with benz[a]anthracene, chrysene, benzo[a]pyrene, and benzo[g,h,i]perylene, and stimulated by incubation with anthracene and pyrene. However, no statistical analysis was performed on these data, and the changes reported are generally within ±10% of control values. In addition, the effects of the PAHs on thromboxane B_2 synthesis are bidirectional, and in many instances, the same compound induced both inhibition and stimulation at different concentrations.

As discussed above, PAHs tend to exert their adverse effects on rapidly proliferating tissues, such as the bone marrow blood forming elements. It is likely that PAH-induced toxicity in this tissue is due to a specific attack on DNA of cells in the S or synthetic phase of mitosis (EPA 1988a).

Although the human data available on PAH-induced hematological toxicity are flawed by confounding factors, they, together with the animal data and the propensity for PAHs to attack rapidly proliferating tissues, indicate that humans exposed to PAHs may be at risk for developing hematological toxicity.

Hepatic Effects. No adverse hepatic effects have been reported in humans following exposure to PAHs. However, hepatic effects have been observed in animals following acute oral, intraperitoneal, or subcutaneous administration of various PAHs. These effects include the induction of preneoplastic hepatocytes, known as y-glutamyl transpeptidase foci, induction of carboxylesterase and aldehyde dehydrogenase activity, an increase in liver weight, and stimulation of hepatic regeneration (an indication of a proliferative effect) (Danz et al. 1991; Gershbein 1975; Kemena et al. 1988; Robinson et al. 1975; Shubik and Porta 1957; Torronen et al. 1981; Tsuda and Farber 1980). These hepatic changes are not considered serious adverse effects, but their incidence and severity have been shown to correlate with the carcinogenic potency of particular PAHs. Thus, monitoring of liver function and tissue integrity may prove useful in the evaluation of PAH exposure.

More serious effects indicative of hepatic injury have been observed in animals. For example, an acute intraperitoneal injection of phenanthrene to rats resulted in liver congestion with a distinct lobular pattern, and an increase in serum aspartate aminotransferase, gamma-GT, and creatinine (Yoshikawa et al. 1987). Similarly, a single intraperitoneal injection of pyrene resulted in minimal swelling of the liver but no significant alterations in serum chemistry. Longer-term administration of PAHs has also been reported to result in adverse hepatic effects in animals. For example, increased absolute and relative liver weight correlated with hepatocellular hypertrophy was seen in male and female mice given 350 mg/kg/day acenaphthene by gavage for 13 weeks (EPA 1989c). Increased liver weight and dose-related centrilobular pigmentation accompanied by an increase in liver enzymes was observed in both male and female mice receiving 250 mg/kg/day fluoranthene by gavage for 13 weeks (EPA 1988e).

Renal Effects. Adverse renal effects associated with PAHs have not been reported in humans. A single injection of anthracene or fluorene had no adverse effect on the kidneys of mice (Shubik and

Porta 1957). Dilated tubules were observed in the kidneys of mice administered pyrene in the diet for 25 days (Rigdon and Giannukos 1964); the toxicological significance of this effect is not known. Renal tubular regeneration, and interstitial lymphocytic infiltrates and/or fibrosis were observed after 13-week oral administration of fluoranthene to female mice at 250 mg/kg/day, and to male mice at 500 mg/kg/day (EPA 1988e). Given the lack of renal toxicity in humans and the limited value of the observations made in animals, the risk to humans for renal toxicity following exposure to PAHs is not known.

Endocrine Effects. There is suggestive evidence that PAHs may adversely affect endocrine function as well. The number of thymic glucocorticoid receptors in 6-week-old rats treated once with 2 mg/kg benzo[a]pyrene was measured (Csaba et al. 1991). It is assumed that the route of exposure was by oral gavage, but this was never explicitly stated. The number of these receptors was decreased by 40% in females and was unaffected in males relative to the vehicle control animals. The statistical significance of these effects was not indicated, nor was the adversity of a decrease in receptor number assessed by examination of functional parameters.

Dermal Effects. The skin is susceptible to PAH-induced toxicity in both humans and animals. Regressive verrucae were reported following intermediate-duration application of benzo[a]pyrene to human skin (Cottini and Mazzone 1939). Although reversible and apparently benign, these changes were thought to represent neoplastic proliferation. Benzo[a]pyrene application also apparently exacerbated skin lesions in patients with pre-existing skin conditions (pemphigus vulgaris and xeroderma pigmentosum) (Cottini and Mazzone 1939). Workers exposed to substances that contain PAHs (e.g., coal tar) experienced chronic dermatitis and hyperkeratosis (EPA 1988a). Coal tar preparations containing PAHs are used in the therapeutic treatment of some skin disorders. Adverse reactions have been noted in these patients, also.

Adverse dermatological effects have also been noted in animals in conjunction with acute and intermediate-duration dermal exposure to PAHs. These effects include destruction of sebaceous glands, skin ulcerations, hyperplasia, and hyperkeratosis (Bock and Mund 1958), and alterations in epidermal cell growth (Albert et al. 1991b; Elgjo 1968).

The observation that PAHs adversely affected the skin in both humans and animals is not surprising. The skin undergoes rapid cell turnover and is thus a likely target for PAH attack on DNA synthesis.

Given the information discussed above, the ubiquitous nature of PAHs in the environment, and the susceptibility of the skin to PAH-induced toxicity, adverse skin effects may occur in individuals exposed to these chemicals by the dermal route.

Immunological and Lymphoreticular Effects. Humoral immunity was depressed in male iron foundry workers exposed to benzo[a]pyrene (Szczeklik et al. 1994). IgG, and IgA were depressed in those workers exposed to high levels. There are reports in the literature concerning the immunotoxicity of PAHs following dermal and parenteral exposure in animals. The carcinogenic PAHs as a group have an immunosuppressive effect. There are limited data that suggest that the degree of immunosuppression correlates with the carcinogenic potency. For example, using spleen cell cultures from C3H/Anf mice, suppression of humoral immunity (as measured by the plaque-forming cell [PFC] response to sheep red blood cells) and cell-mediated immunity (as measured by the one-way mixed lymphocyte response) were observed following incubation with 10^{-5}-10^{-7} mol benzo[a]pyrene (Urso et al. 1986). There was no loss in cell viability at these concentrations. These immunological responses were unaffected by treatment with equivalent concentrations of benzo[e]pyrene. These findings led the authors to speculate that carcinogenic PAHs alter immune function, thereby allowing the induction of carcinogenesis while noncarcinogenic PAHs do not affect immune function. In addition, benzo[a]pyrene, but not benzo[e]pyrene, in the presence of S9 metabolic activation mix, has been shown to inhibit interferon induction by viruses by 60-70% in cultured LLC-MK_2 cells (Hahon and Booth 1986).

Benzo[a]pyrene has been shown to markedly inhibit the immune system, especially T-cell dependent antibody production by lymphocytes exposed either *in vivo* or *in vitro* (Blanton et al. 1986; Lyte and Bick 1985; White and Holsapple 1984). These effects are generally seen at high dose relative to those that can induce cancer in animals.

The effects of benzo[a]pyrene on several parameters of cell-mediated immune function in isolated and T-cell enriched mononuclear cell populations from three strains of mice (C57, C3H, and DBA) given a single intraperitoneal injection of 10-50 mg/kg benzo[a]pyrene or benzo[e]pyrene following stimulation with phytohemagglutinin (PHA) were studied (Wojdani and Alfred 1984). Neither benzo[a]pyrene nor benzo[e]pyrene had an inhibitory effect on lymphocyte blastogenesis induced by PHA; blastogenesis was slightly stimulated at 2.5 and 10 mg/kg of either PAH. Dose-related suppression of cell-mediated cytotoxicity of allosensitized lymphocytes was observed in all strains of

mice treated with benzo[a]pyrene, but no effect on this parameter was observed following treatment with benzo[e]pyrene. The percentage and adherence of macrophages from benzo[a]pyrene-treated mice were increased. The authors suggest that benzo[a]pyrene, but not benzo[e]pyrene, causes alterations in cell-mediated immune function that could compromise the animal's immune function allowing the development of PAH-induced tumors. A major limitation of this study was the lack of statistical analysis, thereby making it difficult to determine the validity of the changes seen. As mentioned previously, relatively high doses of benzo[a]pyrene were employed in these studies.

Benzo[a]pyrene-induced immune suppression was reported in male $B6C3F_1$ mice (Lyte and Bick 1985) and in the offspring of C3H/Anf mice treated intraperitoneally with benzo[a]pyrene (Urso and Gengozian 1980). Cell-mediated and humoral immune function of the liver, thymus, and spleen were evaluated in both maternal animals and the offspring of C3H mice administered one intraperitoneal dose of benzo[a]pyrene (150 mg/kg) during "mid-pregnancy" (Urso et al. 1992). The offspring were evaluated at 1 week and 18 months of age. Suppression of these various aspects of the immune system was observed in both the mothers and the offspring at these relatively high doses. However, the study lacked sufficient detail to adequately assess either the protocol or the results.

Groups of four $B6C3F_1$ female mice were administered single injections of 0, 50, or 200 mg/kg benzo[a]pyrene in corn oil to study the correlation between DNA adduct formation (as measured by ^{32}P-postlabelling analysis) and the suppression of polyclonal immune responses (^{3}H-TdR incorporation following stimulation by *Escherichia coli* lipopolysaccharide [LPS] and concanavalin A [Con A] and IgM secretion) and decreased cell viability in splenic lymphocytes harvested from the treated mice (Ginsberg et al. 1989). Spleen weight was significantly decreased (18%, $p<0.05$) at 50 mg/kg. The polyclonal response to LPS and Con A was suppressed by 30-45%, and this suppression was statistically significant at 200 mg/kg. IgM secretion was also significantly depressed (42%) at 200 mg/kg. These immunosuppressive effects were accompanied by high levels of benzo[a]pyrene/DNA adducts. The authors speculated that the immunosuppressive effects of benzo[a]pyrene were due to a cytotoxic mechanism (as supported by *in vitro* experiments) that in turn resulted partially from the genotoxic effects of benzo[a]pyrene (i.e., the formation of benzo[a]pyrene/DNA adducts).

Benzo[a]pyrene exerts its inhibitory effects on antibody production through alterations on the normal functioning of macrophages, T cells, and B cells (Blanton et al. 1988; Zhao et al. 1990). In contrast,

benzo[a]pyrene has no effect on most cellular immune responses before the appearance of tumors (Dean et al. 1983b), although benzo[a]pyrene exposure does inhibit IL-2-dependent proliferation (Myers et al. 1988).

Benzo[a]pyrene may also induce autoimmune responses. Groups of eight female Sprague-Dawley rats were administered a single subcutaneous injection of 2 mg benzo[a]pyrene or benzo[e]pyrene (11.1 mg/kg) in sesame oil in the right thigh (Faiderbe et al. 1992). The animals were observed for up to 150 days and blood samples were taken at regular intervals to measure anti-phosphatidylinositol (PtdIns) antibodies. Serum levels of anti-PtdIns in animals treated with benzo[a]pyrene exceeded those of the oil-injected controls after day 10, and the difference became statistically significant ($p<0.05$) after day 40. The levels reached a peak at day 60 after which time they reached a plateau. The anti-PtdIns were of the IgG type and specific to phosphatidylinositol. Malignant sarcomas developed at the injection site in the animals treated with benzo[a]pyrene within 100-120 days. Serum levels of anti-PtdIns in animals treated with benzo[e]pyrene did not differ from those of the oil-injected controls. No malignant sarcomas developed at the injection site in 100% of the animals administered benzo[e]pyrene within 100-120 days. The authors speculated that constant stimulation of lymphocytes reactive for PtdIns by an endogenous antigen, of which PtdIns could be a part, was responsible for the increased serum levels of anti-PtdIns. The authors suggested that PtdIns metabolism is altered in rapidly proliferating malignant cells (the neoplasia being stimulated by benzo[a]pyrene), resulting in the synthesis of the PtdIns-containing antigen. The lack of an autoimmune response to benzo[e]pyrene was due to the fact that benzo[e]pyrene was not carcinogenic; there was no neoplastic transformation occurring that could result in the production of PtdIns-containing antigens such as was seen with benzo[a]pyrene. Therefore, this study provides evidence that benzo[a]pyrene-induced neoplasia may cause an alteration in the metabolism of endogenous substances, resulting in the production of autoimmune antibodies to those substances.

The immunotoxic effects of benzo[a]pyrene have been noted *in vitro* as well (e.g., Ladies et al. 1991), and these studies provide some insight into the mechanism of action of benzo[a]pyrene-induced immunological effects. Splenic lymphocytes from $B6C3F_1$ mice were incubated with various concentrations of benzo[a]pyrene for either 2 hours or the entire culture period (Ginsberg et al. 1989). A dose- and duration-related decrease in splenic lymphocyte viability (as measured by ^{3}H-TdR incorporation) and immune response (as measured by IgM secretion) was observed in the absence of S9 activation. Addition of S9 enhanced this effect after acute-duration exposure. However, there was

very little formation of benzo[a]pyrene/DNA adducts at benzo[a]pyrene concentrations of 1-200 µmol in the splenic lymphocytes; this lack of effect was accompanied by a very low level of benzo[a]pyrene metabolism to DNA-adducting metabolites. Benzo[a]pyrene/DNA adducts were measured in liver and lung; however, in the *in vivo* experiment. This led the authors to suggest that benzo[a]pyrene-induced immunotoxicity as expressed by splenic lymphocytes was the result of a cytotoxic effect that was mediated, in part, by a genotoxic mechanism involving the formation of benzo[a]pyrene/DNA adducts remote from the spleen and a direct cytotoxic effect not requiring activation of benzo[a]pyrene to the reactive intermediate.

Incubation of human lymphocytes with 0.1-01.0 µg/mL benzo[a]pyrene resulted in a suppression of lymphokine-activated killer cell (LAK) activity against tumor targets after 3 and 7 days (Lindemann and Park 1989). LAK DNA synthesis was also inhibited after 3 or 7 days of incubation with benzo[a]pyrene. However, benzo[a]pyrene had no effect on LAK binding with tumor targets, and benzo[a]pyrene did not interfere with the cytotoxic effect of natural killer cells added to the incubation medium. Based on these results, the authors concluded that benzo[a]pyrene interferes with the development of the immunological defense killer cells.

Benzo[a]pyrene has also been shown to affect immune responses to viral infection. Benzo[a]pyrene can reversibly inhibit the induction of viral interferon in 32 different mammalian cell lines but only in the presence of S9 metabolic activation (Hahon and Booth 1988). This inhibition must occur at an early level and not affect viral interferon interactions because the activity of exogenous interferon was unaffected. In addition, influenza virus multiplication was also inhibited by activated benzo[a]pyrene. Benzo[e]pyrene had no effect on interferon induction. The authors suggest that benzo[a]pyrene's inhibition of interferon induction may be an early step in compromising the host's immune function, thereby allowing the induction of carcinogenesis.

There is evidence to suggest that PAHs may alter the levels of brain neurotransmitters, which in turn affects the function of the immune system. The levels of two catecholamines, dopamine and norepinephrine, were determined in discrete brain areas in mice in which fibrosarcomas had been induced following a single subcutaneous injection of benzo[a]pyrene (Dasgupta and Lahiri 1992). Both dopamine and norepinephrine levels were significantly decreased in some brain regions (e.g., the corpus striatum and the hypothalamus), and these decreases were evident in both early and late tumor development. The authors state that since immunological function is compromised during

carcinogenesis and certain alterations in brain catecholamines impair immune function, the mechanism by which carcinogens such as benzo[a]pyrene cause immunosuppression and subsequent carcinogenesis may be via depression of brain catecholamines.

Very little information is available on the immunological effects of other PAHs. Mice treated with high doses of dibenz[a,h]anthracene exhibited a reduced serum antibody level in response to antigenic challenge by comparison to controls (Malmgren et al. 1952). The immunosuppressive effects of dibenz[a,h]anthracene were studied in AHH-inducible mice (C57BL/6) and AHH-noninducible mice (DBA/2N) by intraperitoneal and oral administration (Lubet et al. 1984). Immunosuppression occurred in both strains and was more pronounced in the C57BL/6 mice than in the DBA/2N mice, following intraperitoneal administration. However, the DBA/2N mice were more susceptible to immunosuppression following oral administration. These results suggest that PAHs are rapidly metabolized and excreted following oral administration in AHH-inducible mice, whereas in AHH-noninducible mice, the PAHs are absorbed and distributed to target organs. Based on these results, the authors concluded that AHH inducibility plays an important role in the immunosuppressive activity of PAHs.

B-cell lymphopoiesis in mouse bone marrow has been shown to be inhibited by incubation with fluoranthene *in vitro* at concentrations of ≥5 µg/mL (25 µmol). This effect on B-cell precursors may be mediated in part by a stimulation of programmed cell death; as demonstrated by the increase in DNA fragmentation induced by fluoranthene 15-17 hours after addition to the incubation medium. Furthermore, fluoranthene-induced DNA fragmentation always preceded fluoranthene-induced B-cell precursor death. Another mechanism for fluoranthene-induced inhibition of B-cell lymphopoiesis may be alterations in cell growth rates (fluoranthene was shown to slow the rate of B-cell precursor growth at concentrations <5 µg/mL) and/or altered cell survival (Hinoshita et al. 1992).

The lymphoid system, because of its rapidly proliferating tissues, is susceptible to PAH-induced toxicity. The mechanism of action for this effect is most likely inhibition of DNA synthesis. No adverse effects on this system associated with PAH exposure have been reported in humans, but several accounts of lymphoid toxicity in animals are available. A single intraperitoneal injection of benzo[a]pyrene to mice resulted in a small spleen with marked cellular depletion, prominent and edematous trabeculae, and large lymphocytes. These lesions resulted in death (Shubik and Porta 1957). The Shubik and Porta (1957) study was severely limited by the following: the benzo[a]pyrene

was only partly in solution, only one dose was employed, there was a small sample size, the purity of benzo[a]pyrene was not specified, only one sex was tested, and the presence of benzo[a]pyrene in the peritoneal cavity indicates inadequate absorption. No other similar studies were found in the literature.

Even though these effects have not been noted in humans, and the data in animals are contained in only one study, the rapidly proliferating nature of this tissue suggest that humans exposed to PAHs may be a risk for the development of adverse effects on the lymphoid system.

Given the high potential for exposure to PAHs in the vicinity of hazardous waste sites, the evidence from animal studies, and the heterogeneity of human genotypes with regard to enzyme induction capabilities, it would be prudent to consider that PAHs may pose an immunotoxic risk to humans living in areas surrounding hazardous waste sites.

Neurological Effects. No information is available on the short- or long-term neurotoxic effects of exposure to PAHs in humans and animals. Acute-, intermediate-, or chronic-duration studies conducted in animals do not indicate that any of the PAHs tested showed evidence of neurotoxicity, although these tests were not designed to detect subtle neurological changes.

However, there is evidence to suggest that PAHs may alter the levels of brain neurotransmitters. The levels of two catecholamines, dopamine and norepinephrine, were determined in discreet brain areas in mice in which fibrosarcomas had been induced following a single subcutaneous injection of benzo[a]pyrene (Dasgupta and Lahiri 1992). The mice were divided into two groups: early tumor development and late tumor development 3-4 months after administration of the benzo[a]pyrene. Both dopamine and norepinephrine levels were significantly decreased in some brain regions (e.g., the corpus striatum and the hypothalamus), and these decreases were evident in both early and late tumor development. The authors state that because immunological function is compromised during carcinogenesis and because certain alterations in brain catecholamines impair immune function, the mechanism by which carcinogens such as benzo[a]pyrene cause immunosuppression and subsequent carcinogenesis may be via depression of brain catecholamines.

Reproductive Effects. In both prospective and retrospective studies, a decrease in fecundity was observed in women who were exposed prenatally to cigarette smoke (i.e., their mothers smoked when pregnant) (Weinberg et al. 1989; Wilcox et al. 1989). This association was apparent even after

adjustment for age, frequency of intercourse, current smoking status, age at menarche, childhood exposure to cigarette smoking, educational level, reproductive history, body weight, and consumption of alcohol and caffeine. On the other hand, an increase in fecundity was observed in a retrospective study of women who were exposed to cigarette smoke in early childhood. These apparently opposite effects may be partially explained by the fact that when a woman smokes during pregnancy, her fetus is exposed to the components of the cigarette smoke that cross the placenta as well as changes in fetal and placental oxygenation and metabolism that are secondary to changes in maternal metabolism resulting from smoking. However, childhood exposure involves direct inhalation of cigarette smoke. The authors could offer no explanation as to why fecundity should be *increased* as a result of childhood exposure to cigarette smoke (Weinberg et al. 1989; Wilcox et al. 1989).

The testes and ovaries contain rapidly proliferating cells and therefore should be considered susceptible to damage by PAHs. The reproductive toxicity data in animals for the PAHs are limited. The available animal studies exclusively discuss the reproductive effects of benzo[a]pyrene. Adverse effects such as decreased fertility and total sterility in F_1 progeny of CD-1 mice (Mackenzie and Angevine 1981) and decreased incidence of pregnant female rats at parturition (Rigdon and Rennels 1964) were reported following oral exposure to benzo[a]pyrene. However, no adverse reproductive effects were observed in Swiss mice fed benzo[a]pyrene in their diet (Rigdon and Neal 1965). The metabolic differences and method of benzo[a]pyrene administration could account for the differential response to benzo[a]pyrene induced toxicity in these studies. A single intraperitoneal injection of benzo[a]pyrene to female C57BL/6N mice decreased the number of corpora lutea (Swartz and Mattison 1985). The, antiestrogenic effects causing decreased uterine weights in pseudopregnant Sprague-Dawley rats were reported following daily subcutaneous injections of benzo[a]pyrene during days 6-11 of pseudopregnancy (Bui et al. 1986). Similar treatment to pregnant rats during gestation caused resorptions, reduced percentage of viable litters, and decreased uterine weights (Bui et al. 1986; Cervello et al. 1992). Female mice exhibited decreased ovary weights after 13 weeks oral exposure to 700 mg/kg/day acenaphthene (EPA 1989c). The studies conducted on the reproductive effects of benzo[a]pyrene via parenteral routes are briefly discussed below.

Single intraperitoneal injection of benzo[a]pyrene to female C57BL/6N mice at doses as high as 500 mg/kg body weight produced a dose- and time-dependent decrease in the number of corpora lutea (Swartz and Mattison 1985). The NOAEL in this study was 1 mg/kg/day. Groups of 20 C57BL/6N mice were given single intraperitoneal injections of 0-500 mg/kg benzo[a]pyrene (Miller et al. 1992)

and were killed at various intervals after injection. Total ovarian volume, total corpora lutea volume, and total number of corpora lutea per ovary were significantly reduced by doses of benzo[a]pyrene >5 mg/kg in a dose-related manner. These effects resolved in a dose- and time-dependent fashion, so that after 4 weeks, most changes were only evident in the animals treated with the 100 or 500 mg/kg benzo[a]pyrene. Individual corpora lutea volume actually increased in the treated animals, indicating that compensatory hypertrophy was probably occurring. The authors concluded that based on these findings and previous findings, benzo[a]pyrene impairs corpora lutea formation by destroying follicles. In another study, DBA/2N (D2), C57BL/6N (B6), and (DBA/2N x C57BL/6N)F_1 (F_1) mice (7-8/group) were injected with 10 µg of either benzo[a]pyrene or one of three different metabolites of benzo[a]pyrene ([+]7,8-oxide, [-]7,8-dihydrodiol, or [+]-diol-epoxide-2) into the right ovary (Mattison et al. 1989). The left ovary served as a control, and an additional control group injected with the vehicle (DMSO) also served as controls. Ovarian volume, wet weight, and small, growing, and large follicle number were measured in both the treated and contralateral control ovaries. Benzo[a]pyrene and one or more of its'metabolites caused decreases in the treated ovarian weight, the ovarian volume, and the small, growing, and large follicles in one or more strains. In most instances, the contralateral untreated ovary exhibited a compensatory response; ovarian weight and volume increased as compared to the DMSO controls. This study shows that benzo[a]pyrene and some of its metabolites are toxic to the ovaries of mice, and that the ovary is capable of metabolizing benzo[a]pyrene into reactive metabolites. Similarly, administration of benzo[a]pyrene or benzo[e]pyrene into atherosclerosis-susceptible or atherosclerosis-resistant pigeons for 3-5 months of treatment indicated that benzo[a]pyrene, but not benzo[e]pyrene, rendered female pigeons infertile, with ovarian abnormalities (Hough et al. 1993). Cumulatively, these results demonstrate the sensitivity of integrated hypothalamic-pituitary-ovarian function to adverse effects of benzo[a]pyrene.

Daily subcutaneous injection of benzo[a]pyrene beginning on day 6 of gestation for 6 days as opposed to 3 days significantly increased the number of resorptions, and decreased the fetal survival and uterine weights in Sprague-Dawley rats (Bui et al. 1986). In pseudopregnant (i.e., condition occurring following sterile matings in which anatomical and physiological changes occur similar to those of pregnancy) rats, similar benzo[a]pyrene treatment during days 6-11 of pseudopregnancy significantly decreased the cyclic nucleotide levels and uterine weights suggesting an antiestrogenic effect (Bui et al. 1986). Use of a single dosage level precluded the assessment of dose response in these studies.

Pregnant Sprague-Dawley rats were administered subcutaneous injections of benzo[a]pyrene (in DMSO and corn oil) or the vehicle alone on gestation days 7, 9, 11, 13, and 15 (Cervello et al. 1992). The animals were sacrificed on gestation day 16. There were no maternal deaths or signs of maternal toxicity. However, the number of fetuses per litter and number of live fetuses per litter were significantly decreased in the animals treated with benzo[a]pyrene, and the number of resorptions was significantly increased. In addition, uterine weight, and whole uterine gravid weight were significantly decreased and increased, respectively. These results demonstrate the reproductive toxicity of benzo[a]pyrene, but a dose-response relationship could not be established because only one dose was tested.

These results suggest that the potential for adverse reproductive effects may be increased in humans exposed to benzo[a]pyrene in the workplace or at hazardous waste sites.

Developmental Effects. The developmental toxicity data for PAHs are mostly limited to *in utero* exposure of pregnant animals to benzo[a]pyrene via various routes of exposure. The placental transfer of benzo[a]pyrene has been shown in mice following oral and intravenous exposure of dams (Shendrikova and Aleksandrov 1974) and in rats after intratracheal administration (Srivastava et al. 1986). The available data from oral studies in animals indicate that exposure of pregnant dams to benzo[a]pyrene produced resorptions and malformations in fetuses (Legraverend et al. 1984) and sterility in F_1 mouse progeny (Mackenzie and Angevine 1981). Investigations by Legraverend et al. (1984) suggest that benzo[a]pyrene metabolites generated in the fetus rather than in the maternal tissues are responsible for these adverse effects. Also, the genetic differences observed in this study using the oral route were contrary to those induced by intraperitoneal administration of benzo[a]pyrene (Hoshino et al. 1981; Shum et al. 1979), thus emphasizing the importance of route of administration in benzo[a]pyrene metabolism and resulting toxicity.

The developmental effects of benzo[a]pyrene have also been investigated in animals using the parenteral route of administration. Intraperitoneal injection of benzo[a]pyrene to pregnant mice produced stillbirths, resorptions and malformations at a greater incidence in Ah-responsive mice than in Ah-nonresponsive mice (Shum et al. 1979); testicular changes including atrophy of seminiferous tubules with lack of spermatids and spermatozoa; interstitial cell tumors (Payne 1958); immunosuppression (Urso and Gengozian 1980); and tumor induction (Bulay and Wattenberg 1971; Soyka 1980). Adverse effects observed following subcutaneous injection of benzo[a]pyrene include

increased fetal resorptio'ns in rats (Wolfe and Bryan 1939) and lung tumor induction in mice (Nikonova 1977). Decreased fetal survival (Wolfe and Bryan 1939) and lung tumor development (Rossi et al. 1983) were reported in Swiss mice following direct intra-embryonal injection of benzo[a]pyrene.

Results of *in vitro* studies suggest that benzo[a]pyrene may affect a number of enzyme and hormone activities in the human placenta. The effects of benzo[a]pyrene on the binding of epidermal growth factor (EGF) and receptor autophosphorylation were studied in human placental cell cultures from early and late gestation placentas (Guyda et al. 1990). In a subsequent study, the effects of benzo[a]pyrene on the uptake of aminoisobutyric acid (AIB) by early and late gestational human placental cells was also studied (Guyda 1991). Benzo[a]pyrene decreased binding of EGF (37-60%) to the early gestation placental cells, but not the late gestation placental cells. The decrease in binding was due to a decrease in the number of high-affinity EGF binding sites. This effect was specific for EGF receptor sites and not due to a nonspecific effect of benzo[a]pyrene on the membranes because benzo[a]pyrene had no effect on the binding of ^{125}I-labeled insulin and insulin-like growth factors. The authors concluded that the effects of benzo[a]pyrene on EGF binding were specific and related to gestational age. Benzo[a]pyrene stimulated AIB uptake by both early and late gestational cells and enhanced EGF-stimulated AIB uptake in spite of a decrease in the number of EGF receptors. The implications of these finding are that benzo[a]pyrene could alter EGF-induced secretion of human chorionic gonadotrophin and human placental lactogen secretion as well as metabolic functions, thereby affecting the regulation of cell growth and differentiation in human placentas.

The activity of quinone reductase, a major protective enzyme, was increased 2-3-fold in first trimester human placental extracts *in vitro* when incubated for 6 hours with benz[a]anthracene, dibenz[a,h]anthracene, and chrysene at a concentration of 50 µmol (Avigdor et al. 1992). Based on these results, it can be postulated that the early placenta is capable of metabolizing certain toxic xenobiotics such as PAH quinone metabolites to inactive intermediates thereby protecting the developing embryo.

Benzo[a]pyrene (50 µmol) has been shown to stimulate human gonadotropin release by first trimester human placental explants *in vitro* (Bamea and Shurtz-Swirski 1992). This stimulation was evident following static exposure for 24 hours and also in cultures that were superfused, meaning the benzo[a]pyrene had a delayed effect and did not need to be present for this effect to be expressed.

The implication of these findings is that benzo[a]pyrene can alter human placental endocrine function early in pregnancy.

Results of animal and *in vitro* studies suggest that benzo[a]pyrene may produce adverse effects in the offspring of women exposed during pregnancy. Furthermore, the results of genetic studies conducted via oral and intraperitoneal routes emphasize the importance of route of administration in benzo[a]pyrene metabolism and resulting toxicity and the severity of the effect may vary depending upon the genotype of the individual exposed (see Section 2.7, Populations That Are Unusually Susceptible). Based on these observations, it is therefore prudent to consider that the genetically heterogeneous human population may show variation in response to *in utero* exposure to benzo[a]pyrene.

Other PAHs such as anthracene, benzanthracene, chrysene, and dibenz[a,h]anthracene have also been tested for developmental effects via parenteral routes. Of these compounds, dibenz[a,h]anthracene produced fetolethal effects in rats (Wolfe and Bryan 1939), while chrysene produced liver tumors in the mouse progeny (Buening et al. 1979a; Grover et al. 1975)

Genotoxic Effects. As the results presented in Tables 2-4 and 2-5 indicate, benzo[a]pyrene has been thoroughly studied in genetic toxicology test systems. It induces genetic damage in prokaryotes, eukaryotes, and mammalian cells *in vitro* and produces a wide range of genotoxic effects (gene mutations in somatic cells, chromosome damage in germinal and somatic cells, DNA adduct formation, UDS, sister chromatid exchange, and neoplastic cell transformation). In cultured human cells, benzo[a]pyrene binds to DNA and causes gene mutations, chromosome aberrations, sister chromatid exchange, and UDS.

The results of *in vivo* studies indicate that many of the same types of adverse effects observed *in vitro* were seen in mice, rats, and hamsters exposed to benzo[a]pyrene via the oral, dermal, or intraperitoneal routes. The available data also indicate that benzo[a]pyrene is genotoxic in both somatic and germinal cells of intact animals (Table 2-4). The only study that was found regarding genotoxic effects in humans following exposure to benzo[a]pyrene reported no correlation between aluminum plant workers' exposure to PAHs, including benzo[a]pyrene, and sister chromatid exchange frequency (Becher et al. 1984). The findings from assays using human cells as the target, in

TABLE 2-4. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vivo*

Species (test system)	End point	Results	Reference
	ANTHRACENE		
Mammalian systems:			
Chinese hamster/bone marrow	Chromosome aberrations	–	Roszinsky-Kocher et al. 1979
Chinese hamster/bone marrow	Sister chromatid exchange	–	Roszinsky-Kocher et al. 1979
Mouse/bone marrow	Micronuclei	–	Salamone et al. 1981
Mouse	Sperm abnormalities	–	Topham 1980
Host-mediated systems:			
Salmonella typhimurium/mouse host-mediated	Gene mutation	(+)[a]	Simmon et al. 1979
Saccharomyces cerevisiae/mouse host-mediated	Gene mutation	–	Simmon et al. 1979
Chinese hamster V79 cells/mouse host-mediated	Sister chromatid exchange	–	Sirianni and Huang 1978
	BENZ(*a*)ANTHRACENE		
Mammalian systems:			
Chinese hamster/bone marrow	Chromosome aberrations	–	Roszinsky-Kocher et al. 1979
Chinese hamster/bone marrow	Sister chromatid exchange	+	Roszinsky-Kocher et al. 1979
Insect systems:			
Drosophila melanogaster/sex-linked recessives	Gene mutation	–	Zijlstra and Vogel 1984
D. melanogaster/somatic mutation	Gene mutation	–	Fahmy and Fahmy 1980
Host-mediated systems:			
S. typhimurium/mouse host-mediated	Gene mutation	+	Simmon et al. 1979
S. cerevisiae/mouse host-mediated	Gene mutation	–	Simmon et al. 1979
	BENZO(*b*)FLUORANTHENE		
Mammalian systems:			
Chinese hamster/bone marrow	Chromosome aberrations	–	Roszinsky-Kocher et al. 1979
Chinese hamster/bone marrow	Sister chromatid exchange	–	Roszinsky-Kocher et al. 1979
Mouse skin	DNA binding	+	Weyand et al. 1987, 1992a

TABLE 2-4. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vivo* (continued)

Species (test system)	End point	Results	Reference
Rat/lung, liver, peripheral blood lymphocytes	DNA binding	+	Ross et al. 1992
Rat peripheral blood lymphocytes	Sister chromatid exchange	+	Ross et al. 1992
New born mice/lung, liver	DNA binding	+	Weyand et al. 1993b
	BENZO(*j*)FLUORANTHENE		
Mammalian systems:			
Mouse skin	DNA binding	+	La Voie et al. 1991a; Weyand et al. 1987, 1993a
	BENZO(*k*)FLUORANTHENE		
Mammalian systems:			
Mouse skin	DNA binding	+	Weyand et al. 1987
	BENZO(*g,h,i*)PERYLENE		
Host-mediated systems:			
Hamster embryos/transplacental exposure	Transformation	–	Quarles et al. 1979
	BENZO(*a*)PYRENE		
Mammalian systems:			
Mouse/dominant lethals	Gene mutation	+	Epstein 1968; Generoso et al. 1982; Russell 1977
Mouse/spot test	Gene mutation	+	Davidson and Dawson 1976, 1977
Rat hepatocytes/unscheduled DNA synthesis	DNA damage	–	Miralis et al. 1982
Rat hepatocytes/unscheduled DNA synthesis	DNA damage	–	Mullaart et al. 1989
Mouse germ cells/unscheduled DNA synthesis	DNA damage	–	Sega 1979
Mouse skin/lung	DNA binding	+	Mukhtar et al. 1986
Mouse skin	DNA binding	+	Morse et al. 1985; Rice et al. 1984; Weyand and Bevan 1987a

TABLE 2-4. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vivo* (continued)

Species (test system)	End point	Results	Reference
Mouse/bone marrow	DNA binding	+	Wielgosz et al. 1991
Mouse/spleen cells	DNA binding	+	Wielgosz et al.1991
Rat liver parenchymal cells	DNA single strand breaks	+	Mullaart et al. 1989
Rat liver nonparenchymal cells	DNA single strand breaks	–	Mullaart et al. 1989
Rat intestinal cells	DNA single strand breaks	+	Mullaart et al. 1989
Mouse/bone marrow	Chromosome aberrations	+	Adler and Ingwersen 1989
Mouse/bone marrow	Chromosome aberrations	+	Adler et al. 1989
Mouse/embryos	Chromosome aberrations	+	Adler et al. 1989
Chinese hamster/bone marrow	Chromosome aberrations	+	Roszinsky-Kocher et al. 1979
Chinese hamster/bone marrow	Chromosome aberrations	(+)	Bayer 1978
Mouse/heritable translocation	Chromosome aberrations	–	Generoso et al. 1982
Mouse/bone marrow	Chromosome aberrations	+	Wielgosz et al. 1991
Mouse/spleen cells	Chromosome aberrations	+	Wielgosz et al. 1991
Chinese hamster/bone marrow	Sister chromatid exchange	+	Bayer 1978; Roszinsky-Kocher et al. 1979
Mouse/bone marrow	Micronuclei	+	Salamone et al. 1981
Mouse/bone marrow	Micronuclei	–	Bruce and Heddle 1979
Mouse/fetal liver	Micronuclei	+	Harper et al. 1989
Mouse/bone marrow	Micronuclei	+	Harper et al. 1989
Mouse/bone marrow	Micronuclei	+	Awogi and Sato 1989
Mouse/keratinocytes	Micronuclei	+	He and Baker 1991
Mouse/bone marrow	Micronuclei	+	Shimada et al. 1990

TABLE 2-4. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vivo* (continued)

Species (test system)	End point	Results	Reference
Mouse/peripheral blood reticulocytes	Micronuclei	+	Shimada et al. 1992
Rat/peripheral blood reticulocytes	Micronuclei	+	Shimada et al. 1992
Chinese hamster/bone marrow	Micronuclei	–	Bayer 1978
Mouse	Sperm abnormalities	+	Bruce and Heddle 1979; Topham 1980
Mouse	Sperm abnormalities	(+)	Salamone et al. 1988
Mouse	Sperm abnormalities	+	Salamone and Logan 1988
Mouse/bone marrow	Micronuclei	+	Balansky et al. 1994
Mouse/bone marrow	Micronuclei	+	Koratkar et al. 1993
Mouse papilloma cells	Gene mutation	+	Colapietro et al. 1993
Human lung	DNA damage	+	Weston et al. 1993a
Mouse papilloma cells	Gene mutation	+	DiGiovanni et al. 1993
Insect systems:			
D. melanogaster/sex-linked recessive	Gene mutation	(+)	Vogel et al. 1983
D. melanogaster/sex-linked recessive	Gene mutation	–	Valencia and Houtchens 1981; Zijlstra and Vogel 1984
D. melanogaster/somatic mutation	Gene mutation	+	Fahmy and Fahmy 1980
D. melanogaster	Chromosome aberration	(+)	Vogel et al. 1983
Host-mediated systems:			
S. typhimurium/mouse host-mediated	Gene mutation	–	Glatt et al. 1985; Simmon et al. 1979
S. cerevisiae/mouse host-mediated	Gene mutation	–	Simmon et al. 1979
Chinese hamster V79/mouse host-mediated	Sister chromatid exchange	+	Sirianni and Huang 1978
Hamster embryos/transplacental exposure	Transformation	+	Quarles et al. 1979

TABLE 2-4. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vivo* (continued)

Species (test system)	End point	Results	Reference
	BENZO(*e*)PYRENE		
Mammalian systems:			
Chinese hamster/bone marrow	Sister chromatid exchange	(+)	Roszinsky-Kocher et al. 1979
	CHRYSENE		
Mammalian systems:			
Chinese hamster/bone marrow	Chromosome aberrations	–	Roszinsky-Kocher et al. 1979
Chinese hamster/bone marrow	Sister chromatid exchange	+	Roszinsky-Kocher et al. 1979
Host-mediated systems:			
S. typhimurium/mouse host-mediated	Gene mutation	–	Simmon et al. 1979
S. cerevisiae/mouse host-mediated	Gene mutation	–	Simmon et al. 1979
	DIBENZ(*a,h*)ANTHRACENE		
Mammalian systems:			
Chinese hamster/bone marrow	Chromosome aberrations	–	Roszinsky-Kocher et al. 1979
Chinese hamster/bone marrow	Sister chromatid exchange	+	Roszinsky-Kocher et al. 1979
	FLUORANTHENE		
Mammalian systems:			
Mouse/bone marrow	Sister chromatid exchange	–	Palitti et al. 1986
	INDENO(1,2,3-*c,d*)PYRENE		
Mammalian systems:			
Mouse skin	DNA binding	+	Weyand et al. 1987
	PHENANTHRENE		
Mammalian systems:			
Chinese hamster/bone marrow	Chromosome aberrations	–	Bayer 1978; Roszinsky-Kocher et al. 1979

TABLE 2-4. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vivo* (continued)

Species (test system)	End point	Results	Reference
Chinese hamster/bone marrow	Sister chromatid exchange	(+)	Bayer 1978; Roszinsky-Kocher et al. 1979
Chinese hamster/bone marrow	Micronuclei	–	Bayer 1978
Host-mediated systems: *S. typhimurium*/mouse host-mediated	Gene mutation	–	Simmon et al. 1979
S. cerevisiae/mouse host-mediated	*Gene mutation*	–	*Simmon et al. 1979*
Hamster embryos/transplacental exposure	Transformation	–	Quarles et al. 1979
	PYRENE		
Mammalian systems: Mouse/bone marrow	Micronuclei	–	Salamone et al. 1981
Mouse	Sperm abnormalities	–	Salamone et al. 1988
Mouse	Sperm abnormalities	–	Salamone and Logan 1988
Insect systems: *D. melanogaster*/sex-linked recessive	Gene mutation	–	Valencia and Houtchens 1981
Host-mediated systems Chinese hamster V79/mouse host-mediated	Sister chromatid exchange	–	Sirianni and Huang 1978

[a]A positive result was obtained in one experiment; this result was not reproduced in the same laboratory or in a second laboratory.

DNA = deoxyribonucleic acid; – = negative result; + = positive result; (+) = weakly positive result

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
		ACENAPHTHENE		
Prokaryotic organisms:				
Salmonella typhimurium	Gene mutation	–	No data	Pahlman and Pelkonen 1987
Escherichia coli SOS chromotest	Gene mutation	–	No data	Mersch-Sundermann et al. 1992b
		ACENAPHTHYLENE		
Prokaryotic organisms:				
S. typhimurium	Gene mutation	–	No data	Bos et al. 1988
		ANTHRACENE		
Prokaryotic organisms:				
S. typhimurium	Gene mutation	+	–	Sakai et al. 1985
S. typhimurium	Gene mutation	+	No data	Carver et al. 1986
S. typhimurium	Gene mutation	–	–	LaVoie et al. 1983b; 1985; Rosenkranz and Poirier 1979; Simmon 1979a
S. typhimurium	Gene mutation	–	No data	Bos et al. 1988; LaVoie et al. 1979; Pahlman and Pelkonen 1987
Escherichia coli/Pol A	DNA damage	–	–	Rosenkranz and Poirier 1979
E. coli WP2-WP100/rec-assay	DNA damage	–	No data	Mamber et al. 1983
E. coli/differential killing	DNA damage	–	–	Tweats 1981
E. coli SOS chromotest	DNA damage	–	No data	Mersch-Sundermann et al. 1992b
E. coli SOS chromotest	DNA damage	–	–	Mersch-Sundermann et al. 1992a
Eukaryotic organisms:				
Fungi: *Saccharomyces cerevisiae D3*	Miotic recombination	–	–	Simmon 1979b
S. cerevisiae D4-RDII	Gene conversion	No data	–	Siebert et al. 1981

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
Mammalian cells:				
Fischer rat embryo cells	Gene mutation	No data	–	Mishra et al. 1978
Mouse lymphoma L5178Y/TK$^{+/-}$	Gene mutation	(+)	No data	Amacher and Turner 1980
Mouse lymphoma L5178/TK$^{+/-}$	Gene mutation	–	No data	Amacher et al. 1980
Human lymphoblasts TK6	Gene mutation	–	No data	Barfknecht et al. 1982
Human epithelial cells EUE	Gene mutation	No data	–	Rochhi et al. 1980
HeLa cells/unscheduled DNA synthesis	DNA damage	–	–	Martin et al. 1978
Human skin fibroblasts	DNA damage	No data	–	Milo et al. 1978
Rat liver cells RL1	Chromosome aberrations	No data	–	Dean 1981
Rat liver cells ARL18	Sister chromatid exchange	No data	–	Tong et al. 1981
Hamster BHK21 clone 13	Transformation	–	No data	Greb et al. 1980
Syrian hamster embryo cells	Transformation	No data	–	Dunkel et al. 1981
Mouse C3H/10T1/2 clone 8	Transformation	No data	–	Dunkel et al. 1981
Mouse Balb/3T3 cells	Transformation	No data	–	Lubet et al. 1983b; Peterson et al. 1981
Fischer rat embryo cells	Transformation	No data	–	Mishra et al. 1978
Fischer rat embryo cells/leukemia virus transformation	Transformation	No data	–	Dunkel et al. 1981
	BENZ[a]ANTHRACENE			
Prokaryotic organisms:				
S. typhimurium	Gene mutation	+	–	Norpoth et al. 1984; Simmon 1979a

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
S. typhimurium	Gene mutation	+	No data	Bos et al. 1988; Carver et al. 1986; Coombs et al. 1976; Hermann 1981; Pahlman and Pelkonen 1987
S. typhimurium	Gene mutation	+[a]	No data	Phillipson and Ioannides 1989
S. typhimurium	Gene mutation	–[b]	No data	Phillipson and Ioannides 1989
S. typhimurium	Gene mutation	–	–	Rosenkranz and Poirier 1979
E. coli/Pol A	DNA damage	–	–	Rosenkranz and Poirier 1979
E. coli SOS chromotest	DNA damage	+	–	Mersch-Sundermann 1992a
E. coli SOS chromotest	DNA damage	+	No data	Mersch-Sundermann 1992a
Eukaryotic organisms: Fungi: *S. cerevisiae* D3	Mitotic recombination	–	–	Simon 1979b
Mammalian cells:				
Mouse lymphoma L5178Y/TK$^{+/-}$	Gene mutation	+	No data	Amacher et al. 1980
Mouse lymphoma L5178Y/TK$^{+/-}$	Gene mutation	+	–	Amacher and Turner 1980; Amacher and Paillet 1982
Mouse lymphoma L5178Y/TK$^{+/-}$	Gene mutation	–	–	Amacher and Paillet 1983
Chinese hamster V79	Gene mutation	–	–	Huberman 1975
Chinese hamster V79	Gene mutation	–	No data	Huberman 1975
Human lymphoblasts TK6	Gene mutation	+	No data	Barfknecht et al. 1982
Human epithelial cells EUE	Gene mutation	No data	–	Rochhi et al. 1980
Human keratinocytes	Gene mutation	No data	–	Allen-Hoffmann and Rheinwald 1984
HeLa cells/unshceduled DNA synthesis	DNA damage	+	No data	Martin et al. 1978

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
Rat liver cells ARL18	Sister chromatid exchange	No data	(+)	Tong et al. 1981
Hamster BHK21 clone 13	Transformation	+	No data	Greb et al. 1980
Hamster embryo cells	Transformation	No data	(+)	DiPaolo et al. 1969, 1971
Hamster embryo cells	Transformation	–	No data	Grover et al. 1971
Syrian hamster embryo cells	Transformation	No data	+	Dunkel et al. 1981
Syrian hamster lung cells FSHL	Transformation	No data	+	Emura et al. 1980
Mouse ventral prostate C3H clone G23	Transformation	No data	–	Grover et al. 1971; Marquardt et al. 1972
Mouse Balb/3T3 cells	Transformation	No data	(+)	Dunkel et al. 1981
Fischer rat embryo cells/leukemia virus transformation	Transformation	No data	+	Dunkel et al. 1981
	BENZO[b]FLUORANTHENE			
Prokaryotic organisms:				
S. typhimurium	Gene mutation	+	No data	Amin et al. 1984; Hermann 1981; LaVoie et al. 1979
S. typhimurium	Gene mutation	–	No data	Mossanda et al. 1979
S. typhimurium/fluctuation test	Gene mutation	–	No data	Mossanda et al. 1979
E. coli PQ37 SOS chromotest	DNA damage	+	–	Mersch-Sundermann et al. 1992b
Mammalian cells:				
Chinese hamster V79	Gene mutation	–	–	Huberman 1975
Hamster BHK21 clone 13	Transformation	+	No data	Greb et al. 1980
Syrian hamster lung cells FSHL	Transformation	No data	+	Emura et al. 1980

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
BENZO[j]FLUORANTHENE				
Prokaryotic organisms:				
S. typhimurium	Gene mutation	+	No data	LaVoie et al. 1979
S. typhimurium/fluctuation test	DNA binding	+	No data	Marshall et al. 1992; Weyand et al. 1992
S. typhimurium/fluctuation test	Gene mutation	+	+	Marshall et al. 1993
E. coli SOS chromotest	DNA damage	+	No data	Mersch-Sundermann et al. 1992b
BENZO[k]FLUORANTHENE				
Prokaryotic organisms:				
S. typhimurium	Gene mutation	+	No data	Amin et al. 1985b; LaVoie et al. 1979; LaVoie et al. 1980; Weyand et al. 1988
Mammalian cells:				
Syrian hamster lung cells FSHL	Transformation	No data	–	Emura et al. 1980
BENZO[g,h,i]PERYLENE				
Prokaryotic organisms:				
S. typhimurium	Gene mutation	+	–	Andrews et al. 1978; Sakai et al. 1985
S. typhimurium	Gene mutation	+	No data	Carver et al. 1986; LaVoie et al. 1979; Mossanda et al. 1979
S. typhimurium/fluctuation test	Gene mutation	(+)	No data	Mossanda et al. 1979
E. coli SOS chromotest	DNA damage	+	–	Mersch-Sundermann et al. 1992a
E. coli SOS chromotest	DNA damage	+	No data	Mersch-Sundermann et al. 1992b
BENZO[a]PYRENE				

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
Prokaryotic organisms:				
S. typhimurium	Gene mutation	+	–	Glatt et al. 1987; Grolier et al. 1989; Prasanna et al. 1987; Rosenkranz and Poirier 1979; Sakai et al. 1985; Simmon 1979a
S. typhimurium	Gene mutation	+	No data	Alfheim and Randahl 1984; Alzieu et al. 1987; Ampy et al. 1988; Andrews et al. 1989; Antignac et al. 1990; Bos et al. 1988; Bruce and Heddle 1979; Carver et al. 1986; Hermann 1981; LaVoie et al. 1979; Lee and Lin 1988; Marino 1987; Norpoth et al. 1984; Pahlman and Pelkonen 1987
S. typhimurium	Gene mutation	+	No data	Phillipson and Ioannides 1989a
S. typhimurium	Gene mutation	–	No data	Gao et al. 1991
S. typhimurium	Gene mutation	–	No data	Phillipson and Ioannides 1989b
S. typhimurium TM677	Gene mutation	+	–	Rastetter et al. 1982
S. typhimurium TM677	Gene mutation	+	No data	Babson et al. 1986
S. typhimurium	Gene mutation	+	No data	Balansky et al. 1994
E. coli WP2-WP100/rec-assay	DNA damage	+	No data	Mamber et al. 1983
E. coli/PoLA		+	–	Rosenkranz and Poirier 1979
E. coli/differential killing	DNA damage	+	–	Tweats 1981
E. coli/SOS chromotest	DNA damage	+	–	Mersch-Sundermann et al. 1992b
Eukaryotic organisms: Fungi: *S. cerevisiae* D3	Mitotic recombination	–	–	Simmon 1979b
S. cerevisiae D4-RDII	Mitotic recombination	No data	–	Siebert et al. 1981

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
Animal systems:				
Chinese hamster V79	Gene mutation	+	No data	Arce et al. 1987; Diamond et al. 1980; Huberman 1975
Chinese hamster V79	Gene mutation	+	–	Huberman 1975
Chinese hamster CHO	Gene mutation	+	(+)	Gupta and Singh 1982
Fischer rat embryo cells/OUA®	Gene mutation	No data	+	Mishra et al. 1978
Mouse lymphoma L5178Y/TK$^{+/-}$	Gene mutation	+	–	Amacher and Paillet 1983; Clive et al. 1979
Mouse lymphoma L5178Y/TK$^{+/-}$	Gene mutation	+	No data	Amacher et al. 1980; Amacher and Turner 1980; Arce et al. 1987
Mouse lymphoma L5178Y/HGPRT	Gene mutation	(+)	No data	Clive et al. 1979
Human lymphoblasts AHH	Gene mutation	No data	+	Crespi et al. 1985
Human lymphoblasts TK6	Gene mutation	(+)	No data	Crespi et al. 1985
Human lymphoblasts	Gene mutation	+	No data	Danheiser 1989
Human epithelial cells EUE	Gene mutation	No data	+	Barfknecht et al. 1982; Rocchi et al. 1980
Human fibroblasts HSC172	Gene mutation	+	–	Gupta and Goldstein 1981
Human keratinocytes	Gene mutation	No data	+	Allen-Hoffmann and Rheinwald 1984
Rat hepatocytes/DNA repair	DNA damage	No data	+	Williams et al. 1982
Rat tracheal epithelial cells	DNA damage	No data	+	Cosma and Marchock 1988; Cosma et al. 1988
Mouse C3H/10T1/2 clone 8	DNA damage	No data	(+)	Lubet et al. 1983b
HeLa cells/unscheduled DNA synthesis	DNA damage	+	NR	Martin et al. 1978
Human skin fibroblasts	DNA damage	No data	+	Milo et al. 1978
Human mammary cells	DNA damage	No data	+	Leadon et al. 1988

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
Human fibroblasts/unscheduled DNA synthesis	DNA damage	+	No data	Agrelo and Amos 1981
Human fibroblasts WI-38/unscheduled DNA synthesis	DNA damage	+	–	Robinson and Mitchell 1981
Human lymphocyte	DNA damage	No data	+	Wienke et al. 1990
Calf thymus DNA	DNA binding	+	No data	Cavalieri et al. 1988a
Chick embryo fibroblasts	DNA binding	No data	+	Liotti et al. 1988
Chick embryo hepatocytes	DNA binding	No data	+	Liotti et al. 1988
Chinese hamster V79	DNA binding	No data	No data	Arce et al. 1987
Mouse lymphoma L5178Y/TK$^{+/-}$	DNA binding	+	No data	Arce et al. 1987
Mouse C3H/10T1/2	DNA binding	+	No data	Arce et al. 1987
Syrian hamster embryo SHE	DNA binding	No data	+	Arce et al. 1987
Rat bladder epithelial cells	DNA binding	No data	+	Moore et al. 1982
Rat mammary epithelial cells	DNA binding	No data	+	Moore et al. 1987
Human liver HepG2 cells	DNA binding	No data	+	Diamond et al. 1980
Human mammary cells	DNA binding	No data	+	Leadon et al. 1988; Moore et al. 1987
Human bladder cells	DNA binding	No data	+	Moore et al. 1982
Human endometrial cells	DNA binding	No data	+	Dorman et al. 1981
Human bronchus cells	DNA binding	No data	+	Harris et al. 1984
Human colon cells	DNA binding	No data	+	Harris et al. 1984
Human lymphocytes	DNA binding	No data	+	Pavanello and Levis 1992

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
Chinese hamster V79-4	Chromosome aberrations	–	–	Popescu et al. 1977
Chinese hamster CHL	Chromosome aberrations	+	–	Matsuoka et al. 1979
Mouse lymphoma L5178Y/TK$^{+/-}$	Chromosome aberrations	+	No data	Arce et al. 1987
Rat liver cells RL1	Chromosome aberrations	No data	+	Dean 1981
Human fibroblasts WI-38	Chromosome aberrations	+	–	Weinstein et al. 1977
Chinese hamster V79	Sister chromatid exchange	+	No data	Arce et al. 1987; Mane et al. 1990
Chinese hamster V79	Sister chromatid exchange	+	–	Popescu et al. 1977; Wojciechowski et al. 1981
Chinese hamster bone marrow	Sister chromatid exchange	No data	+	Roszinsky-Kocher et al. 1979
Chinese hamster Don-6	Sister chromatid exchange	No data	+	Abe et al. 1983b
Chinese hamster CHO	Sister chromatid exchange	+	–	Husgafvel-Pursiainen et al. 1986
Rat pleural mesothelial cells	Sister chromatid exchange	No data	+	Achard et al. 1987
Rat liver cells ARL18	Sister chromatid exchange	No data	+	Tong et al. 1981
Rat hepatoma Reuber H4-II-E	Sister chromatid exchange	No data	+	Dean et al. 1983a
Rat esophageal tumor R1	Sister chromatid exchange	No data	+	Abe et al. 1983b
Rat ascites hepatoma AH66-B	Sister chromatid exchange	No data	+	Abe et al. 1983b
Human fibroblasts TIG-II	Sister chromatid exchange	+	(+)	Huh et al. 1982
Human hepatoma C-HC-4	Sister chromatid exchange	No data	+	Abe et al. 1983a, 1983b
Human hepatoma C-HC-20	Sister chromatid exchange	No data	+	Abe et al. 1983a, 1983b
Human lymphocyte	Sister chromatid exchange	+	–	Lo Jacono et al. 1992
Human lymphocyte	Sister chromatid exchange	No data	+	Wienke et al. 1990

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
Golden hamster embryo cells	Transformation	+	No data	Mager et al. 1977
Hamster BHK21 clone 13	Transformation	+	–	Greb et al. 1980
Hamster embryo cells/SA7 virus transformation	Transformation	No data	+	Casto et al. 1977
Syrian hamster embryo cells	Transformation	No data	+	DiPaolo et al. 1969, 1971; Dunkel et al. 1981
Syrian hamster embryo cells/focus assay	Transformation	No data	+	Casto et al. 1977
Syrian hamster lung FSHL	Transformation	No data	+	Emura et al. 1980, 1987
Syrian hamster SHE/SA7 virus transformation	Transformation	No data	+	Arce et al. 1987
Mouse C3H/10T1/2	Transformation	No data	+	Arce et al. 1987; Lubet et al. 1983b; Peterson et al. 1981
Mouse Balb/3T3	Transformation	No data	+	Dunkel et al. 1981
Mouse Balb/3T3 clone A31-1-1	Transformation	No data	+	Little and Vetroys 1988
Fischer rat embryo cells	Transformation	No data	+	Mishra et al. 1978
Rat embryo cells/SA7 virus transformation	Transformation	No data	+	DiPaolo and Casto 1976
Fischer rat embryo cells/leukemia virus transformation	Transformation	No data	+	Dunkel et al. 1981
Human breast cancer cells	Gene expression	+	No data	Moore et al. 1994
Human breast epithelial cells	Transformation	No data	+	Calaf et al. 1993
Rat heptocyte	Sister chromatid exchange	+	No data	Kulka et al. 1993
Chinese hamster cells	Sister chromatid exchange	No data	+	Kulka et al. 1993

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
Mouse Balb/c-3T3 cells	Transformation	No data	+	Matthews 1994
Hamster tracheal cells	DNA damage	No data	+	Roggeband et al. 1994
Rat tracheal cells	DNA damage	No data	+	Roggeband et all. 1994
		BENZO[e]PYRENE		
Prokaryotic organisms:				
S. typhimurium	Gene mutation	+	No data	Andrews et al. 1978
S. typhimurium	Gene mutation	(+)	No data	Wood et al. 1979b
S. typhimurium	Gene mutation	+[c]	No data	Wood et al. 1979b
S. typhimurium	Gene mutation	+	No data	LaVoie et al. 1979b
E. coli SOS chromotest	DNA damage	+	No data	Mersch-Sundermann et al. 1992b
E. coli SOS chromotest	DNA damage	(+)	–	Mersch-Sundermann et al. 1992a
Mammalian cells:				
Chinese hamster V79 ovary cells	Sister chromatid exchange	–	No data	Mane et al. 1990
Prokaryotic organisms:				
S. typhimurium	Gene mutation	+	–	Sakai et al. 1985
S. typhimurium	Gene mutation	+	No data	Bos et al. 1988; Carver et al. 1986; Hermann 1981; LaVoie et al. 1979; Pahlman and Pelkonen 1987
S. typhimurium	Gene mutation	(+)	No data	Wood et al. 1977
S. typhimurium	Gene mutation	–	–	Rosenkranz and Poirier 1979; Simmon 1979a
E. coli/PolA	DNA damage	–	–	Rosenkranz and Poirier 1979
E. coli SOS chromotest	DNA damage	+	–	Mersch-Sundermann et al. 1992a
E. coli SOS chromotest	DNA damage	+	No data	Mersch-Sundermann et al. 1992b

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
Eukaryotic organisms:				
Fungi: *S. cerevisiae* D3	Mitotic recombination	–	–	Simmon 1979b
S. cerevisiae D4-RDII	Mitotic recombination	No data	–	Siebert et al. 1981
Mammalian cells:				
Chinese hamster V79	Gene mutation	–	No data	Huberman 1975
Human lymphoblasts TK6	Gene mutation	+	No data	Barfknecht et al. 1982
Human ephithelial cells EUE	Gene mutation	No data	–	Rocchi et al. 1980
Hamster BHK21 clone 13	Tranformation	+	No data	Greb et al. 1980
Mouse ventral prostrate C3H clone G23	Transformation	No data	–	Marquardt et al. 1972
	DIBENZ[a,h]ANTHRACENE			
Prokaryotic organisms: *S. typhimurium*	Gene mutation	+	No data	Andrews et al. 1978; Carver et al. 1986; Hermann 1981; Lecoq et al. 1991b; Pahlman and Pelkonen 1987; Wood et al. 1978
S. typhimurium	Gene mutation	–[a,b]	No data	Phillipson and Ioannides 1989
E. coli SOS chromotest	DNA damage	+	–	Mersch-Sundermann et al. 1992a
E. coli SOS chromotest	DNA damage	+	No data	Mersch-Sundermann et al. 1992b
Eukaryotic organisms: Fungi: *Neurospora crassa*	Gene mutation	No data	+	Barrat and Tatam 1958
S. cerevisiae D4-RDII	Mitotic recombination	No data	–	Siebert et al. 1981
Mammalian cells:				
Chinese hamster V79	Gene mutation	(+)	No data	Huberman 1975
Human epithelial cells EUE	Gene mutation	No data	(+)	Rocchi et al. 1980

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
HeLa cells/unscheduled DNA synthesis	DNA damage	+	NR	Martin et al. 1978
Human bronchus cells	DNA binding	No data	+	Harris et al. 1984
Hamster embryo cells	Transformation	–	No data	Grover et al. 1971
Hamster embryo cells/SA7 virus transformation	Transformation	No data	+	Casto 1973; Casto et al. 1977
Syrian hamster embryo cells	Transformation	No data	+	DiPaolo et al. 1969
Syrian hamster embryo cells/focus assay	Transformation	No data	+	Casto et al. 1977
Hamster BHK21 clone 13	Transformation	+	–	Greb et al. 1980
Mouse ventral prostate C3H clone G23	Transformation	No data	–	Marquardt et al. 1972
Mouse C3H/10T$^{1/2}$ clone 8	Transformation	No data	(+)	Lubet et al. 1983b
Rat embryo cells/SA7 virus transformation	Transformation	No data	+	DiPaolo and Casto 1976
Prokaryotic organisms:				
S. typhimurium	Gene mutation	+	No data	Bos et al. 1988; Carver et al. 1986; Hermann 1981; LaVoie et al. 1979
S. typhimurium	Gene mutation	(+)	No data	Bos et al. 1987
S. typhimurium	Gene mutation	–	No data	Mossanda et al. 1979
S. typhimurium/fluctuation test	Gene mutation	+	No data	Mossanda et al. 1979
S. typhimurium/fluctuation test	Gene mutation	+	–	Bhatia et al. 1987
S. typhimurium/taped plate assay	Gene mutation	+	–	Bos et al. 1987
S. typhimurium TM 677	Gene mutation	+	–	Rastetter et al. 1982

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
S. typhimurium TM 677	Gene mutation	+	No data	Babson et al. 1986
E. coli SOS chromotest	DNA damage	+	–	Mersch-Sundermann et al. 1992a
E. coli SOS chromotest	DNA damage	+	No data	Mersch-Sundermann et al. 1992b
Mammalian cells:				
Human lymphoblasts AHH1	Gene mutation	No data	–	Crespi et al. 1985
Human lymphoblasts TK6	Gene mutation	+	No data	Barfknecht et al. 1982
Chinese hamster CHO-1	Sister chromatid exchange	+	–	Palitti et al. 1986
Prokaryotic organisms:				
S. typhimurium	Gene mutation	–	–	Sakai et al. 1985
S. typhimurium	Gene mutation	–	No data	Bos et al. 1988; Hermann 1981; LaVoie et al. 1979; Pahlman and Pelkonen 1987
E. coli WP2-WP100/rec-assay	DNA damage	–	No data	Mamber et al. 1983
E. coli SOS chromotest	DNA damage	–	–	Mersch-Sundermann et al. 1992a
E. coli SOS chromotest	DNA damage	–	No data	Mersch-Sundermann et al. 1992b
Mammalian cells:				
Chinese hamster lung cell	Chromosome abberrations	+	–	Matsuoka et al. 1991
IDENO[1,2,3-c,d]PYRENE				
Prokaryotic organisms:				
S. typhimurium	Gene mutation	+	–	Rice et al. 1985b
S. typhimurium	Gene mutation	+	No data	LaVoie et al. 1979
E. coli SOS chromotest	DNA damage	+	–	Mersch-Sundermann et al. 1992a
E. coli SOS chromotest	DNA damage	+	No data	Mersch-Sundermann et al. 1992b

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
Mammalian cells:				
Syrian hamster lung cells FSHL	Transformation	No data	+	Emura et al. 1980
		PHENANTHRENE		
Prokaryotic organisms:				
S. typhimurium	Gene mutation	+	–	Sakai et al. 1985
S. typhimurium	Gene mutation	+	No data	Carver et al. 1986; Oesch et al. 1981
S. typhimurium	Gene mutation	(+)	No data	Bos et al. 1988
S. typhimurium	Gene mutation	–	–	LaVoie et al. 1981b; Rosenkranz and Poirier 1979; Simmon 1979a
S. typhimurium	Gene mutation	–	No data	Hermann 1981; LaVoie et al. 1979; Pahlman and Pelkonen 1987
E. coli/PolA	DNA damage	–	–	Rosenkranz and Poirier 1979
E. coli SOS chromotest	DNA damage	+	–	Mersch-Sundermann et al. 1992a
E. coli SOS chromotest	DNA damage	+	No data	Mersch-Sundermann et al. 1992b
Eukaryotic organisms:				
Fungi: *S. cerevisiae* D3	Mitotic recombination	–	–	Simmon 1979b
S. cerevisiae D4-RDII	Mitotic recombination	No data	–	Siebert et al. 1981
Mammalian cells:				
Fischer rat embryo cells	Gene mutation	No data	–	Mishra et al. 1978
Chinese hamster V79	Gene mutation	–	No data	Huberman 1975
Human lymphoblasts TK6	Gene mutation	(+)	No data	Barfknecht et al. 1982
Human skin fibroblasts	DNA damage	No data	–	Milo et al. 1978
Chinese hamster V79-4	Chromosome aberrations	–	–	Popescu et al. 1977

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
Chinese hamster Don	Chromosome aberrations	No data	–	Abe and Sasaki 1977
Chinese hamster CHL	Chromosome aberrations	No data	–	Ishidate and Odashima 1977
Chinese hamster CHL	Chromosome aberrations	–	–	Matsuoka et al. 1979
Chinese hamster V79-4	Sister chromatid exchange	–	–	Popescu et al. 1977
Chinese hamster Don	Sister chromatid exchange	No data	–	Abe and Sasaki 1977
Syrian hamster embryo cells	Transformation	No data	–	DiPaolo et al. 1969; Dunkel et al. 1981
Hamster BHK21 clone 13	Transformation	–	No data	Greb et al. 1980
Hamster embryo cells/SA7 virus transformation	Transformation	No data	–	Casto et al. 1977
Mouse ventral prostate C3H clone G23	Transformation	No data	–	Marquardt et al. 1972
Mouse C3H/10T$^{1/2}$	Transformation	No data	–	Lubet et al. 1983b; Peterson et al. 1981
Mouse Balb/3T3 cells	Transformation	No data	–	Dunkel et al. 1981
Fischer rat embryo cells	Transformation	No data	–	Mishra et al. 1978
Fischer rat embryo cells/leukemia virus transformation	Transformation	No data	–	Dunkel et al. 1981
Prokaryotic organisms:				
S. typhimurium	Gene mutation	+	–	Sakai et al. 1985
S. typhimurium	Gene mutation	+	No data	Bos et al. 1988
S. typhimurium	Gene mutation	–	No data	Carver et al. 1986; Hermann 1981; LaVoie et al. 1979
S. typhimurium/fluctuation test	Gene mutation	+	+	Bhatia et al. 1987
S. typhimurium/taped plate	Gene mutation	+	No data	Bos et al. 1988
E. coli WP2-WP100/rec-assay	DNA damage	–	No data	Mamber et al. 1983

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
E. coli/differential killing	DNA damage	–	–	Tweats 1981
E. coli/SOS chromotest	DNA damage	–	–	Mersch-Sundermann et al. 1992a
E. coli/SOS chromotest	DNA damage	–	No data	Mersch-Sundermann et al. 1992b
Mammalian cells:				
Fisher rat embryo cells	Gene mutation	No data	+	Mishra et al. 1978
Chinese hamster V79	Gene mutation	–	–	Huberman 1975
Chinese hamster V79	Gene mutation	–	No data	Huberman 1975
Mouse lymphoma L5178Y/TK$^{+/-}$	Gene mutation	–	No data	Amacher et al. 1980
Human lymphoblasts TK6	Gene mutation	–	No data	Barfknecht et al. 1982
HeLa cells/unscheduled DNA synthesis	DNA damage	–	–	Martin et al. 1978
Rat hepatocytes/DNA repair	DNA damage	No data	–	Williams et al. 1982
Human skin fibroblasts	DNA damage	No data	–	Milo et al. 1978
Human skin fibroblasts	DNA damage	–	No data	Agrelo and Amos 1981
Human fibroblasts WI-38 unscheduled DNA synthesis	DNA damage	+	–	Robinson and Mitchell 1981
Chinese hamster V79-4	Chromosome aberrations	+	–	Popescu et al. 1977
Human fibroblasts WI-38	Chromosome aberrations	–	–	Weinstein et al. 1977
Rat liver cells RL1	Chromosome aberrations	No data	–	Dean 1981
Chinese hamster V79-4	Sister chromatid exchange	–	–	Popescu et al. 1977
Rat liver cells ARL18	Sister chromatid exchange	No data	–	Tong et al. 1981
Syrian hamster embryo cells	Transformation	No data	–	DiPaolo et al. 1969
Fischer rat embryo cells	Transformation	No data	–	Mishra et al. 1978

TABLE 2-5. Genotoxicity of Polycyclic Aromatic Hydrocarbons *In Vitro (continued)*

Species (test system)	End point	Result		Reference
		With activation	Without activation	
Hamster embryo cells/SA7 virus transformation	Transformation	No data	–	Casto et al. 1977
		Chrysene		
Prokaryotic organisms: *S. typhimurium*	Gene mutation	+	No data	Glatt et al. 1993
S. typhimurium	Gene mutation	+	No data	Cheung et al. 1993

[a]Noninduced hamster S9
[b]Noninduced mouse, rat, pig and human S9
[c]Synthetically prepared diol epoxide was strongly mutagenic

AHH = aromatic hydrocarbon hydroxylase; CHO = Chinese hamster ovary; DNA = deoxyribonucleic acid; FSHL = female sex hormone lutenizing; NR = Not reported; PAHs = polycyclic hydrocarbons; SOS = DNA repair assay; – = negative result; + = positive result; (+) = weakly positive result

conjunction with the data from whole animal experiments, suggest that benzo[a]pyrene would probably have similar deleterious effects on human genetic material.

Because the genotoxic activity of benzo[a]pyrene is well established, it is frequently used as a positive control to demonstrate the sensitivity of various test systems to detect the genotoxic action of unknown compounds. It also serves as the model compound for PAHs, and the available information on the formation of metabolites and structure of benzo[a]pyrene can theoretically be used to predict potential genotoxicity/carcinogenicity of other PAHs that have not been as extensively studied.

Benzo[a]pyrene is generally considered to be biologically inert but can be metabolized by enzyme systems into at least 27 identified metabolites; however, only a few of these metabolites are reactive species that can damage DNA (De Bruin 1976). Benzo[a]pyrene 7,8-diol-9,10-epoxide is thought to be the ultimate mutagenic/carcinogenic metabolite. The primary metabolic pathway leading to the formation of the genotoxic/carcinogenic diol epoxides is assumed to be cytochrome P-450-dependent mixed-function oxidases (MFO), which in the case of PAHs are called AHHs. AHH is an ubiquitous enzyme system and has been found in a variety of tissues including liver, lung, and gastrointestinal tract of rats, mice, hamsters, and monkeys. AHH has also been detected in human liver, lung, placenta, lymphocytes, monocytes, and alveolar macrophages (Singer and Grunberger 1983). The evidence indicating that a variety of human tissues including human lymphocytes (GAO 1991; Wiencke et al. 1990), human lymphoblasts (Danheiser et al. 1989), and human mammary epithelial cells (Mane et al. 1990) can serve as a source of exogenous metabolic activation tends to support the role of AHH systems in initiating the conversion of benzo[a]pyrene to genotoxic forms. However, human erythrocytes, which do not contain an effective cytochrome P-450 system, were more efficient than induced rat liver fractions in converting benzo[a]pyrene to a genotoxin as indicated by higher sister chromatid exchange and micronuclei frequencies observed in human lymphocytes co-cultivated with human erythrocytes (Lo Jacono et al. 1992). The findings, while unconfirmed, suggest that enzymatic systems other than AHH may yield reactive intermediates. Similar evidence that uninduced lung, kidney, or spleen from Sprague-Dawley rats or BALB/c mice did not convert benzo[a]pyrene to a mutagen in *S. typhimurium* was reported by Ampy et al. (1988) who concluded that these tissues may, therefore, not be at risk from exposure. Superficially, the data from the studies conducted by Phillipson and Ioannides (1989) (indicating that neither benzo[a]pyrene nor benz[a]anthracene were mutagenic in *S. typhimurium* TA100 in the presence of noninduced hepatic fractions from rats, mice, pigs, or humans) would tend to support the data reported by Lo Jacono et al. (1992) and Ampy et al.

(1988) (suggesting either that other enzyme systems are involved in the bioactivation of these compounds or that certain tissues are not at risk). However, it is important to note, as pointed out by Phillipson and Ioannides (1989), that the level of P-450 isoenzyme proteins in unexposed animals is relatively low. Support for this statement was provided by the data demonstrating that uninduced hamster liver fractions, which contain high cytochrome P-448 levels, converted both benzo[a]pyrene and benz[a]anthracene to mutagens. By inference, it can reasonably be assumed that repeated exposures are required to induce the requisite enzyme systems to metabolize these promutagens to ultimate mutagenic/carcinogenic forms. It can further be assumed that the tissues of any species, including humans, that contain the appropriate inducible enzyme system are at risk.

The function of other enzyme systems in the biotransformation of benzo[a]pyrene should not be ruled out. However, the evidence that cytochrome P-448 plays a major role in this process was further substantiated by the observation that rat liver enzymes induced by PAHs such as 3-MC or dibenz[a,h]anthracene were more efficient in metabolizing benzo[a]pyrene, dibenz[a,h]anthracene, and benz[a]anthracene to mutagenic metabolites for *S. typhimurium* than was phenobarbital (Teranishi et al. 1975). This finding is consistent with the well-documented observation that various inducing agents such as phenobarbital and 3-MC cause the preferential synthesis of specific forms of cytochrome P-450. In the case of 3-MC, cytochrome P-448 is the principal form of induced cytochrome (Singer and Grunberger 1983).

Epoxidation is thought to be the major pathway for benzo[a]pyrene metabolism pertinent to macromolecular interaction. The metabolic attack consists of the cytochrome P-450/P-448-dependent MFO system converting the benzo[a]pyrene molecule into an epoxide; the epoxide is acted upon by epoxide hydrolase to form a dihydrodiol, and a second cytochrome MFO reaction gives rise to the ultimate mutagenic/carcinogenic form, benzo[a]pyrene 7,8-diol-9,10-epoxide. One of the unique structural features of the diol epoxide is that it appears to form in the area of the PAH molecule referred to as the bay region (i.e., a deep-pocketed area formed when a single benzo ring is joined to the remainder of the multiple ring system to form a phenanthrene nucleus). The location of the bay region(s) for the various PAHs in this profile is depicted in Chapter 3 (Table 3-1).

An additional feature of bay region diol epoxides is the ease of carbonium ion formation, which renders the PAH molecule highly reactive and susceptible to attack by nucleophiles (Jerina 1980; Singer and Grunberger 1983). The carbonium ion is more likely to form in structures where the

epoxide is part of the bay region of a saturated terminal angular ring than in an area where the diol epoxide is not associated with a bay region. Further enhancement of bay region epoxides can occur by the formation of an intramolecular hydrogen bond between the oxygen molecule of the epoxide and an associated hydroxyl group. These metabolites are also more resistant to enzymatic detoxification by epoxide hydrolase and glutathione transferase. The increased reactivity conferred by intramolecular hydrogen bonding and the decreased rate of further metabolism favor the interaction with DNA.

Analysis of the bay region diol epoxides and their contribution to the DNA binding, genotoxicity, and carcinogenicity of various PAHs has provided the basis for the bay region hypothesis (Wood et al. 1979a). For example, DNA adducts formed with non-bay region diol epoxides of benzo[a]pyrene have low mutagenic potential (MacLeod et al. 1994). The hypothesis further predicts that structures with more reactive bay regions would probably be more genotoxic and more carcinogenic. The body of evidence on the mutagenic and tumorigenic activity of the PAHs that form bay region diol epoxides (benzo[a]pyrene, benz[a]anthracene, chrysene, dibenz[a,h]anthracene; benzo[b]fluoranthene, benzo[j]fluoranthene, benzo[k]fluoranthene, and indeno[1,2,3-c,d]pyrene) supports this hypothesis.

Based on these considerations, the available genetic toxicology results from studies conducted with the other PAHs in this profile are discussed relative to the bay region hypothesis. It is cautioned, however, that while the use of structural relationships to predict potentially reactive compounds is a powerful tool, it is not infallible, nor does it replace *in vitro* or *in vivo* testing. The formation of bay region epoxides is not an absolute requirement for carcinogenic activity because several PAHs that cannot form bay region epoxides are known to be carcinogens. It can, nevertheless, serve as a warning system to alert regulatory agencies to a potential health hazard and to enable investigators to establish priority lists for testing PAHs.

There is no convincing evidence that the PAHs lacking a bay region structure (acenaphthene, acenaphthylene, and fluorene) are genotoxic; the results for acenaphthene and acenaphthylene are consistently negative. The induction of chromosome aberrations only, at a single dose in Chinese hamster lung cells exposed to fluorene (Matsuoka et al. 1991), is not sufficient to conclude that fluorene is a clastogen. However, none of these compounds have been extensively studied in *in vitro* assays, and they have not been tested *in vivo.*

The majority of the data for anthracene and pyrene were negative. Although isolated positive results were obtained, particularly in microbial systems, neither compound produced consistent genotoxic effects in mammalian cells *in vitro*, and both were negative in the limited *in vivo* studies that have been performed.

The results obtained with fluoranthene, the remaining PAH without a bay region configuration, illustrate the need to apply the bay region hypothesis judiciously. There is ample evidence indicating that fluoranthene induced gene mutations in bacteria and human lymphoblasts and sister chromatid exchange in Chinese hamster ovary cells. Based on the evidence of a powerful response in the *Escherichia coli* PQ37 SOS DNA repair assay (SOS chromotest), Mersch-Sundermann et al. (1992a) predicted that fluoranthene has a relatively high probability of being genotoxic (80%). However, fluoranthene did not induce sister chromatid exchanges in mouse bone marrow cells (Palitti et al. 1986). The work of Busby et al. (1984) in newborn mice, suggests that fluoranthene should be classified as a carcinogen.

The occurrence of a bay region structure on the phenanthrene molecule suggests that this compound is genotoxic. However, the overall findings from the genetic toxicology studies do not support such a prediction. Similarly, the reported observation that the intraperitoneal injection of phenanthrene resulted in sister chromatid exchange induction in Chinese hamster bone marrow cells was not convincing (Bayer 1979; Roszinsky-Kocher et al. 1979). In both studies, the sister chromatid exchange increase over background was less than 1.5 fold and comparable doses did not cause chromosome aberrations. As stated earlier, the occurrence of a bay region on the molecule in conjunction with the reactivity of the bay region appear to be the determinants of genotoxic/carcinogenic activity. It is, therefore, probable that the bay region on phenanthrene is not very reactive, which would account for the lack of genotoxicity and for the low carcinogenicity index (<2) assigned to this compound (Arcos et al. 1968). Similarly, quantum mechanical calculations indicate a low probability of carbonation formation for the bay region diol epoxide of phenanthrene (Jerina 1980).

The lack of genotoxicity for phenanthrene is thought to be related to the metabolism of this substance to its 9,10-dihydrodiol. However, specific methylated phenanthrenes, which direct the metabolic fate of this tricyclic hydrocarbon towards the formation of a classical bay region dihydrodiol epoxide, have exhibited significant genotoxicity (LaVoie et al. 1983a). It was demonstrated that the presence of a

methyl group at or adjacent to the K-region of phenanthrene can inhibit the formation of the 9,10-dihydrodiol and produce powerful mutagens in *Salmonella.* Additionally, the presence of a halogen at the K-region site produced similar results, which further support the association between inhibition of 9,10-dihydrodiol formation and mutagenic potency of substituted phenanthrenes. The study authors concluded that derivatives of phenanthrene that can inhibit metabolism at this site have a greater probability of exerting genotoxic effects. Additionally, methylated derivatives of phenanthrene may act as tumor initiators, as shown on mouse skin (LaVoie et al. 1981b).

The weight of evidence from the *in vitro* and *in vivo* studies conducted with benz[a]anthracene, dibenz[a,h]anthracene, and chrysene indicates that these three agents are genotoxic and that they exert their genotoxic effects through the binding of bay region diol epoxides to cellular DNA. Similarly, there is a substantive body of evidence that confirms the hypothesis implicating the formation of bay region diol epoxides as the major mechanism of action for both the genotoxicity and carcinogenicity induced by these PAHs (Cheung et al. 1993; Fuchs et al. 1993a, 1993b; Glatt et al. 1993; Lecoq et al. 1989, 1991a; Wood 1979). It is also of note that these three compounds, as well as benzo[a]pyrene, induced neoplastic cell transformation in at least one cell line (see Table 2-5).

Both benzo[b]fluoranthene and indeno[1,2,3-c,d]pyrene are known to exhibit mutagenic activity in *S. typhimurium* TA100 in the presence of rat liver homogenate (Amin et al. 1984; Hermann 1981; LaVoie et al. 1979; Rice et al. 1985b). Both of these agents were positive for *in vitro* cell transformation (Emura et al. 1980; Greb et al. 1980) and were shown to bind to mouse skin DNA *in vivo* (Hughes et al. 1993; Weyand 1989; Weyand et al. 1987). In addition, benzo[b]fluoranthene formed DNA adducts in the lungs and livers of adult rats (Ross et al. 1992) and newborn mice (Weyand et al. 1993b) and formed DNA adducts as well as induced sister chromatid exchange in peripheral blood lymphocytes of treated rats (Ross et al. 1992). These data are consistent with reports on the tumorigenic activity of these PAHs in rodents and their potential to act as carcinogens in humans.

Studies on the mutagenic activity of benzofilfluoranthene and benzo[k]fluoranthene have also indicated that these nonalternant PAHs are mutagenic in *S. typhimurium* TAl00 (Amin et al. 1985b; LaVoie et al. 1979, 1980a; Weyand et al. 1988, 1992). There is also evidence that application of either of these PAHs to mouse skin results in DNA adduct formation (Hughes et al. 1993; LaVoie et al. 1991a, 1991b; Weyand et al. 1987, 1993a). The relative extent of binding to mouse skin DNA (i.e.,

benzo[j]fluoranthene > benzo[k]fluoranthene) parallels the relative tumorigenic potency of these hydrocarbons on mouse skin (i.e., benzo[j]fluoranthene is more potent than benzo[k]fluoranthene as a tumor initiator) (LaVoie et al. 1982).

Benzo[g,h,i]perylene has been reported to be mutagenic in *S. typhimurium* and to cause DNA damage in *E. coli.* Benzo[g,h,i]perylene has been shown to be responsible for the formation of DNA adducts isolated after topical application of pharmaceutical grade coal tar to the skin of mice (Hughes et al. 1993). However, the few studies that were found were insufficient to draw meaningful conclusions.

The final compound in this group, benzo[e]pyrene, contains two equivalent bay regions. *In vivo,* benzo[e]pyrene induced a marginal increase in sister chromatid exchanges but did not cause structural chromosome aberrations in bone marrow cells harvested from Chinese hamsters receiving two daily intraperitoneal doses of 450 mg/kg (Roszinsky-Kocher et al. 1979). Similarly, sister chromatid exchange frequencies were not increased in V-79 cells co-cultivated with rat mammary epithelial cells as the source of exogenous metabolic activation (Mane et al. 1990). Benzo[e]pyrene was, however, reported to be weakly mutagenic in *S. typhimurium* (Andrews et al. 1978) and weakly genotoxic in the *E. coli* SOS chromotest (Mersch-Sundermann et al. 1992a, 1992b).

The weak genotoxicity and the very weak carcinogenicity of benzo[e]pyrene appear to contradict the bay region diol epoxide hypothesis. Quantum mechanical analysis of the ringed structure strongly suggests the likelihood of carbonium ion formation and an associated chemical reactivity equivalent to the bay region diol epoxide of dibenz[a,h]anthracene (Wood et al. 1979a). Similarly, synthetically prepared bay region tetrahydro-epoxides of benzo[e]pyrene were found to be highly mutagenic in bacteria and mammalian cells, suggesting that bay region diol epoxide(s), if formed, would also be mutagenic. However, the parent compound was not metabolized to a reactive state by Aroclor 1254 S9 or by purified cytochrome P-450 derived from rat livers induced with Aroclor 1254. From these results, Wood et al. (1979a) concluded that the lack of mutagenicity for benzo[e]pyrene may be associated with the failure of the cytochrome P-450-dependent monooxygenase system to catalyze the critical oxidations necessary to form the bay region diol. Specifically, there was very little formation of the bay region 9,10-dihydrodiol and low conversion of authentic 9,10-dihydrodiol to the bay region diol epoxide. Subsequent studies with authentic bay region diol epoxides of benzo[e]pyrene showed that they had relatively low mutagenic and tumorigenic activity as a result of the diaxial conformation of the diol. The diaxial conformation of the 9,10-dihydrodiol also provides an explanation for the low

formation of the bay region diol epoxide since metabolism is shifted away from the adjacent isolated double bond (Chang et al. 1981; Wood et al. 1980). Since structural-activity analysis suggests that the bay region diol epoxides would have biological activity, Wood et al. (1979a) caution that extrapolation of these findings to *in vivo* metabolic events in species other than rats should be approached with caution. It is conceivable that benzo[e]pyrene would be genotoxic in species capable of carrying out the appropriate enzymatic steps.

In summary, several general conclusions can be reached for the unsubstituted PAHs evaluated in this profile. The formation of diol epoxides that covalently bind to DNA appears to be the primary mechanism of action for both genotoxicity and carcinogenicity of several of the unsubstituted PAHs that are genotoxins (benzo[a]pyrene, benz[a]anthracene, dibenz[a,h]anthracene, chrysene, benzo[b]fluoranthene, benzo[j]fluoranthene). There was insufficient evidence to draw meaningful conclusions regarding the genotoxic potential of benzo[g,h,i]perylene, although some evidence does exist.

With regard to the unsubstituted PAHs that either lack a bay region configuration (acenaphthene, acenaphthylene, anthracene, fluorene, and pyrene) or appear to have a weakly reactive bay region (phenanthrene), there is no compelling evidence to suggest that they interact with or damage DNA. The five PAHs that appear to be exceptions to the bay region diol epoxide hypothesis are fluoranthene, benzo[k]fluoranthene, benzo[j]fluoranthene, and indeno[1,2,3-cd]pyrene (no bay region), and benzo[e]pyrene (two bay regions). The evidence does suggest, however, that fluoranthene possesses genotoxic properties while benzo[e]pyrene is either weakly mutagenic or nonmutagenic.

Cancer. Evidence exists to indicate that mixtures of PAHs are carcinogenic in humans. The evidence in humans comes primarily from occupational studies of workers exposed to mixtures containing PAHs as a result of their involvement in such processes as coke production, roofing, oil refining, or coal gasification (e.g., coal tar, roofing tar, soot, coke oven emissions, soot, crude oil) (Hammond et al. 1976; Lloyd 1971; Maclure and MacMahon 1980; Mazumdar et al. 1975; Redmond et al. 1976; Wynder and Hoffmann 1967). PAHs, however, have not been clearly identified as the causative agent. Cancer associated with exposure to PAH-containing mixtures in humans occurs predominantly in the lung and skin following inhalation and dermal exposure, respectively. Some ingestion of PAHs is likely because of swallowing of particles containing PAHs subsequent to mucocilliary clearance of these particulates from the lung.

Certain PAHs are carcinogenic to animals by the oral route (e.g., benz[a]anthracene, benzo[a]pyrene, and dibenz[a,h]anthracene) (Berenblum and Haran 1955; Chu and Malmgren 1965; Klein 1963; McCormick et al. 1981; Neal and Rigdon 1967; Rigdon and Neal 1966; Snell and Stewart 1963; Spamins et al. 1986; Wattenberg and Leong 1970). The results of dermal studies indicate that benz[a]anthracene, benzo[a]pyrene, benzo[b]fluoranthene, benzo[j]fluoranthene, benzo[k]fluoranthene, chrysene, dibenz[a,h]anthracene, and indeno[1,2,3-c,d]pyrene are tumorigenic in mice following dermal exposure (Albert et al. 1991b; Cavalieri 1988b; Habs et al. 1984; Levin et al. 1984; Warshawsky and Barkley 1987; Wilson and Holland 1988; Wynder and Hoffmann 1959b). The sensitivity of mouse skin to PAH tumorigenesis forms the basis for the extensive studies performed using dermal administration. This tumorigenicity can be enhanced or modified with concomitant exposure to more than one PAH, long straight-chain hydrocarbons (i.e., dodecane), or similar organic compounds commonly found at hazardous waste sites. Thus, humans exposed to PAHs in combination with these substances could be at risk for developing skin cancer.

For many of the carcinogenic PAHs discussed in this profile, it appears that the site of tumor induction is influenced by the route of administration and site of absorption, i.e., forestomach tumors are observed following ingestion, lung tumors following inhalation, and skin tumors following dermal exposure. However, the observations (discussed below) that (1) mammary tumors are induced following intravenous injection in Sprague-Dawley rats, (2) the susceptibility to tumor development on the skin after dermal application is not similar in rats and mice, and (3) oral cavity tumors are not observed when benzo[a]pyrene is administered in the diet, suggest that the point of first contact may not always be the site of PAH-induced tumors. The results of carcinogenicity studies conducted with the 17 PAHs discussed in this profile by parenteral routes of exposure are summarized in Table 2-6.

TABLE 2-6. Summary of Carcinogenicity Studies with Polycyclic Aromatic Hydrocarbons Using Parenteral Routes of Exposure

Chemical	Species	Route	Duration	Result/Site	Reference
Anthracene	Rat	Lung implantation	1 dose, 55-week observation	–	Stanton et al. 1972
	Newborn mouse	Subcutaneous	Single dose	–/lung	Platt et al. 1990
	Rat	Intrapulmonary	Single dose	+/lung	Deutsch-Wenzel et al. 1983
Benz[a]anthracene	Mouse	Subcutaneous	10 weeks	+/injection site	Boyland and Sims 1967
		Intramuscular	No data	+/fibrosarcomas, hemangioendotheliomas	Klein 1952
	Newborn mouse	Intraperitoneal	3 days	+/lung	Levin et al. 1984
	Hamster	Intratracheal	30 weeks	–	Sellakumar and Shubik 1974
Benzo[a]pyrene	Mouse	Subcutaneous	Single dose	+/injection site sarcomas	Pfeiffer 1977
	Newborn mouse	Intraperitoneal	Single dose	+/liver	LeVoie et al. 1987
	Newborn mouse	Intraperitoneal	No data	+/lung	Busby et al. 1984
	Rat	Intramammary	Single dose	+/mammary gland	Cavalieri et al. 1988b, 1988c
	Mouse	Intravaginal	5 months	+/cervix	Naslund et al. 1987
	Rat	Intrapulmonary	Single dose	+/lung	Deutsch-Wenzel et al. 1983
	Hamster	Intratracheal	Chronic	–	Kunstler 1983
	Rat	Tracheal implant	Intermediate	+/tracheal	Nettesheim et al. 1977
	Rat	Intrapulmonary	Single dose	+/lung	Iwagawa et al. 1989
	Newborn mouse	Subcutaneous	15 days	+/lung	Busby et al. 1989
	Rat	Intramammary	Single dose	+/mammary gland	Cavalieri et al. 1991
	Mouse	*In utero*	2 days	+/lung	Turusov et al. 1990
	Rat	Tracheal explant	Single dose	+/lung	Topping et al. 1981
	Rat	Intrapulmonary	Single dose	+/lung	Wenzel-Hartung et al. 1990
	Mouse	Intraperitoneal	Single dose	+/lung	Mass et all. 1993
	Hamster	Silastic implant	170 d	+/lung	Hammond and Benfield 1993
	Hamster	Intratracheal	1 time, for 6 weeks	+/lung	Kimizuka et al. 1993
Benzo[b]fluoranthene	Newborn mouse	Intraperitoneal	Single dose	+/liver	LaVoie et al. 1987
	Rat	Intrapulmonary	Single dose	+/lung	Deutsch-Wenzel et al. 1983
	Hamster	Intratracheal	30 weeks	–	Sellakumar and Shubik 1974
Benzo[e]pyrene	Rat	Tracheal explant	Single dose	–/trachea	Topping et al. 1981
	Rat	Intrapulmonary	Single dose	–/lung	Deutsch-Wenzel et al. 1983
Benzo[j]fluoranthene	Rat	Intrapulmonary	Single dose	+/lung	Deutsch-Wenzel et al. 1983
Benzo[g,h,i]perylene	Mouse	Subcutaneous	Single dose	–	IARC 1983
	Rat	Intrapulmonary	Single dose	+	Deutsch-Wenzel et al. 1983
Benzo[k]fluoranthene	Newborn mouse	Intraperitoneal	Single dose	–	LaVoie et al. 1987
	Rat	Intrapulmonary	Single dose	+/lung	Deutsch-Wenzel et al. 1983

TABLE 2-6. Summary of Carcinogenicity Studies with Polycyclic Aromatic Hydrocarbons Using Parenteral Routes of Exposure (continued)

Chemical	Species	Route	Duration	Result/Site	Reference
Anthracene	Rat	Lung implantation	1 dose, 55-week observation	–	Stanton et al. 1972
Chrysene	Newborn mouse	Intraperitoneal	No data	–	Buening et al. 1979a
	Newborn mouse	Intraperitoneal	Single dose, 70-week, week observation	+/liver	Grover et al. 1975
	Mouse	Subcutaneous	10 weeks	+/injection site tumors	Boyland and Sims 1967
	Rat	Intrapulmonary	Single dose	+/lung	Wenzel-Hartung et al. 1990
Dibenz[a,h]anthracene	Newborn mouse	Intraperitoneal	No data	+/lung	Buening et al. 1979b
	Mouse	Subcutaneous	10 weeks	+/injection site tumors	Boyland and Sims 1967
	Hamster	Intratracheal	30 weeks	–	Sellakumar and Shubik 1974
	Newborn mouse	Subcutaneous	Single dose	+/lung	Platt et al. 1990
	Newborn mouse	Subcutaneous	Single dose	+/injection site sarcoma	O'Gara et al. 1965
	Rat	Intrapulmonary	Single dose	+/lung	Wenzel-Hartung et al. 1990
Fluoranthene	Mouse	Intraperitoneal	15 days	+/lung	Busby et al. 1984
	Mouse	Intraperitoneal	3 doses in 15 days, 9-month observation	+/lung	Wang and Busby 1993
Fluorene	Mouse	Subcutaneous	Single dose	–	Roe 1962; Shear and Luter 1941; Steiner 1955
Ideno[1,2,3-c,d]pyrene	Newborn mouse	Intraperitoneal	Single dose	–	LaVoie et al. 1987
	Rat	Intrapulmonary	Single dose	+/lung	Deutsch-Wenzel et al. 1983
Phenanthrene	Newborn mouse	Intraperitoneal	No data	–	Buening et al. 1979a
	Rat	Intrapulmonary	Single dose	–/lung	Wenzel-Hartung et al. 1990
Pyrene	Hamster	Intratracheal	30 weeks	–	Sellakumar and Shubik 1974
	Newborn mouse	Subcutaneous	Single dose	–/lung	Busby et al. 1989

+ = increased incidence of tumors; – = no increase in tumor incidence

EPA has performed weight-of-evidence evaluations of several of the PAHs discussed in this profile. The carcinogenicity classifications currently verified by EPA's Carcinogenicity Risk Assessment Verification Endeavor Work Group (EPA 1994) are listed below:

PAH	EPA Classification
Acenaphthylene	D (not classifiable as to human carcinogenicity)
Anthracene	D
Benz[a]anthracene	B2 (probable human carcinogen)
Benzo[b]fluoranthene	B2
Benzo[k]fluoranthene	B2
Benzo[g,h,i]perylene	D
Benzo[a]pyrene	B2
Chrysene	B2
Dibenz[a,h]anthracene	B2
Fluoranthene	D
Fluorene	D
Indeno[1,2,3-c,d]pyrene	B2
Phenanthrene	D
Pyrene	D

A quantitative cancer risk estimate (i.e., cancer potency factor) has thus far been developed for benzo[a]pyrene only (EPA 1992). This cancer potency factor (q_1^*) is 7.3 per (mg/kg)/day and is based on the geometric mean of risk estimates calculated from the Neal and Rigdon (1967) and Brune et al. (1981) studies.

EPA and others have developed a relative potency estimate approach for the PAHs (EPA 1993a; Nisbet and LaGoy 1992). By using this approach, the cancer potency of the other carcinogenic PAHs can be estimated based on their relative potency to benzo[a]pyrene. Following are the toxicity equivalence factors (based on carcinogenicity) calculated for PAHs discussed in this profile considered by the authors of one of these approaches to be of most concern at hazardous waste sites (Nisbet and LaGoy 1992):

Compound	Toxicity Equivalency Factor (TEF)
Dibenz[a,h]anthracene	5
Benzo[a]pyrene	1
Benz[a]anthracene	0.1
Benzo[b]fluoranthene	0.1
Benzo[k]fluoranthene	0.1
Indeno[1,2,3-c,d]pyrene	0.1
Anthracene	0.01
Benzo[g,h,i]perylene	0.01
Chrysene	0.01
Acenaphthene	0.001
Acenaphthylene	0.001
Fluoranthene	0.001
Fluorene	0.001
Phenanthrene	0.001
Pyrene	0.001

EPA (1993) has derived the following relative potency estimates based on mouse skin carcinogenesis:

Compound	Relative Potency[a]
Benzo[a]pyrene	1.0
Benz[a]anthracene	0.145
Benzo[b]fluoranthene	0.167
Benzo[k]fluoranthene	0.020
Chrysene	0.0044
Dibenz[a,h]anthracene	1.11
Indeno[1,2,3-c,d]pyrene	0.055[b]

[a]Model was $P(d)=1-\exp[-a(1+bd)^2]$ for all but indeno[1,2,3-c,d]pyrene

[b]Simple mean of relative potencies (0.021 and 0.089); the latter derived using the one-hit model

2.5 BIOMARKERS OF EXPOSURE AND EFFECT

Biomarkers are broadly defined as indicators signaling events in biologic systems or samples. They have been classified as markers of exposure, markers of effect, and markers of susceptibility (NAS/NRC 1989).

A biomarker of exposure is a xenobiotic substance or its metabolite(s), or the product of an interaction between a xenobiotic agent and some target molecule(s) or cell(s) that is measured within a compartment of an organism (NRC 1989). The preferred biomarkers of exposure are generally the substance itself or substance-specific metabolites in readily obtainable body fluid(s) or excreta. However, several factors can confound the use and interpretation of biomarkers of exposure. The body burden of a substance may be the result of exposures from more than one source. The substance being measured may be a metabolite of another xenobiotic substance (e.g., high urinary levels of phenol can result from exposure to several different aromatic compounds). Depending on the properties of the substance (e.g., biologic half-life) and environmental conditions (e.g., duration and route of exposure), the substance and all of its metabolites may have left the body by the time samples can be taken. It may be difficult to identify individuals exposed to hazardous substances that are commonly found in body tissues and fluids (e.g., essential mineral nutrients such as copper, zinc, and selenium). Biomarkers of exposure to PAHs are discussed in Section 2.5.1.

Biomarkers of effect are defined as any measurable biochemical, physiologic, or other alteration within an organism that, depending on magnitude, can be recognized as an established or potential health impairment or disease (NAS/NRC 1989). This definition encompasses biochemical or cellular signals of tissue dysfunction (e.g., increased liver enzyme activity or pathologic changes in female genital epithelial cells), as well as physiologic signs of dysfunction such as increased blood pressure or decreased lung capacity. Note that these markers are not often substance specific. They also may not be directly adverse, but can indicate potential health impairment (e.g., DNA adducts). Biomarkers of effects caused by PAHs are discussed in Section 2.5.2.

A biomarker of susceptibility is an indicator of an inherent or acquired limitation of an organism's ability to respond to the challenge of exposure to a specific xenobiotic substance. It can be an intrinsic genetic or other characteristic or a preexisting disease that results in an increase in absorbed

dose, a decrease in the biologically effective dose;or a target tissue response. If biomarkers of susceptibility exist, they are discussed in Section 2.7, Populations That Are Unusually Susceptible.

2.5.1 Biomarkers Used to Identify or Quantify Exposure to Polycyclic Aromatic Hydrocarbons

PAHs and their metabolites can be measured in the urine of exposed individuals. In workers exposed to PAHs and dermatology patients treated with coal tar, the PAH metabolite 1-hydroxypyrene has been detected in the urine at concentrations of 0-40 µg/g creatinine or 290 ng/g creatinine, respectively (Jongeneelen et al. 1985). The amount of 1-hydroxypyrene detected in urine samples taken during the weekend was less than that detected during the weekdays, when the exposure was presumably higher than on the weekends. No correlation was found between occupational exposure levels and urine levels, so it is not known whether urinary metabolites could be detected following exposure to low levels of PAHs (as might be expected to occur in individuals living in the vicinity of hazardous waste sites). The presence of 1-hydroxypyrene in urine has also been demonstrated in workers exposed to PAHs in several different environments (creosote-impregnating plant, road workers laying asphalt, and workers exposed to diesel exhaust fumes) (Jongeneelen et al. 1988). In another study, the levels of urinary 1-hydroxypyrene significantly correlated with the environmental levels of pyrene and benzo[a]pyrene in coke plants, steel plants, and several Chinese cities where coal burning occurs (Zhao et al. 1990). The usefulness of monitoring urinary 1-hydroxypyrene concentration by liquid chromatography in occupationally exposed individuals as a biomarker for exposure to environmental PAHs was assessed. Postshift 1-hydroxypyrene urinary levels were significantly increased over preshift 1-hydroxypyrene levels in exposed workers as compared to nonexposed controls (the net mean change was 17-fold higher in the exposed workers as opposed to the nonexposed controls), and smoking status did not affect this result. In addition, in this work setting (an aluminum production plant), environmental levels of pyrene were strongly correlated with the environmental levels of total PAHs, indicating that pyrene is an appropriate environmental PAH marker in this situation. Thus, 1-Hydroxypyrene levels in urine may be used as a biomarker of exposure to PAHs in certain situations (Tolos et al. 1990). Additional studies have evaluated the usefulness of determining PAH or metabolite levels in human urine as a measure of exposure in industrial and environmental exposure settings (Granella and Clonfero 1993; Hansen et al. 1993; Herikstad et al. 1993; Kanoh et al. 1993; Likhachev et al. 1993; Ovrebo et al. 1994; Santella et al. 1993; Strickland et al. 1994; Van Hummelen et al. 1993; Van Rooij et al. 1993a, 1993b; Viau et al. 1993). Based on these results, the identification

of PAH metabolites in the urine could serve as a method of biological monitoring of exposed workers, and possibly individuals living in the vicinity of hazardous waste sites where PAHs have been detected although it would be very difficult to distinguish exposures resulting from hazardous waste sites form those resulting from normal human activities.

Autopsies performed on cancer-free patients found PAH levels of 11-2,700 ppt in fat samples. Several PAHs were detected, including anthracene, pyrene, benzo[e]pyrene, benzo[k]fluoranthene, benzo[a]pyrene, and benzo[g,h,i]perylene, with pyrene being detected in the highest concentrations (Obana et al. 1981). A similar study done on livers from cancer-free patients found levels of 6-500 ppt of all of the same PAHs except benzo[e]pyrene, which was not detected in the liver. As in the fat samples studies, pyrene appeared in the highest concentrations in the liver, but the overall levels were less than in fat (Obana et al. 1981). However, because of the ubiquitous nature of PAHs in the environment, detection of PAH metabolites in the body tissues or fluids is not specific for exposure to PAHs from hazardous waste sites. In addition, it is impossible to determine from these biological media whether exposure was to high or low levels of PAHs or if the exposure duration was acute, intermediate, or chronic. Benzo[a]pyrene and 1-nitropyrene were determined in excised lung samples from Chinese and Japanese cancer patients (Tokiwa et al. 1993). Exposure to the two marker compounds was from burning coal (Chinese, benzo[a]pyrene) or oil (Japanese, 1-nitropyrene). Compound levels in the lung correlated with individual exposure history. Using a large sample population, total PAH levels in lung tissue has also been shown to correlate to cancer incidence (Seto et al. 1993).

PAHs form DNA adducts that can be measured in body tissues or blood in both humans and laboratory animals following exposure to PAHs or mixtures containing PAHs (e.g., Assennato et al. 1993; Bjelogrlic et al. 1994; Chou et al. 1993; Culp and Beland 1994; Day et al. 1990; Fuchs et al. 1993a, 1993b; Garg et al. 1993; Garner et al. 1988; Gallagher et al. 1993; Herberg et al. 1990; Hughes and Phillips 1990; Hughes et al. 1993; Jones et al. 1993; Khanduja and Majid 1993; Lee et al. 1993; Lewtas et al. 1993; Likhachev et al. 1993; Lu et al. 1993; Mass et al. 1993; Mumford et al. 1993; Newman et al. 1988, 1990; Nowak et al. 1992; Oueslati et al. 1992; Roggeband et al. 1994; Ross et al. 1990, 1991; Shamshuddin and Gan 1988; Van Schooten et al. 1991, 1992; Weston et al. 1988, 1993a; Weyand et al. 1993a, 1993b). PAHs also form adducts with other cellular macromolecules, such as hemoglobin, globin, and other large serum proteins (e.g., Bechtold et al. 1991; Sherson et al. 1990; Weston et al. 1988). Again, these PAH-DNA and PAH-protein adducts are not specific for any

particular source of PAHs, and the adducts measured could have been from exposure to other sources of PAHs, such as complex mixtures that contain PAHs (e.g., crude oils, various high-boiling point distillates, complex petroleum products, coal tars, creosote, and the products of coal liquification processes), as well as vehicle exhausts, wild fires, agricultural burning, tobacco smoke, smoke from home heating of wood, cereals, grains, flour, bread, vegetables, fruits, meat, processed or pickled foods, beverages, and grilled meats. It is impossible to determine from these adducts whether exposure was to high or low levels of PAHs or if the exposure duration was short or long.

In another study, an evaluation of mutations in peripheral lymphocytes was conducted in workers in or near an iron foundry; data were examined for correlations to benzo[a]pyrene exposure determined by personal monitors. Exposure levels for benzo[a]pyrene were 2-60 ng/m^3, which are the lowest levels yet analyzed in foundry workers. Mutations at the hypoxanthine guanine phosphoribosyl transferase (HPRT) and glycophorin A (GPA) loci, which are measures of molecular effects in lymphocytes and erythrocytes, respectively, were assessed to demonstrate their relationship to external exposure at these low levels. The rate of mutation was also compared to PAH-DNA adducts in the blood (Santella et al. 1993). Workers were classified into three exposure categories, low (<5), medium (5-12), and high (>12). HPRT mutant frequencies for these groups were 1.04, 1.13, and 1 .82x10^{-6} cells, respectively, and demonstrated an upward trend that was marginally significant. In contrast, HPRT mutations were highly correlated with PAH-DNA adducts (Santella et al. 1993). GPA variants were not correlated with PAH exposure. These results support the use of both biomonitoring and personal environmental monitoring in the determination of exposure.

Three methods were evaluated for their usefulness as biomarkers of exposure to benzo[a]pyrene in Wistar rats administered a single dose of l-200 mg/kg (Willems et al. 1991). These three methods were mutagenicity observed in urine and fecal extracts, chromosome aberrations and sister chromatid exchanges in peripheral blood lymphocytes, and DNA adduct formation in peripheral blood lymphocytes and liver. Mutagens were measured in urine and feces at levels of 10 and 1 mg/kg, respectively. DNA adduct formation (measured by ^{32}P-postlabelling) could be detected at doses of ≥10 mg in lymphocytes and ≥100 mg in liver, and the levels were twice as high in the lymphocytes as in the liver. Only a slight increase in sister chromatid exchanges and no enhanced frequency of chromosomal aberrations were seen. These results indicate that mutagenicity observed in excreta and DNA adducts in lymphocytes are both useful biomarkers of exposure in the rat, with mutagenic activity in feces being the more sensitive.

The ability of phenanthrene, fluoranthene, pyrene, benz[a]anthracene, chrysene, benzo[a]pyrene, benzo[b]fluoranthene, benzo[j]fluoranthene, indeno[1,2,3-c,d]pyrene, and dibenz[a]anthracene to bind to mouse hemoglobin and serum proteins after tail vein injection was investigated (Singh and Weyand 1994). Urinary excretion of these compounds was also investigated. A direct correlation between urinary excretion and hydrocarbon molecular weight was observed. Binding to both globin and serum proteins was detectable, with binding to serum proteins 10-fold higher than to globin. These results provide an assessment of the potential usefulness of various PAHs as biomarkers of exposure to complex mixtures.

2.5.2 Biomarkers Used to Characterize Effects Caused by Polycyclic Aromatic Hydrocarbons

The available genotoxicity data indicate that several of the 17 PAHs discussed in this profile are genotoxic in both nonmammalian and mammalian systems and are indirect mutagens (i.e., requiring the presence of an exogenous mammalian metabolic system). There were no tests reported for humans exposed to benzo[a]pyrene (the most widely tested PAH) *in vivo*, but several types of cultured human tissue cells demonstrated positive results for benzo[a]pyrene-induced genotoxicity (as evidenced by the induction of chromosomal aberrations, sister chromatid exchange) and binding of benzo[a]pyrene to DNA. The measurement of DNA adduct formation as well as the induction of sister chromatid exchange in human lymphocytes has been proposed as a biomarker of benzo[a]pyrene-induced effects for human monitoring programs (Wiencke et al. 1990). It is probable, however, that the analysis of DNA adducts would be the more sensitive diagnostic tool since hundreds of benzo[a]pyrene-DNA adducts per nucleus would be required to yield a detectable increase in the sister chromatid exchange frequency for an exposed population. Although these results are exclusively from *in vitro* tests and the limited genotoxicity tests conducted on urine obtained from humans exposed to creosote (a complex mixture containing PAHs) have been negative, the genotoxic effects observed in human tissue cells, particularly DNA adduct formation, may serve as a biomarker of effects for at least one of the PAHs, benzo[a]pyrene. It would not be possible to identify the source.of the benzo[a]pyrene, however.

PAHs have been shown to cause noncancer adverse effects on rapidly proliferating tissues such as the hematopoietic system, the lymphoid system, and the skin in both humans and animals. The skin is susceptible to PAH-induced toxicity in both humans and animals. Regressive verrucae were reported following intermediate-duration application of benzo[a]pyrene to human skin (Cottini and Mazzone

1939). Although reversible and apparently benign, these changes were thought to represent neoplastic proliferation. Benzo[a]pyrene application also apparently exacerbated skin lesions in patients with pre-existing skin conditions (pemphigus vulgaris and xeroderma pigmentosum) (Cottini and Mazzone 1939). Workers exposed to substances that contain PAHs (e.g., coal tar) experienced chronic dermatitis and hyperkeratosis (EPA 1988a). However, none of these end points is specific to PAHs, and all can be seen with other agents. No other biomarkers of effect (specific or otherwise) have been identified following exposure to PAHs.

For more information on biomarkers for renal and hepatic effects of chemicals see ATSDR/CDC Subcommittee Report on Biological Indicators of Organ Damage (1990) and for information on biomarkers for neurological effects see OTA (1990). Additional information can be found in a series of reports on biomarkers issued by the National Research Council (NRC 1989, 1992).

2.6 INTERACTIONS WITH OTHER SUBSTANCES

Because humans are usually exposed to PAHs in complex mixtures rather than to individual PAHs, it is important to understand the potential interactions between the PAHs and other components of the mixture. Interactions may occur among chemicals in a mixture prior to exposure, or may occur after exposure as a result of differing effects of the mixture components on the body. Synergistic and/or antagonistic interactions with regard to the development of health effects, particularly carcinogenesis, may occur.

The extent of human exposures to PAH mixtures in occupational settings is generally not known in quantitative terms. However, exposures to complex chemical mixtures that include PAHs, such as use of tobacco products and exposure to roofing tar emissions, coke oven emissions, coal tar, and shale oils, have been associated with adverse health effects in humans. The biological consequences of human exposure to complex mixtures of PAHs depend on the interaction of the various strongly carcinogenic, weakly carcinogenic, or noncarcinogenic PAHs. For example, there is evidence to suggest that PAHs in cigarette smoke require other components in the smoke in order to exert their tumorigenic effect (Akin et al. 1976).

The interaction between noncarcinogenic and carcinogenic PAHs has been extensively examined in animals. Noncarcinogenic PAHs exhibit co-carcinogenic potential and tumor-initiating and promoting

activity when applied with benzo[a]pyrene to the skin of mice. Simultaneous administration of weakly carcinogenic or noncarcinogenic PAHs including benzo[e]pyrene, benzo[g,h,i]perylene, fluoranthene, or pyrene significantly elevated the benzo[a]pyrene-induced tumor incidence. Benzo[e]pyrene, fluoranthene, and pyrene were more potent co-carcinogens than benzo[g,h,i]perylene (Van, Duuren and Goldschmidt 1976; Van Duuren et al. 1973). Benzo[e]pyrene, fluoranthene, and pyrene have also demonstrated weak tumor-promoting activity following initiation with benzo[a]pyrene, and these compounds increased benzo[a]pyrene-DNA adduct formation (Di Giovanni et al. 1982; Lau and Baird 1992; Rice et al. 1984, 1988; Slaga et al. 1979; Smolarek et al. 1987; Van Duuren and Goldschmidt 1976; Van Duuren et al. 1973).

Interactions between selected noncarcinogenic PAHs and carcinogenic benzo[a]pyrene have also been documented to reduce the carcinogenic potential of benzo[a]pyrene in animals. Benzo[a]fluoranthene, benzo[k]fluoranthene, chrysene, perylene, and a mixture of anthracene, phenanthracene, and pyrene significantly inhibited benzo[a]pyrene-induced injection-site sarcomas. However, other PAHs including anthracene, benzo[g,h,i]perylene, fluorene, and indeno[1,2,3-c,d]pyrene had no antagonistic effects (Falk et al. 1964). Coexposure of tracheal explants to benzo[e]pyrene and benzo[a]pyrene resulted in an increased incidence of tracheal epithelial sarcomas over that seen with either PAH alone (Topping et al. 1981). Phenanthrene administration with benzo[a]pyrene decreased the DNA adduct formation in mice (Rice et al. 1984).

There is evidence to suggest that benz[a]anthracene may serve as an anticarcinogen when administered with benzo[a]pyrene. Coadministration of benz[a]anthracene and benzo[a]pyrene decreased benzo[a]pyrene metabolism, benzo[a]pyrene-DNA adduct formation, and reduced the mutagenic activity of benzo[a]pyrene on hamster embryo cells. It has been postulated that the antimutagenic effect of benz[a]anthracene results from competition with benzo[a]pyrene for MFO enzymes, rather than the induction of detoxifying enzymes (Smolarek et al. 1986).

The synergistic effect of individual PAHs on the mutagenicity of benzo[a]pyrene has also been demonstrated. Anthracene and benzo[e]pyrene enhanced the mutagenicity of benzo[a]pyrene, the maximal increase being obtained with anthracene. Benzo[e]pyrene (at a ratio of 2:l) had no effect on benzo[a]pyrene-induced mutation frequencies in V79 cells, but at a ratio of 15:1, benzo[e]pyrene inhibited the benzo[a]pyrene-induced mutations by approximately 10-fold. Benzo[e]pyrene inhibited the metabolism of benzo[a]pyrene by cultured hamster embryo only at high doses, but at both low and

high doses, the proportion of metabolites formed was altered by benzo[e]pyrene (Baird et al. 1984). The percentage of water-soluble metabolites was decreased, whereas the percentage of diols was increased. The authors postulated that benzo[e]pyrene alters the activity of other PAHs by inhibiting the conversion of the proximate carcinogenic diol of a particular PAH to a diol epoxide.

Benzo[a]pyrene and dibenz[a,h]anthracene in combination with 10 noncarcinogenic PAHs were less potent tumor-inducers than was dibenz[a,h]anthracene alone or in combination with benzo[a]pyrene. The noncarcinogenic or weakly carcinogenic PAHs include benzo[e]pyrene, phenanthrene, anthracene, pyrene, fluoranthene, chrysene, perylene, benzo[g,h,i]pyrene, and coronene. Dose-response relationships for tumor incidences were observed for benzo[a]pyrene and dibenz[a,h]anthracene either alone or in combination with the 10 noncarcinogenic PAHs; however, no treatment-related sarcoma incidences were observed for any of the 10 noncarcinogenic PAHs (Pfeiffer 1977).

Phenanthrene, a noncarcinogenic PAH, demonstrated a dose-related inhibition of dibenz[a,h]anthracene-induced carcinogenicity in mice. Phenanthrene significantly reduced the incidence of injection-site sarcomas elicited by dibenz[a,h]anthracene, especially at low doses. However, when triethylene glycol was the vehicle administered in combination with phenanthrene and dibenz[a,h]anthracene, a substantial increase (50%) in the rate of tumor induction was observed (Falk et al. 1964).

Several experiments have shown that most PAH mixtures are considerably less potent than individual PAHs. Various combustion emissions and benzo[a]pyrene have been examined for carcinogenic potency and tumor initiation activity on mouse skin. In all cases, PAH mixtures were much less potent than benzo[a]pyrene. The authors calculated relative potency estimates that ranged from 0.007 for coke oven emissions extract to less than 0.002 for diesel engine exhaust extract, using papillomas per mouse per milligram of the mixture as the end point (Slaga et al. 1980b). Another study demonstrated that the relative tumorigenicities, as compared to benzo[a]pyrene, of automobile exhaust .condensate (AEC), diesel emission condensate, and a representative mixture of carcinogenic PAHs were 0.0053, 0.00011, and 0.36, respectively, following chronic application to mouse skin (Misfeld 1980). AEC has also exhibited an antagonistic influence on benzo[a]pyrene carcinogenicity when subcutaneously administered to mice; this effect was particularly augmented at higher benzo[a]pyrene concentrations (Pott et al. 1977).

Carcinogenic and noncarcinogenic PAHs, comprising a quantitative fraction of automobile exhaust gas condensate, were selected for carcinogenicity testing via dermal exposure of female NMRI mice. The purpose was to identify interactions between mixtures of the carcinogenic and noncarcinogenic PAHs (Schmahl et al. 1977). The carcinogenic PAHs were benzo[a]pyrene, dibenz[a,h]anthracene, benz[a]anthracene, benzo[b]fluoranthene; and the noncarcinogenic PAHs were phenanthrene, anthracene, fluoranthene, pyrene, chrysene, benzo[e]pyrene, and benzo[g,h,i]perylene. Treatment was carried out twice a week, for the natural lifetime of the animals. Although the carcinogenic action observed could be attributed almost entirely to the action of the carcinogenic PAHs, in relatively small doses, addition of the noncarcinogenic PAHs did not inhibit carcinogenesis, but had an additive effect.

Predicting the toxicity of a complex mixture on the basis of one of several of its components may be misleading, because the interactions among the components may modify toxicity. Since PAHs require metabolic activation by monoxygenases to elicit carcinogenic effects, any alteration in these metabolic pathways will influence the observed toxicity. There are two primary mechanisms by which chemicals interact with PAHs to influence toxicity. A compound may compete for the same metabolic activating enzymes and thereby reduce the toxicity of carcinogenic PAHs, or it may induce the metabolizing enzyme levels to result in a more rapid detoxification of the carcinogenic PAHs (Levin et al. 1982). Chaloupka et al. (1993) showed that a mixture of PAHs, produced as by-products from a manufactured gas plant, was 706 times more potent than expected, based on its benzo[a]pyrene content (0.17%) at inducing mouse hepatic microsomal ethoxyresorufin O-deethylase. Alternatively, compounds may compete for a deactivating pathway, thereby increasing the toxicity of PAHs (Furman et al. 1991). Many monooxygenase inducers are ubiquitous in the environment, and they may have an effect on the toxicity of PAHs. For example, environmental contaminants such as tetrachlorodibenzo-p-dioxin (TCDD), polychlorinated biphenyls (PCBs) and 3,3',4,4'-tetrachlorobiphenyl (TCBP) can increase microsomal enzyme activity and consequently affect PAH toxicity (Jacob et al. 1987; Kouri et al. 1978). The dermal absorption of benzo[a]pyrene was measured in the presence or absence of complex organic mixtures derived from coal liquefaction processes (Dankovic et al. 1989). The dermal half-life of benzo[a]pyrene was 3.0 hours when applied alone, 6.7 hours when measured as a component of a mixture, and ranged from 7.8 to 29.7 hours in the presence of different mixtures. The authors proposed that these mixtures inhibit the dermal absorption of benzo[a]pyrene by inhibiting the metabolism of benzo[a]pyrene at the application site. Interactions. can thus play important modulatory roles in the expression of PAH toxicity that may not be adequately reflected based on the toxicity of a single PAH.

2. HEALTH EFFECTS

The majority of human exposures to PAHs occur in the presence of particles that affect the pharmacokinetics of PAHs in a manner that can enhance their carcinogenicity. Coadministration of benzo[a]pyrene and particulate material, such as hematite (Fe_2O_3) and arsenic trioxide (As_2O_3), greatly increases respiratory tract tumor yields in laboratory animals following intratracheal instillation (Pershagen et al. 1984; Saffiotti et al. 1972; Stenback and Rowland 1979; Stenback et al. 1976). The effects of particles on the potential human carcinogenicity of PAHs are likely to be similar. When benzo[a]pyrene is particle-bound, clearance from hamster lungs is slower than that of pure benzo[a]pyrene aerosol, increasing the length of time the lungs are exposed and increasing the dose to the gastrointestinal tract as a result of mucocilliary clearance. Respirable benzo[a]pyrene-containing particulates such as diesel exhaust, when coated with the phospholipid component of a pulmonary surfactant, are genotoxic (Wallace et al. 1987). Dusts can increase the rates of pulmonary cell proliferation (Harris et al. 1971; Stenback and Rowland 1979; Stenback et al. 1976), which in turn increases the cells' susceptibility to an initiation event in the presence of a carcinogen.

Environmental exposure to PAHs can also occur along with exposure to other environmental pollutants. The effects of exposure to SO_2 (either by inhalation or systemically with endogenous sulfite/bisulfite anions that accumulated as a result of induced sulfite oxidase deficiency) on benzo[a]pyrene-induced lung tumors were studied in male Sprague-Dawley rats (Gunnison et al. 1988). The animals, were administered benzo[a]pyrene (1 mg) by weekly intratracheal instillation for 15 weeks during which time they were exposed daily by inhalation to 30 or 60 ppm SO_2 or were maintained on a high tungsten to molybdenum diet. There were no statistically significant differences between the benzo[a]pyrene only and the benzo[a]pyrene + SO_2 or benzo[a]pyrene + sulfite/bisulfite groups with respect to the incidence of squamous cell carcinomas of the lung, latency for tumor development, or rate of appearance. Although benzo[a]pyrene alone induced almost 100% tumor incidence leaving little room for an SO_2-induced enhanced response, a shortened latency or increased rate of appearance would have suggested that SO_2 potentiates the carcinogenicity of benzo[a]pyrene, and this did not occur. Therefore, the authors concluded that SO_2 does not potentiate the carcinogenicity of benzo[a]pyrene in the lung.

Concomitant exposure to solvents may also occur, particularly in an occupational setting. It has been demonstrated that pretreatment of rats with toluene (1 g/kg intraperitoneally) inhibits the total cytochrome P-450 content in microsomes isolated from the lungs (Furman et al. 1991). In addition, formation of 3-hydroxybenzo[a]pyrene (a nontoxic metabolite) was inhibited by 36% by the

microsomes *in vitro* whereas the formation of several diols (reactive intermediates) was unaffected by toluene pretreatment. These results indicate that toluene alters the balance between toxification and detoxification of benzo[a]pyrene by cytochrome P-450 in the lung, favoring the formation of reactive genotoxic/carcinogenic intermediates. Therefore, the authors suggested that concomitant exposure to solvents, such as toluene, and PAHs may result in an increased risk for lung cancer.

Asbestos exerts a synergistic influence on cigarette smoke (which contains several PAHs) in the development of bronchopulmonary cancers. This has important implications for workers occupationally exposed to asbestos, who also smoke. The interaction between cigarette smoke and asbestos may be explained partly by differences in the kinetics of PAH cell uptake when PAHs are preadsorbed on asbestos (Foumier and Pezerat 1986). Plutonium oxide (PuO_2) has also been shown to enhance benzo[a]pyrene-induced lung carcinogenesis following simultaneous inhalation of both compounds (Metivier et al. 1984).

Another component of cigarette smoke, nicotine, may also affect the toxicokinetics of PAHs. When introduced in the perfusion medium with benzo[a]pyrene, nicotine inhibited the elimination of benzo[a]pyrene from the lung (Foth et al. 1988a).

Naturally occurring compounds have been found to induce the enzymes that metabolize PAHs, leading to either increased or decreased toxicity. Compounds that exert a protective effect against the carcinogenicity of PAHs and are enzyme inducers include plant flavonoids, plant phenols, antioxidants, retinoids (vitamin A), garlic oil, selenium, molybdenum, turmeric extracts, nitrates, soy sauce, and Chinese herbs. Plant flavonoids can induce microsomal monooxygenases and reduce the carcinogenicity of benzo[a]pyrene (Weibel 1980). Flavones administered orally or dermally increased benzo[a]pyrene hydroxylase activity in the small intestine and skin, respectively, and prevented the formation of pulmonary adenomas and forestomach and skin tumors initiated by benzo[a]pyrene (Rahimtula et al. 1977; Wattenberg and Leong 1970). A series of flavonoids and isoflavonoids, compounds that are found in fruits and vegetables, were tested for their ability to inhibit metabolism of benzo[a]pyrene in cultured hamster embryo cells (Chae et al. 1992). The results indicated that the flavonoids are generally more active than the isoflavonoids, and that two hydroxyl, two methoxyl, or methyl and hydroxyl substituents at the 5- and 7-positions and a 2,3-double bond are the structural characteristics required for inhibition of benzo[a]pyrene metabolism to reactive intermediates. Two of these compounds, acacetin and kaempferide also inhibited benzo[a]pyrene-induced mutation in Chinese

hamster V79 cells. Therefore, the authors proposed that the protective effect of these compounds may be due to their ability to inhibit metabolism of benzo[a]pyrene to reactive intermediates. Similar results have been obtained with pine cone extracts, tested in the *Salmonella typhimurium* assay (Lee et al. 1993). These results suggest that these compounds may be useful as potential chemopreventive agents in individuals exposed to genotoxic/carcinogenic PAHs.

Dietary plant phenols, such as tannic acid, quercetin, myricetin, and anthraflavic acid exhibit a protective effect against the tumorigenicity of benzo[a]pyrene and other PAHs by altering the metabolic pathways that detoxify and activate PAHs to their ultimate carcinogenic metabolites, thus suppressing PAH metabolism and subsequent PAH-DNA adduct formation. It has been suggested that the possible mechanism for the anticarcinogenic effect of these plant phenols may be an inhibitory effect on the binding of the ultimate carcinogen to the target tissue DNA (Mukhtar et al. 1988). Oral administration of these compounds has been associated with a decrease in tumorigenesis induced by benzo[a]pyrene in mouse forestomach (Katiyar et al. 1993a, 1993b; Zheng et al. 1993). Antioxidants also affect benzo[a]pyrene hydroxylation by rat liver microsomal MFOs, and reduce the bacterial mutagenicity of benzo[a]pyrene in the presence of rat liver microsomes and cofactors (Rahimtula et al. 1977). Antioxidants such as BHA, BHT, phenothiazine, phenothiazine methosulfate, and ethoxyquin all can reduce the quantitative yield of benzo[a]pyrene metabolites in incubations with rat liver microsomes (Sullivan et al. 1978).

Retinoids, of which vitamin A is a member, have demonstrated an antagonistic effect on benzo[a]pyrene-induced carcinogenicity. (Vitamin A has been shown to prevent and/or reverse the genetic damage caused by benzo[a]pyrene.) Similarly, the ability of benzo[a]pyrene (75 mg/kg, oral administration) to induce micronuclei *in vivo* was completely inhibited in Swiss mice orally administered doses of vitamin A ranging from 750 to 1,500 mg/kg 1 hour prior to benzo[a]pyrene treatment (Rao and Nandan 1990). Although the protective mechanism has not been fully elucidated, it has been suggested that vitamin A interferes with the activation of benzo[a]pyrene to its reactive metabolites, thus reducing the amount of benzo[a]pyrene-DNA binding in rat liver and target tissues (i.e., stomach) to prevent the mutagenic action of benzo[a]pyrene. It has also been suggested that vitamin A can enhance DNA repair (McCarthy et al. 1987; Rao et al. 1986). Conversely, vitamin A deficiency enhances the mutagenicity and carcinogenic effect of cigarette smoke and benzo[a]pyrene. This activity is related to a decreased level of free radical scavengers like ascorbic acid and glutathione in the liver (Alzieu et al. 1987). Another study observed that vitamin A deficient animals exposed to

cigarette smoke via inhalation exhibited enhanced benzo[a]pyrene-DNA adduct formation (Gupta et al. 1987, 1990). This has important implications for humans who smoke and consume diets deficient in vitamin A. Mammary tumor incidence was reduced by 27% (from 67% to 40%) in female rats receiving retinyl acetate before, during, and after the administration of either a single dose or eight weekly doses of benzo[a]pyrene. These results demonstrate that retinyl acetate is capable of inhibiting benzo[a]pyrene-induced mammary tumor formation in rats when given before, during, and after carcinogen treatment (McCormick et al. 1981).

The oral gavage administration of 25 mg/kg *n*-acetylcysteine (NAC) prevented the formation of benzo[a]pyrene-diol-epoxide-DNA adducts in rats receiving benzo[a]pyrene by intratracheal instillation for 3 consecutive days (25 mg/kg in 2% Tween 80) (De Flora et al. 1991). Inhibition of DNA adduct formation was more efficient in the liver than in the lungs. Similarly, micronuclei induction in the benzo[a]pyrene-treated rats was completely reversed by NAC. These results suggest that NAC, which is a glutathione precursor, may be effective in preventing or reversing the binding of the reactive intermediates of PAHs to cellular macromolecules and, therefore, may prevent the subsequent toxic effects of PAHs.

Coumarin, also known to be anticarcinogenic, inhibited benzo[a]pyrene-induced micronuclei in male ICR mice pretreated with 65 or 130 mg/kg/day coumarin for 6 days prior to the intraperitoneal administration of 150 mg/kg benzo[a]pyrene (Morris and Ward 1992). However, pretreatment with either dose of coumarin did not alter the genotoxicity of benzo[a]pyrene when females were included in the study.

Garlic oil also exhibits an antagonistic effect on benzo[a]pyrene by inhibiting benzo[a]pyrene-induced skin carcinogenesis in Swiss mice during the initiation phase (Sadhana et al. 1988). A primary constituent of garlic oil, allyl methyl trisulfide (ATM), has also demonstrated an inhibitory effect on benzo[a]pyrene induced neoplasia of the forestomach in mice (Spamins et al. 1986).

Selenium has been shown to reduce the mutagenicity of benzo[a]pyrene as well as AHH activity (Lee and Lin 1988). Selenium also inhibits the metabolism of benzo[a]pyrene *in vitro* (Bompart and Claments 1990). Several different salts of molybdenum inhibited the formation of certain metabolites of benzo[a]pyrene by lung and liver microsomes *in vitro* obtained from rats pretreated with 3-methylcholanthrene (Bompart et al. 1989). In a later study, it was demonstrated that benzo[a]pyrene

metabolism *in vitro* by lung and liver microsomes isolated from rats that were exposed to 40 or 80 mg/kg of ammonium heptamolybdate for 8 weeks was inhibited (Bompart 1990). These results suggest that molybdenum interferes with the cytochrome P-450 enzymes responsible for the activation of benzo[a]pyrene, and thus may have a protective effect against benzo[a]pyrene-induced toxicity/carcinogenicity.

Ferric oxide has been shown to increase the metabolism of benzo[a]pyrene by hamster alveolar macrophages (Greife and Warshawsky 1993). Alveolar macrophages, the primary lung defense cell, have been shown to metabolize benzo[a]pyrene to a more biologically active form, and then release the metabolites. Concurrent exposure of hamster alveolar macrophages to benzo[a]pyrene-coated ferric oxide resulted in a significant increase in the amount of benzo[a]pyrene metabolites and superoxide anions, which have been shown to produce localized lipid peroxidation and edema *in vivo.*

Lindane, an isomer of hexachlorocyclohexane, is an organochlorine pesticide which is extensively used in agricultural and public health programs in developing countries (Khan et al. 1993). Pretreatment of rat lungs with lindane by intratracheal injection inhibited benzo[a]pyrene hydoxlase activity in the lungs. Reduced elimination of intravenously administered benzo[a]pyrene from the lungs of rats after lindane pretreatment was also observed, suggesting that lindane may alter the clearance of benzo[a]pyrene from the lungs.

Prostacyclin has been shown to significantly reduce genetic damage caused by benzo[a]pyrene to mouse bone marrow cells, using the micronucleus test (Koratkar et al. 1993).

Chinese herbs commonly used in anti-cancer drugs have also been demonstrated to inh.ibit the mutagenicity of benzo[a]pyrene (Lee and Lin 1988).

Aqueous extracts of turmeric, curcumin-free aqueous turmeric extract, and curcumin were tested for their ability to inhibit benzo[a]pyrene-induced mutagenicity in the *S. typhimurium* assay and the bone marrow micronucleus test in Swiss mice (Azuine et al. 1992). A dose-dependent inhibition of benzo[a]pyrene-induced mutagenicity was observed in two strains of *Salmonella* in the presence of Aroclor-1254-induced rat liver homogenate, and 3 mg/kg of these three extracts also significantly inhibited benzo[a]pyrene-induced bone marrow micronuclei formation by 43%, 76%, and 65%. Female Swiss mice were treated with either aqueous turmeric extract (3 mg/day), curcumin-free

aqueous tumeric extract (1 mg/day), or curcumin (1 mg/day) 5 days/week for 2 weeks prior to receiving twice weekly gavage administrations of 20 mg/kg benzo[a]pyrene for 4 weeks. The treatment with the turmeric extracts continued for another 2 weeks after the cessation of benzopyrene treatment, and the animals were observed until they were 180 days old. A group receiving just benzo[a]pyrene served as a control. The benzo[a]pyrene-only animals exhibited 100% tumor incidence with 9.1±0.6 papillomas/mouse. All three extracts significantly ($p<0.00l$) inhibited the formation of forestomach papillomas by benzo[a]pyrene by 53%, and the average numbers of papillomas per mouse was also significantly decreased. The authors suggested that turmeric extracts may be useful as chemopreventive agents, but that there are probably several mechanisms of action for these inhibitory effects.

Pumark, a mixture of solvent extracts of tumeric, betel leaf, and catechu, was tested for its chemopreventative activity against benzo[a]pyrene-induced DNA damage (Ghaisas and Bhide 1994) Sister chromatid exchange and micronuclei formation in human lymphocyte culture were used as markers to assess the protective effect of Pumark. Pumark gave 50-60% protection against benzo[a]pyrene-induced chromosomal damage.

Other environmentally ubiquitous substances, such as nitrites and nitrates, have been shown to interact with PAHs. Pyrene is not mutagenic in the *Salmonella typhimurium* assay. However, when injected intraperitoneally into mice at doses of 10-200 mg/kg in combination with inhalation exposure to 50 or 100 ppm nitrous oxide (NO_2) mutagenic metabolites of pyrene were recovered from the urine (Kanoh et al. 1990). In addition, 1-hydroxypyrene (the major urinary metabolite of pyrene) administration in combination with NO_2 exposure also produced mutagenic metabolites. These results suggest that combined exposure to pyrene, a prevalent environmental PAH, and nitrogen compounds could result in the formation of nitrogenated mutagenic metabolites of pyrene. The effects of nitrite (in drinking water) and/or soy sauce (in food) on the forestomach tumors induced by twice weekly gavage administration of eight total doses of benzo[a]pyrene were studied in mice (Benjamin et al. 1988). The combination of nitrite and soy sauce resulted primarily in a significant reduction in the number of tumors per animal induced by benzo[a]pyrene, and also a reduction in tumor incidence. Neither substance alone had much effect on the carcinogenicity of benzo[a]pyrene alone. The mechanism for this protective effect of the combination of nitrite and soy sauce is not known.

The fungicide (prochloraz), the topical antifungal agent (miconazole) and 7,8-benzoflavone (a strong inhibitor of cytochrome P-450) limited the conversion of benzo[a]pyrene to a mutagen in S. *typhimurium.* The order of inhibitory action was 7,8-benzoflavone ≥ prochloraz ≥ miconazole (Antignac et al. 1990).

Diet (i.e., dietary fat levels) can also have an effect on the disposition and toxicity of PAHs. The metabolism of benzo[a]pyrene in hepatocytes *in vitro* from rats fed high-fat (as corn oil) diets was decreased (Zaleski et al. 1991). This effect was not due to a decrease in the activity of AHH. The authors postulated that the high-fat diets allowed benzo[a]pyrene, which is highly lipophilic, to become sequestered in lipid droplets and, therefore, become inaccessible to the P-450 enzymes. Another study suggests that caloric restriction, per se, can reduce the metabolic activation capacity of the liver, thereby reducing the production of mutagenic metabolites from PAHs (Xiao et al. 1993).

Organosulphur compounds, e.g., S-methyl cysteine sulphoxide (SMCSO) and its metabolite methyl methane thiosulphinate, both naturally occurring compounds present in Brassica vegetables (broccoli, cabbage) were found to inhibit benzo[a]pyrene-induced micronucleus formation in mouse bone marrow by 31 and 33%, respectively, after oral administration (Marks et al. 1993).

o-Cresol, often found in conjunction with PAHs in industrial waste from coking, oil processing, shale processing, and other industries, was found to protect mice from benzo[a]pyrene-induced forestomach tumors after oral administration, when o-cresol was administered before or after benzo[a]pyrene (Yanysheva et al. 1993).

Topical application of 1% croton oil twice weekly at 4 weeks of age had an inhibitory effect on tumor formation in offspring of ICF/Ha female mice treated with intraperitoneal injections of benzo[a]pyrene in sesame oil on the llth, 13th and 15th days of pregnancy (Bulay and Wattenberg 1971).

Administration of a diet containing 3% myo-inositol to mice beginning one week after oral benzo[a]pyrene administration reduced the number of pulmonary adenomas by 40% but did not prevent forestomach tumors (Estensen and Wattenberg 1993). Under the same conditions, administration of 0.5% dexamethasone in the diet inhibited pulmonary adenomas by 57% and also inhibited forestomach tumor formation to a similar degree. A combination of the two compounds resulted in additive chemoprevention.

The ubiquitous nature of PAHs in the environment, particularly as constituents of complex mixtures such as automobile emissions, coal tar, coke oven emissions, and combustion products of tobacco, increases the likelihood that the type of interactions discussed will occur. Thus, interactions may play a decisive role in the expression of toxicity and the development of cancer in exposed populations.

2.7 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

A susceptible population will exhibit a different or enhanced response to PAHs than will most persons exposed to the same level of PAHs in the environment. Reasons include genetic make-up, developmental stage, age, health and nutritional status (including dietary habits that may increase susceptibility, such as inconsistent diets or nutritional deficiencies), and substance exposure history (including smoking). These parameters result in decreased function of the detoxification and excretory processes (mainly hepatic, renal, and respiratory) or the pre-existing compromised function of target organs (including effects or clearance rates and any resulting end-product metabolites). For these reasons we expect the elderly with declining organ function and the youngest of the population with immature and developing organs will generally be more vulnerable to toxic substances than healthy adults. Populations who are at greater risk due to their unusually high exposure are discussed in Section 5.6, Populations With Potentially High Exposure.

Data suggest that specific subsections of the population may be susceptible to the toxic effects produced by exposure to PAHs. These include people with various conditions, such as aryl hydrocarbon hydroxylase (AHH) that is particularly susceptible to induction, nutritional deficiencies, genetic diseases that influence the efficiency of DNA repair, and immunodeficiency due to age or disease. Other subsections of the population that may be susceptible to the toxic effects of PAHs are people who smoke, people with a history of excessive sun exposure, people with liver and skin diseases, and women, especially of child-bearing age. Human fetuses may also be particularly susceptible to the toxic effects produced by exposure to PAHs. Data also indicate that the general population may be at increased risk of developing lung cancer following prolonged inhalation of PAH-contaminated air, and skin cancer following concurrent dermal exposure to PAHs and sunlight. There is some limited evidence that indicates that all people could be sensitive at some point to the toxic effects of environmental contaminants, such as PAHs, as a result of stress and/or circadian rhythms.

Pre- and post-natal exposure to PAHs could produce adverse reproductive and developmental effects in human fetuses. Most PAHs and their metabolites cross the placenta because of their lipid solubility (Calabrese 1978; Shendrikova and Aleksandrov 1974). Fetuses are susceptible to the toxic effects produced by maternal exposure to PAHs, such as benzo[a]pyrene, because of an increased permeability of the embryonic and fetal blood-brain barrier and a decreased liver-enzyme conjugating function (Calabrese 1978; Shendrikova and Aleksandrov 1974). Because of PAH exposure, higher incidences of embryo- and fetolethality, stillbirths, resorptions, and malformations of the kidney and bladder have been observed in animals (Legraverend et al. 1984; Urso and Gengozian 1980; Urso and Johnson 1987). Delayed effects have been observed in the progeny of mothers exposed to PAHs, such as benzo[a]pyrene (Urso and Gengozian 1980). These .delayed effects include sterility of progeny, immune suppression, possible alteration of endocrine function, and cancer in rodents (Csaba and Inczefi-Gonda 1992; Csaba et al. 1991; Legraverend et al. 1984; Mackenzie and Angevine 1981). Tobacco smoke contains both PAHs and particulate matter. These could interact synergistically in pregnant women who smoke to produce decreased birth weight, increased perinatal morbidity and mortality, and other diseases of the newborn (NRC 1983). PAHs in cigarette smoke, such as benzo[a]pyrene, have been associated with the induction of AHH activity in human placental tissue and a decrease in placental size (NRC 1983). Results of *in vitro* studies indicate that benzo[a]pyrene alters human placental endocrine and metabolic function (Avigdor et al. 1992; Bamea and Shurtz-Swirski 1992; Guyda 1991; Guyda et al. 1990).

People with AHH that is particularly susceptible to induction may also be susceptible to the possible carcinogenic effect of exposure to PAHs. This enzyme is mixed function oxidase (MFO) that is involved in the metabolism of PAHs to certain reactive intermediates that can cause cell transformation, mutagenicity, and cytotoxicity. The incidence of this inducible genetic trait is low in 53%, intermediate in 37%, and high in 10% of the white population in the United States (Calabrese 1978). It has been proposed that genetically expressed AHH inducibility is related to the development of bronchogenic carcinoma in persons exposed to PAHs contained in tobacco smoke. On the other hand, individuals with a greater ability to induce AHH may be able to rapidly detoxify PAHs and eliminate them, thus making them less susceptible to the toxic effects of PAHs. Based on the population frequency of genetically controlled AHH induction, some scientists predict that approximately 45% of the general population are considered to be at high risk, and 9% of the 45% are considered to be at very high risk, of developing bronchogenic carcinoma following exposure to PAHs (Calabrese 1978).

Certain nutritional deficiencies have been associated with an increased cancer incidence in PAH-exposed animals. These include deficiencies in vitamins A and C, iron, and riboflavin (Calabrese 1978). It is estimated that at least 25% of all children between the ages of 7 and 12 years and all children of low-income families consume less than the recommended dietary allowance (RDA) of vitamin A. It has also been estimated that between 10% and 30% of the infants, children, and adults of low-income groups consume less than the RDA for vitamin C, 98% of all children consume less than the RDA for iron, and 30% of women and 10% of men between the ages of 30 and 60 years consume less than two-thirds of the RDA for riboflavin (Calabrese 1978). Other nutrients such as vitamin D, selenium, and protein can also influence the cancer incidence in animals exposed to PAHs (NRC 1983; Prasanna et al. 1987). Several studies have been conducted to investigate the interaction between nutrition and PAH exposure by administering benzo[a]pyrene to laboratory animals. The nutritional factors listed above either reduced the amount of benzo[a]pyrene binding to DNA in rat liver or forestomach tissue (McCarthy et al. 1987), prevented or reversed genetic damage (Rao et al. 1986), or reduced the activity of AHH (Prasanna et al. 1987). It has also been observed that fasted rats showed altered toxicokinetics of PAHs resulting from benz[a]anthracene and chrysene exposure. This altered toxicokinetics included reduced hepatic clearance because of decreased AHH activity and the acceleration of the depletion of cytochrome P-450 and other microsomal enzymes required to metabolize PAHs (Fiume et al. 1983).

Individuals who undergo a rapid reduction in body fat may be at risk from increased toxicity because of the systemic release and activation of PAHs that had been stored in fat. The metabolism of benzo[a]pyrene in hepatocytes *in vitro* from rats fed high-fat (as corn oil) diets was decreased (Zaleski et al. 1991). This effect was not due to a decrease in the activity of AHH. The authors postulated that the high-fat diets allowed benzo[a]pyrene, which is highly lipophilic, to become sequestered in lipid droplets and, therefore, become inaccessible to the P-450 enzymes.

People exposed to PAHs in conjunction with particulates from tobacco smoke, fossil-fuel combustion, coal fly ash, and asbestos fibers are at increased risk of developing toxic effects, primarily cancer. Even people not susceptible to the toxic effects of PAHs may become affected when exposure occurs in conjunction with exposure to particulates (NRC 1983). This enhanced effect results from the adsorption of PAHs onto the particulates. They are vacuolized into cells, and distributed differently in tissues depending on the size and type of particulate matter. This increased PAH uptake may result in more efficient induction of AHH activity at low PAH concentrations. This activity also increases the

dose to the gastrointestinal tract as a result of mucocilliary clearance (NRC 1983). This synergistic action between PAHs and particulate matter in air pollution has been associated with the occurrence of stomach cancer in humans (Fraumeni 1975).

Immunocompetence is an important factor in decreasing or preventing human susceptibility to toxicity and disease after exposure to environmental contaminants. Small children have an immature immune system, and the elderly may have a deficient immune system due to age, genetic factors, or disease (Calabrese 1978; NRC 1983). It is possible that individuals whose immune systems are compromised could be at an increased risk of carcinogenesis, including that produced by PAHs. Some genetic diseases that may predispose a person to immune deficiency include ataxia telangiectasia, Wiskott-Aldrich syndrome, Bloom's syndrome, common variable immunodeficiency, selective IgA deficiency, Bruton's agammaglobulinemia, severe combined immunodeficiency, selective IgM deficiency, AIDS, and immunodeficiency with normal or increased immunoglobulins (NRC 1983).

Genetic diseases that reduce DNA-repair capabilities also increase an individual's susceptibility to PAH-related malignancy by reducing the efficiency of DNA repair. In fact, the level of benzo[a]pyrene/DNA adducts in peripheral lymphocytes was slightly but significantly higher in 22 lung cancer patients who had at least one "first-degree" relative with lung cancer than in 30 healthy controls (Nowak et al. 1992). This finding led the authors to speculate that altered metabolic activation and deactivation and increased formation of adducts may indicate a genetic predisposition for lung cancer. Some of the diseases that reduce DNA repair capability are also associated with an abnormality of the immune system (NRC 1983). Diseases that may be associated with DNA-repair deficiencies are classical and variant xeroderma pigmentosum, ataxia telangiectasia, Bloom's syndrome, Fanconi's anemia, familial retinoblastoma, D-deletion retinoblastoma, progeria (Hutchinson-Gilford) syndrome, Down's syndrome, dyskeratosis congenita, Cockayne's syndrome, actinia keratosis, and cutaneous malignant melanoma (NRC 1983).

Women may be at increased risk of reproductive dysfunction following exposure to high levels of PAHs. Data from animal studies indicate that oocyte and follicle destruction occurs following dosing with PAHs (Mattison et al. 1989; Miller et al. 1992; Urso and Gengozian 1980; Urso and Johnson 1987). Benzo[a]pyrene exposure may reduce fertility and the ability to bear children (Mackenzie and Angevine 1981; Rigdon and Rennels 1964). Exposure may also reduce fertility of exposed women by

causing ovarian dysfunction (Swartz and Mattison 1985). However, the doses that produced the effects discussed above are high relative to expected environmental exposures to PAHs.

Subsections of the population that suffer from liver and skin diseases may be at increased risk of developing adverse effects from exposure to PAHs. People with pre-existing skin conditions, such as pemphigus vulgaris and xeroderma pigmentosum, and those with normal skin may be at increased risk of developing adverse dermal effects ranging from rashes to cancer following exposure to some PAHs, such as benzo[a]pyrene, anthracene, benz[a]anthracene, and pyrene (Bingham and Falk 1969; Cavalieri et al. 1977, 1988b; Cottini and Mazzone 1939; Forbes et al. 1976; Habs et al. 1980; Shubik and Porta 1957). Exposure to more than one PAH may enhance or reduce tumor development (Slaga et al. 1979; Van Duuren and Goldschmidt 1976; Van Duuren et al. 1973). Skin cancer induction in laboratory animals has been associated with exposure to benz[a]anthracene, benzo[a]pyrene, benzo[b]fluoranthene, benzohlfluoranthene, benzo[k]fluoranthene, chrysene, dibenz[a,h]anthracene, and indeno[1,2,3-c,d]pyrene.

People with significant exposure to ultraviolet radiation, such as from sunlight, may also be at increased risk of developing skin cancer due to PAH exposure. Ultraviolet radiation has a synergistic influence on PAH-induced skin cancer following dermal exposure. It enhances benzo[a]pyreneinduced skin carcinogenesis in the mouse, which is dependent on the dose of benzo[a]pyrene (Gensler 1988). Combined exposure to anthracene and sunlight could produce mutagenic lesions (Blackbum and Taussig 1975; Forbes et al. 1976). Laboratory animals exposed concurrently to chronic ultraviolet irradiation and to PAHs were at a higher risk of skin tumor induction (Mukhtar et al. 1986).

2.8 METHODS FOR REDUCING TOXIC EFFECTS

This section will describe clinical practice and research concerning methods for reducing toxic effects of exposure to PAHs. However, because some of the treatments discussed may be experimental and unproven, this section should not be used as a guide for treatment of exposures to PAHs. When specific exposures have occurred, poison control centers and medical toxicologists should be consulted for medical advice.

2.8.1 Reducing Peak Absorption Following Exposure

General recommendations to reduce absorption follo.wing acute exposure to PAHs include removing the individual from the source of exposure, removing contaminated clothing, and decontaminating exposed areas of the body. It has been suggested that contaminated skin should be washed with soap and water, and eyes exposed to PAHs should be flushed with water or saline (Stutz and Janusz 1988). Administration of activated charcoal following ingestion of PAHs is recommended; however, it has not been proven to reduce absorption of PAHs in the gastrointestinal system (Stutz and Janusz 1988). The use of emetics as a means of gastrointestinal decontamination of PAHs is not recommended (Bronstein and Currance 1988). There is a risk of causing chemical pneumonitis in the patient by the aspiration of the PAHs.

2.8.2 Reducing Body Burden

There are no known methods currently available for reducing the body burden of PAHs. Evidence from acute-duration studies in experimental animals indicates that PAHs are rapidly metabolized and conjugated to form water-soluble metabolites that are essentially completely eliminated in the urine and feces within a matter of days (see Sections 2.3.3 and 2.3.4). No data are available on the kinetics of PAHs following chronic exposure, so it is not known if PAHs or their metabolites bioaccumulate in these exposure situations. Given the relatively rapid and complete excretion observed following short-term exposures, it is not likely that PAHs bioaccumulate to an appreciable degree. However, PAHs are lipophilic, so it is conceivable that unmetabolized parent compound could accumulate in tissue fat stores. In fact, diet (i.e., dietary fat levels) may have an effect on the disposition and toxicity of PAHs. The metabolism of benzo[a]pyrene in hepatocytes *in vitro* from rats fed high-fat (as corn oil) diets was decreased (Zaleski et al. 1991). This effect was not due to a decrease in the activity of AHH. The authors postulated that the high-fat diets allowed benzo[a]pyrene, which is highly lipophilic, to become sequestered in lipid droplets and, therefore, become inaccessible to the P-450 enzymes. Therefore, high-fat diets may favor the accumulation of parent PAHs in lipids so that they are not metabolized to reactive intermediates or water-soluble conjugates. Alternatively, rapid fat loss may result in the release of sequestered parent PAHs, making them available to the P-450 enzymes to be metabolized to reactive intermediates as well as water-soluble conjugates that can be easily excreted. Thus, modulating body fat content may reduce body burden of PAHs by hastening

their metabolism to water-soluble conjugates. However, the result may also be an increase in toxicity due to increased metabolism to reactive intermediates.

2.8.3 Interfering with the Mechanism of Action for Toxic Effects

As discussed in Sections 2.3.5 and 2.4, it is currently believed that the toxic and carcinogenic effects of PAHs are mediated by reactive diol-epoxide intermediates that interact directly with DNA and RNA, producing adducts. The formation of these adducts leads to neoplastic transformation as well as interfering with the normal functioning of rapidly proliferating tissues. As discussed above, these reactive intermediates are formed when PAHs are biotransformed by the P-450 enzymes. Interference with these metabolic pathways, by inactivation of the activated diol epoxides, reduction in tissue levels of cytochrome P-450, and direct inhibition of the cytochrome P-450 enzymes responsible for the formation of the reactive intermediates, could reduce the toxic and carcinogenic effects of PAHs. A number of drugs, such as cobaltous chloride, SKF-525-A, and 6-nitro- 1,2,3-benzothioadiazole, have been reported to inhibit P-450 enzymes. In addition, as discussed in Section 2.7, other compounds that exert a protective effect against the carcinogenicity of PAHs by interfering with cytochrome P-450 enzymes include plant flavonoids, plant phenols, antioxidants (such as BHA, BHT, phenothiazine, phenothiazine methosulfate, and ethoxyquin), retinoids (vitamin A), garlic oil, selenium, organosulphur compounds, o-cresol, myo-inositol, lindane, and molybdenum (Bompart 1990; Bompart et al. 1989; Chae et al. 1992; Estensen and Wattenberg 1993; Ghaisas and Bhide 1994; Katiyar et al. 1993a, 1993b; Khan et al. 1993; Lee and Lin 1988; Lee et al. 1993; Marks et al. 1993; Mukhtar et al. 1988; Rahimtula et al. 1977; Rao and Nandan 1990; Sullivan et al. 1978; Weibel 1980, Yanysheva et al. 1994; Zheng et .al. 1993). Reduced caloric intake has also been shown to cause decreased metabolism of PAHs by liver microsomes, thus protecting against genotoxic effects (Xiao et al. 1993). P-450 metabolism also results in products that can be more readily eliminated than can the parent compound. Hence, any side products of the drugs or substances listed above, along with their potential to increase the biological half-life of the PAHs, would also need to be considered in any protocol. Further research to determine which cytochrome P-450 isozymes are involved in the metabolism to the reactive intermediates, as well as which isozymes are involved in enhancing the elimination of PAHs, could lead to the development of strategies to selectively inhibit specific isozymes and, thus, reduce the toxic effects of PAHs.

It has also been suggested that some of these compounds may act at other points in the activation, macromolecular binding sequence described above. For instance, vitamin A can also enhance DNA repair (McCarthy et al. 1987; Rao et al. 1986).

Because PAHs are detoxified by conjugation with substances such as glutathione (see Sections 2.3.3 and 2.3.4), sufficient glutathione stores in the body may reduce the chances of toxic effects following acute exposure to PAHs. For example, the oral gavage administration of NAC prevented the formation of benzo[a]pyrene-diol-epoxide-DNA adducts in rats receiving benzo[a]pyrene (De Flora et al. 1991). Inhibition of DNA adduct formation was more efficient in the liver than in the lungs. Similarly, micronuclei induction in the benzo[a]pyrene-treated rats was completely reversed by NAC. These results suggest that NAC, which is a glutathione precursor, may be effective in preventing or reversing the binding of the reactive intermediates of PAHs to cellular macromolecules and, therefore, may prevent the subsequent toxic effects of PAHs.

2.9 ADEQUACY OF THE DATABASE

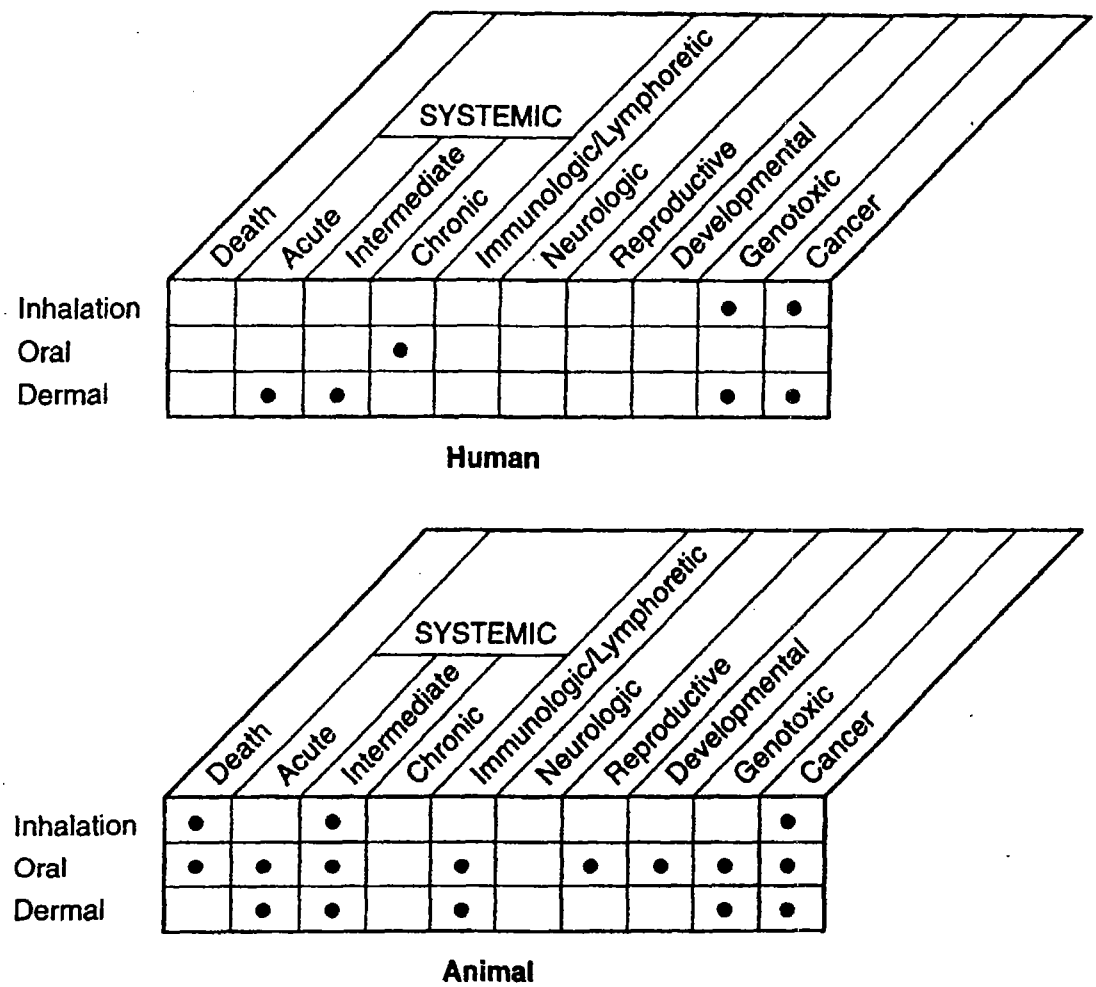
Section 104(i)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of PAHs is available. Where adequate information is not available, ATSDR, in conjunction with the National Toxicology Program (NTP), is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of PAHs.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

2.9.1 Existing Information on Health Effects of Polycyclic Aromatic Hydrocarbons

The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to PAHs are summarized in Figure 2-5. The purpose of this figure is to illustrate the existing

FIGURE 2-5. Existing Information on Health Effects of Polycyclic Aromatic Hydrocarbons



● Existing Studies

information concerning the health effects of PAHs. Each dot in the figure indicates that one or more studies provide information associated with that particular effect. The dot does not imply anything about the quality of the study or studies. Gaps in this figure should not be interpreted as "data needs." A data need, as defined in ATSDR's Decision Guide for Identifying Substance-Specific Data Needs Related to Toxicological Profiles (ATSDR 1989), is substance-specific information necessary to conduct comprehensive public health assessments. Generally, ATSDR defines a data gap more broadly as any substance-specific information missing from the scientific literature.

The vast majority of literature reviewed concerning the health effects of PAHs in humans described case reports and chronic-duration studies in workers linking the occurrence of lung and skin cancer and adverse noncancer skin effects with exposure to PAH-containing mixtures such as coke oven emissions, roofing-tar emissions, shale oils, and soot, and exposure to cigarette smoke. The predominant routes of exposure in the studies are inhalation and dermal, but the possibility of some degree of oral exposure cannot be ruled out, especially in light of muco-cilliary clearance and ingestion following inhalation exposure. Because of the lack of quantitative exposure information and the presence of other potentially carcinogenic substances in these mixtures, it is impossible to evaluate the contribution of an individual PAH or even the PAHs as a class to the effects observed.

The database for the health effects of PAHs in experimental animals consists primarily of older animal studies that would be considered inadequate by current standards, and two-stage dermal carcinogenesis studies. As can be seen in Figure 2-5, very little information is available on the effects of inhalation exposure to PAHs in animals. However, oral and dermal exposures to relatively high doses of PAHs have been shown in numerous studies to induce skin, lung, and forestomach tumors in animals, and noncancer adverse effects in rapidly proliferating tissues such as bone marrow, lymphoid organs, gonads, and intestinal epithelium. Benzo[a]pyrene is by far the most extensively studied of the PAHs; therefore, the adverse effects of other less-studied PAHs must generally be inferred from the results obtained with benzo[a]pyrene. This may over- or underestimate the health risk associated with the various PAHs.

2.9.2 Identification of Data Needs

Acute-Duration Exposure. Little is known regarding the adverse health effects associated with acute-duration inhalation exposure to any of the PAHs in either humans or animals. Limited

information is available on the effects of acute-duration oral and dermal exposures to PAHs in animals; the skin and the liver have been identified as target organs of PAH toxicity in animals (Iwata et al. 1981; Nousiainen et al. 1984). Available information is insufficient to derive an acute inhalation or oral MRL. Identification of target organs (other than the developing fetus) from acute-duration animal studies following inhalation and oral exposures would be helpful in order to assess the risk associated with the acute inhalation of contaminated air or ingestion of PAH-contaminated water or soils by humans living in areas surrounding hazardous waste sites. Additional inhalation and oral studies in animals involving a range of exposure concentrations and employing sensitive histological and biochemical measurements of injury to a comprehensive set of end points would be useful for establishing dose-response relationships and identifying thresholds for these effects. This information would be useful for determining levels of significant exposure to PAHs that are associated with adverse health effects. Both routes are considered significant for individuals living in the vicinity of hazardous waste sites because exposures to particulate PAHs in air and PAHs bound to soil particles, sediments in water, and contaminated food are possible in such areas. Furthermore, the pharmacokinetic data on PAHs are insufficient to determine whether similar effects may be expected to occur across different routes of exposure. Additional studies should be conducted on the effects of PAHs after acute-duration dermal exposure, since dermal exposure may be important to populations around hazardous waste sites. It is known that acute-duration dermal exposure to PAHs results in adverse dermal effects. Further studies determining the relative importance of exposure by this route, with regard to subsequent toxicity, would be useful. Studies describing dermal and oral absorption of PAHs from complex mixtures, including soil and other mixtures that may actually be the vehicles of human exposure, would be useful in furthering understanding of the toxicity of these compounds. The studies should be conducted with benzo[a]pyrene, because this PAH has been found at the highest number of NPL sites and it is a representative altemant PAH; studies should also be conducted with a representative nonaltemant PAH such as fluoranthene, benzo[b]fluoranthene, or benzo[j]fluoranthene. In addition, since PAHs rarely occur alone, but are found in the environment in combinations and mixtures, studies, particularly feeding studies, addressing mixtures of PAHs should be conducted. In all cases, research should be cOnducted to determine the most appropriate animal species for extrapolation to humans.

Intermediate-Duration Exposure. Little is known regarding the adverse health effects associated with intermediate-duration inhalation exposure to any of the PAHs in either humans or animals. One inhalation study in rats failed to establish an effect level (Wolff et al. 1989c). Information is available

on the effects of intermediate-duration exposures to some of the PAHs in humans (dermal) and in animals (oral and dermal). Regressive verrucae and other epidermal changes were noted in the skin of human volunteers treated with topically applied benzo[a]pyrene (Cottini and Mazzone 1939). Intermediate-duration dermal exposure to benzo[a]pyrene in patients with preexisting dermal conditions of pemphigus vulgaris and xeroderma pigmentosum was associated with an exacerbation of the abnormal skin lesions (Cottini and Mazzone 1939). Target organs identified in animal studies with some of the PAHs were the skin, the liver, and the hemolymphatic system (Legraverend et al. 1983; Old et al. 1963; Robinson et al. 1975). The available information is insufficient to derive an intermediate inhalation MRL for PAHs because no intermediate-duration inhalation animal studies exist that adequately describe the effects of inhalation exposure to PAHs. Intermediate duration MRLs have been derived for acenaphthene, fluoranthene, fluorene, and anthracene, based on 90-day gavage studies in mice (EPA 1988e; 1989c; 1989d, 1989e). For acenaphthene, fluoranthene, and fluorene, liver effects, supported by effects in other organ systems were identified as the target toxicity. For anthracene, no effect was seen in the liver or any other organ system, even at the highest dose of 1,000 mg/kg/day. The PAHs in these studies were administered by gavage, a route that does not mimic the potential exposure of people living near hazardous waste sites. Identification of target organs from intermediate-duration animal studies following inhalation and oral (drinking water) exposures would be useful in order to assess the risk associated with the intermediate-duration inhalation of contaminated air or ingestion of PAH-contaminated water or soils by humans living in areas surrounding hazardous waste sites. Ninety-day studies in animals by the inhalation and oral (drinking water) routes would be helpful to establish dose-response relationships and to identify other possible target organs or systems in individuals living around hazardous waste sites who can be exposed to low levels of PAHs for an intermediate-duration period of time. Both routes are considered important for individuals living in the vicinity of hazardous waste sites because exposure to particulate PAHs in air and PAHs bound to soil particles, sediments in water, and contaminated food are significant routes of exposure for individuals living in the vicinity of hazardous waste sites. Furthermore, the pharmacokinetic data on PAHs are insufficient to determine whether similar effects may be expected to occur across different routes of exposure. Additional studies should be conducted on the effects of PAHs after intermediate-duration dermal exposure, since dermal exposure may be important to populations around hazardous waste sites. It is known that acute-duration dermal exposure to PAHs results in adverse dermal effects. Further studies determining the relative importance of exposure by this route, with regard to subsequent toxicity, would be useful. Studies describing dermal and oral absorption of PAHs from complex mixtures, including soil and other

mixtures that may actually be the vehicles of human exposure, would be useful in furthering the understanding of the toxicity of these compounds. The studies should be conducted with benzo[a]pyrene, because it has been found at the hi.ghest number of NPL sites and it is a representative altemant PAH, and with a representative nonaltemant PAH such as fluoranthene, benzo[b]fluoranthene, or benzofilfluoranthene. In addition, since PAHs rarely occur alone, but are found in the environment in combinations and mixtures, studies, particularly feeding studies, addressing mixtures of PAHs should be conducted. In all cases, research should be conducted to determine the most appropriate animal species for extrapolation to humans.

Chronic-Duration Exposure and Cancer. Few controlled epidemiological studies have been reported in humans on the effects of exposure to PAHs or PAH-containing mixtures; such studies would be difficult to conduct because of the presence of too many confounding factors. However, information is available on the effects of chronic-duration dermal exposures to PAH-containing mixtures in humans. Workers exposed to substances that contain PAHs (e.g., coal tar) experience chronic dermatitis and hyperkeratosis (EPA 1988a). Several chronic ingestion, intratracheal installation, and skin-painting studies have been conducted in animals using various PAHs, but none identified adverse effects other than cancer. Therefore, threshold levels for chronic-duration inhalation and oral exposure have not been thoroughly investigated, and no MRLs have been developed from this database. Although the existing animal studies are inadequate to establish threshold levels and dose-response relationships for toxic effects resulting from chronic exposure to PAHs, the data from 90-day studies recommended above should be evaluated before chronic studies are conducted. Inhalation and ingestion are probably the most significant routes of exposure for individuals living in the vicinity of hazardous waste sites contaminated with PAHs. Low dose chronic studies are needed to mimic these exposures.

Human data on the carcinogenicity of PAHs are available only for mixtures containing PAHs. Animal carcinogenicity data are available for only benzo[a]pyrene following inhalation exposure, for a limited number of PAHs following ingestion, and for almost all of the 17 PAHs following dermal exposure. A large database on carcinogenicity exists on complex mixtures that contain PAHs (such as crude oils, various high boiling point distillates, complex petroleum products, coal tars, creosote, and the products of coal liquification processes). It is difficult to ascertain the carcinogenicity of the component PAHs in these mixtures because of the potential interactions that could occur and the presence of other carcinogenic substances in the mixtures. Furthermore, the levels of PAHs were not quantified in any

of these reports. However, most of the available information on the carcinogenicity of PAHs in humans must be inferred from studies that reported the effects of exposure to complex mixtures that contain PAHs. Epidemiologic studies have shown increased mortality due to lung cancer in humans exposed to coke oven emissions (Lloyd 1971; Mazumdar et al. 1975; Redmond et al. 1976), roofing-tar emissions (Hammond et al. 1976), and cigarette smoke (Maclure and MacMahon 1980; Wynder and Hoffmann 1967). Despite the limitations inherent in these studies, reports of this nature provide qualitative evidence of the potential for mixtures containing PAHs to cause cancer in humans, and more definitive studies in humans on individual PAHs are not recommended at this time.

Inhalation exposure to benzo[a]pyrene has been shown to induce respiratory tract tumors in hamsters (Thyssen et al. 1981). Certain PAHs are carcinogenic to animals by the oral route (e.g., benz[a]anthracene, benzo[a]pyrene, and dibenz[a,h]anthracene), and tumors have been noted in the liver, mammary gland, and respiratory and gastrointestinal tracts following oral administration of these compounds (Neal and Rigdon 1967; Rigdon and Neal 1969). However, only a few PAHs have been assayed by the oral route. The results of dermal studies indicate that benz[a]anthracene, benzo[a]pyrene, benzo[b]fluoranthene, benzo[j]fluoranthene, benzo[k]fluoranthene, chrysene, dibenz[a,h]anthracene, and indeno[1,2,3-c,d]pyrene are tumorigenic in rats and mice following dermal exposure. Although many of these studies would be considered inadequate by current standards, the results nevertheless indicate that these PAHs can induce skin tumors as well as act as tumor initiators and promoters (Habs et al. 1984; Warshawsky and Barkley 1987; Wynder and Hoffmann 1959b). Therefore, additional studies on the carcinogenicity of PAHs in animals are probably not necessary at this time.

Genotoxicity. The genotoxic potential of several of the PAHs (both altemant and nonaltemant) has been extensively investigated using both *in vivo* and *in vitro* assays. All but three of the PAHs (acenaphthene, acenaphthylene, and fluorene) were reported to be mutagenic in at least one *in vitro* assay with the bacteria *S. typhimurium.* No further genotoxicity data are considered necessary at this time.

Reproductive Toxicity. No data were located regarding reproductive effects of PAHs in humans, and the available information regarding reproductive effects of PAHs in animals is limited; data exist on only one of the PAHs (benzo[a]pyrene), and these data are conflicting. Adverse effects such as decreased fertility and total sterility in F1 progeny of CD-1 mice (Mackenzie and Angevine 1981) and

decreased incidence of pregnant female rats at parturition (Rigdon and Rennels 1964) were reported following oral exposure to benzo[a]pyrene. However, no adverse reproductive effects were observed in Swiss mice fed benzo[a]pyrene in their diet (Rigdon and Neal 1965). The metabolic differences and method of benzo[a]pyrene administration could account for the differential response to benzo[a]pyrene-induced toxicity in these studies. Parenteral studies in animals have also demonstrated adverse reproductive effects (Bui et al. 1986; Cervello et al. 1992; Mattison et al. 1992; Miller et al. 1992; Swartz and Mattison 1985). The limited animal data suggest that PAHs may be reproductive toxicants, but these data are not extensive enough to draw firm conclusions. Furthermore, the testes and ovaries contain rapidly proliferating cells and therefore should be considered susceptible to damage by PAHs. The 90-day studies identified above should be conducted with special emphasis on reproductive organ pathology. If reproductive effects are observed in these studies, multigeneration animal studies could then be conducted to evaluate properly the relevance of this end point. In addition, since PAHs rarely occur alone, but are found in the environment in combinations and mixtures, studies, particularly feeding studies, addressing mixtures of PAHs should be conducted. In all cases, research should be conducted to determine the most appropriate animal species for extrapolation to humans. Future epidemiological studies should give special emphasis to evaluation of reproductive toxicity.

Developmental Toxicity. No studies were located regarding developmental effects in humans exposed to PAHs by any route. However, results of *in vitro* studies suggest that human placental endocrine and hormonal function may be affected by exposure to benzo[a]pyrene (Avigdor et al. 1992; Bamea and Shurtz-Swirski 1992; Guyda 1991). Only limited data are available in animals on a few PAHs (mostly benzo[a]pyrene). These data indicate that ingested or parenterally administered PAHs have a potential to induce adverse developmental effects such as resorptions and malformations (Legraverend et al. 1984; Shum et al. 1979), sterility in F_1 progeny (Mackenzie and Angevine 1981), testicular changes including atrophy of seminiferous tubules with lack of spermatids and spermatozoa, interstitial cell tumors (Payne 1958), immunosuppression (Urso and Gengozian 1980), and tumor induction (Bulay and Wattenberg 1971; Soyka 1980). However, another study found no developmental effects when benzo[a]pyrene was administered orally to mice (Rigdon and Neal 1965). The available animal data suggest that PAHs may be developmental toxicants. However, most of the data are from parenteral routes of exposure, and there are no inhalation data. The oral data are limited because of conflicting results across studies, the use of inconsistent protocols (e.g., varying numbers of animals, administration of the test compound during different times of gestation), the use of only one

dose, lack of study details, and the fact that data are available only on benzo[a]pyrene. Furthermore, some studies have shown that the toxic manifestations of benzo[a]pyrene are dependent on the route of exposure. Therefore, a two-species developmental toxicity study would be helpful to assess fully the potential for PAHs to affect development in humans. The route of exposure should be determined following evaluation of the reproductive organs in the 90-day studies to see if any particular route of exposure has a greater effect. The pharmacokinetic data on PAHs are insufficient,to determine whether similar effects may be expected to occur across different routes of exposure. Developmental toxicity should also be assessed in future animal reproductive toxicology testing and human epidemiological studies. In addition, since PAHs rarely occur alone, but are found in the environment in combinations and mixtures, studies, particularly feeding studies, addressing mixtures of PAHs should be conducted. In all cases, research should be conducted to determine the most appropriate animal species for extrapolation to humans.

Immunotoxicity. No studies were located regarding immunological effects in humans after exposure to PAHs by any route, or in animals following inhalation exposure. In the one oral exposure study in animals that was located, a single dose of fluorene failed to affect thymus or spleen weight (Danz and Brauer 1988). However, there is information available in animals on the immunotoxicity of several PAHs following dermal exposure (contact hypersensitivity) (Old et al. 1963) and intraperitoneal or subcutaneous administration (suppression of both humoral and cellular immunity) (Blanton et al. 1986, 1988; Lubet et al. 1984; Lyte and Bick 1985; White and Holsapple 1984). In general, the degree of immunosuppression correlates with the individual PAH's carcinogenic potency. Because of the information in animals that suggests that PAHs may affect the immune system, Tier I testing to assess PAH-induced immunotoxicity, as recently defined by the NTP (Luster et al. 1988) is recommended. The parameters that should be measured include immunopathology, humoral-mediated immunity, cell-mediated immunity, and nonspecific immunity. Although relatively high doses of PAHs must be used to obtain immunotoxicity in animals, much information could be gained from these studies. In addition, since PAHs rarely occur alone, but are found in the environment in combinations and mixtures, studies, particularly feeding studies, addressing mixtures of PAHs should be conducted. In all cases, research should be conducted to determine the most appropriate animal species for extrapolation to humans. Future epidemiologic studies should also place emphasis on evaluation of this end point.

Neurotoxicity. The potential for short- or long-term neurotoxic effects following exposure to PAHs by any route has not been specifically studied in humans or animals. Although acute-, intermediate-, and chronic-duration studies conducted in animals do not indicate that any of the PAHs tested showed gross evidence of neurotoxicity, these tests were not designed to detect subtle neurological changes. It is recommended that neurobehavioral as well as neuropathological end points be included in future 90-day toxicity testing of PAHs. If these preliminary data indicate that any of the PAHs are neurotoxicants, then a more comprehensive neurotoxicity battery, using sensitive functional and neuropathological tests, could be conducted to characterize further the neurotoxic potential of these PAHs. In addition, since PAHs rarely occur alone, but are found in the environment in combinations and mixtures, studies, particularly feeding studies, addressing mixtures of PAHs should be conducted. In all cases, research should be conducted to determine the most appropriate animal species for extrapolation to humans.

Epidemiological and Human Dosimetry Studies. There are no epidemiological studies available that have investigated the effects of single PAHs by any route of exposure. Most of the available information on the effects of PAHs in humans comes from reports of occupational exposures to PAH-containing mixtures. For example, epidemiologic studies have shown increased mortality due to lung cancer in humans exposed to coke oven emissions (Lloyd 1971; Mazumdar et al. 1975; Redmond et al. 1976), roofing-tar emissions (Hammond et al. 1976), and cigarette smoke (Maclure and MacMahon 1980; Wynder and Hoffmann 1967). Each of these mixtures contains benzo[a]pyrene, chrysene, benz[a]anthracene, benzo[b]fluoranthene, and dibenz[a,h]anthracene as well as other potentially carcinogenic PAHs and other carcinogenic and potentially carcinogenic chemicals, tumor promoters, initiators, and co-carcinogens such as nitrosamines, coal tar pitch, and creosote. Limitations inherent in these studies include unquantified exposure concentrations and durations, as well as concomitant exposure to other potentially toxic substances. Despite their inadequacies, studies in humans suggest that PAH-containing mixtures are dermal irritants and carcinogens following inhalation and/or dermal exposure. If either worker or general populations with appropriate exposure can be identified, epidemiologic studies should be undertaken with special emphasis placed upon evaluation of cancer (of the skin and other organs) and other adverse skin effects, reproductive/ developmental toxicity, and immunotoxicity. However, such studies would be difficult to conduct. With a group of chemicals that are as ubiquitous as PAHs, it would be extremely difficult to distinguish between exposed and nonexposed populations. The more these groups overlap, the higher the chance for misclassification bias. In addition, the statistical power of an epidemiological study

depends partially on the variance of the exposure measurements. If there is enormous variation in the exposure levels among the exposed and nonexposed groups, then the population size needed to obtain statistical significance in the study would be unmanageable and would most likely not be found in any one occupational setting or hazardous waste site. Furthermore, because of the size of the population needed, it would be very difficult to control for confounding factors such as smoking, geographical location, lifestyle.

Biomarkers of Exposure and Effect.

Exposure. Sensitive analytical methods are available to quantify PAH exposure in humans. Although PAHs can be detected in the body fluids and tissues, because of the ubiquitous nature of PAHs in the environment, these biomarkers are not specific for any particular source of PAH exposure. PAHs and their metabolites (e.g., 1-hydroxypyrene) can be measured in the urine of exposed individuals. PAHs form DNA adducts that can be measured in body tissues or blood following exposure to PAHs and mixtures that contain PAHs. Studies attempting to identify suitable and reliable biomarkers from phenanthrene, chrysene, and fluoranthene have been conducted (e.g., Grimmer et al. 1988). However, no other biomarkers (specific or otherwise) that have practical utility have been identified following exposure to PAHs. Further work on developing biomarkers that enable exposure to be quantified would be useful to ascertain whether individuals have been exposed to potentially toxic levels of PAHs. In addition, since PAHs rarely occur alone, but are found in the environment in combinations and mixtures, studies addressing mixtures of PAHs should be conducted.

Effect. The available biomarkers of effect for PAHs are not specific for effects induced by PAHs. The available genotoxicity data indicate that several of the 17 PAHs considered here are genotoxic in both nonmammalian and mammalian systems and are indirect mutagens (i.e., requiring the presence of an exogenous mammalian metabolic system). There were no tests reported for humans exposed to benzo[a]pyrene (the most widely tested PAH) *in vivo*, but several types of cultured human tissue cells demonstrated positive results for benzo[a]pyrene-induced genotoxicity (as evidenced by the induction of chromosomal aberrations, sister chromatid exchange) and binding of benzo[a]pyrene to DNA. Thus, although these results are exclusively from *in vitro* tests and the limited genotoxicity tests conducted on urine obtained from humans exposed to PAHs have been negative, these genotoxic effects observed in human tissue cells may serve as a biomarker of effects for at least one of the PAHs, benzo[a]pyrene. The formation of benzo[a]pyrene-DNA adducts has been demonstrated, and

this may serve as a biomarker of PAH-induced carcinogenicity. Additional studies on the relative sensitivity of DNA adducts and sister chromatid exchanges to identify threshold levels of exposure that could be detected in human populations would be useful. In addition, since PAHs rarely occur alone, but are found in the environment in combinations and mixtures, studies addressing mixtures of PAHs should be conducted.

Absorption, Distribution, Metabolism, and Excretion. The quantitative data on the toxicokinetics of PAHs are based, to a large extent, on short-term exposure to benzo[a]pyrene in animals. Occupational exposure to PAHs generally occurs as a mixture. Therefore, inhalation, oral, and dermal studies exploring how PAHs interact with each other to affect their disposition would be more representative of exposures in humans.

The presence of PAHs and their metabolites in human urine and blood following inhalation, oral, and dermal exposures indicates that PAH absorption occurs in humans (Becher and Bjorseth 1983; Buckley and Lioy 1992; Hecht et al. 1979). However, there was no quantitative information on the extent and rate of PAH absorption in humans. Most of the information regarding the pulmonary and oral absorption and distribution of PAHs in animals is based on acute-duration exposures (Chang 1943; Hecht et al. 1979; Weyand and Bevan 1986, 1987b, 1988; Withey et al. 1991; Wolff et al. 1989c). PAHs appear to be widely distributed in tissues of animals following oral and inhalation exposure; peak tissue concentrations occurred earlier with higher exposure levels. Studies on the absorption and distribution of PAHs following long-term exposures would indicate whether the kinetics are similar to acute-duration exposures. The dermal study conducted by Storer et al. (1984) revealed that several PAHs in a crude coal tar mixture were absorbed, but that benzo[a]pyrene was not. In contrast, animal studies indicate that benzo[a]pyrene was dermally absorbed (Ng et al. 1992; Wester et al. 1990; Yang et al. 1989); however, tissue distribution was not discussed.

PAH metabolism has been extensively reviewed in human and animal tissue homogenates, cultures, and perfused systems (Autrup et al. 1978; Cavalieri et al. 1987; Cohen et al. 1976; Kiefer et al. 1988; Leung et al. 1988). However, these studies are limited to the biotransformation of individual compounds. Since most metabolic pathways have been identified or can be predicted for the individual PAHs, it is now important to understand how these metabolic pathways are affected when the PAHs compete. The carcinogenic and toxic potential of PAHs is associated with their metabolites. Alterations in rates of metabolism and metabolite profiles may affect the toxic consequences of PAHs.

Available data on several of the nonaltemant tumorigenic PAHs discussed in this profile indicate that they exert their adverse effects by mechanisms that differ from those that have been more recently elucidated for altemant PAHs (Amin et al. 1982, 1985b; Rice et al. 1987b). The mechanisms by which benzo[b]fluoranthene and benzo[j]fluoranthene are metabolically activated to genotoxic agents have been elucidated (LaVoie et al. 1993b; Marshall et al. 1993; Weyand et al. 1993a, 1993b). Additional studies designed to assess the potential toxic effects of these reactive metabolites in various species and at various organ sites would be useful.

No studies were located that monitored the rate and extent of PAH excretion in humans. Most studies in animals concentrated on the extent of PAH excretion and the distribution of the compound and its metabolites in urine, feces, and bile following short-term exposures (Bevan and Weyand 1988; Grimmer et al. 1988; Petridou-Fischer et al. 1988; Weyand and Bevan 1986; Wolff et al. 1989c; Yamazaki and Kakiuchi 1989). Data regarding the excretion pattern and rate following long-term exposure to PAHs would be useful to determine if bioaccumulation occurs.

In addition, since PAHs rarely occur alone, but are found in the environment in combinations and mixtures, studies, particularly feeding studies, addressing mixtures of PAHs should be conducted. In all cases, research should be conducted to determine the most appropriate animal species for extrapolation to humans.

Comparative Toxicokinetics. Occupational studies provide evidence that inhaled PAHs are absorbed. Animal studies also show that pulmonary absorption of benzo[a]pyrene occurs, but the extent of absorption is not known. Ingestion of benzo[a]pyrene is low in humans while oral absorption in animals varies among the PAH compounds depending on the lipophilicity. The absorption and distribution of PAHs in various species would be expected to be similar based on the lipophilicity of the compounds. In general, percutaneous absorption of PAHs in several animal species appears to be rapid and high (Ng et al. 1992; Sanders et al. 1986; Wester et al. 1990; Yang et al. 1989). This suggests that dermal absorption in humans may also occur rapidly; however, the extent of absorption may vary depending on the vehicle.

There was no information available on the distribution of PAHs in humans. In general, tissue distribution of benzo[a]pyrene following inhalation exposure is qualitatively similar for different species (Bevan and Weyand 1988; Weyand and Bevan 1986, 1987a, 1988; Wolff et al. 1989c). In

general, orally absorbed PAHs were rapidly and widely distributed in the rat (Bartosek et al. 1984; Withey et al. 1991; Yamazaki and Kakiuchi 1989). Qualitative similarities in distribution among species suggest that distribution in humans would also be similar. Placental transfer of PAHs in mice and rats appears to be limited (Neubert and Tapken 1988; Withey et al. 1992); therefore, human fetuses may be exposed to PAHs, but levels would not be as high as maternal levels.

Qualitatively, metabolism and excretion would be relatively similar in humans and animals, but variability in specific activities of enzymes will alter the metabolic profiles among the species. Knowledge of these differences in enzyme activity in various species would assist in predicting which pathways and metabolites would prevail. For instance, AHH activity is not induced by PAHs in some strains of mice. Therefore, it would be useful to examine the metabolism of those less-well-studied PAHs in several species (i.e., rodent and nonrodent) so that the carcinogenic potential of PAHs in various species could be predicted. The feces (via the bile) appears to be the major excretion route, but the extent of elimination of PAHs varies among species (Bevan and Weyand 1988; Grimmer et al. 1988; Ng et al. 1992; Petridou-Fischer et al. 1988; Sanders et al. 1986; Weyand and Bevan 1986; Wolff et al. 1989c). Further comparative studies on excretion would be useful because differences in human and animal excretion rates are not known. In addition, many of the toxicity tests have used mice, while a larger proportion of toxicokinetic studies have used rats. Thus, more kinetic studies should be conducted in mice to provide data to correspond to the toxicity data. Further, since PAHs rarely occur alone, but are found in the environment in combinations and mixtures, studies, particularly feeding studies, addressing mixtures of PAHs should be conducted. In all cases, research should be conducted to determine the most appropriate animal species for extrapolation to humans.

Methods for Reducing Toxic Effects. Efforts are currently underway to develop ways to mitigate the adverse effects of PAHs, especially with regard to natural products. Efforts to reduce or eliminate cigarette smoking in the general population also contribute toward reducing exposure to and toxic effects of PAHs. The target organs of PAHs have been identified (i.e., the skin and rapidly proliferating tissue such as the hematopoietic and lymphoid systems). Furthermore, several PAHs are considered to be carcinogenic. The mechanism of action for altemant PAH-induced carcinogenicity is fairly well understood. However, additional information would be useful to understand the mechanism of nonaltemant PAH-induced carcinogenicity, how PAHs exert their adverse effects on rapidly proliferating tissue, and how various interactions between PAHs can affect their toxicity and carcinogenicity.

2.9.3 Ongoing Studies

Ongoing research on the health effects and toxicokinetics of PAHs is summarized in Table 2-7.

TABLE 2-7. Ongoing Studies on Polycyclic Aromatic Hydrocarbons[a]

Investigator	Affiliation	Research description	Sponsor
E.J. La Voie	Rutgers State University, New Brunswick, NJ	Environmental polyclics—Metabolism and activation (mice, humans)	National Institute of Environmental Health Sciences
S.P. Mudzinski	Albany Medical College of Union University, Albany, NY	Immunotoxicologic screening of chemical carcinogens (mice)	National Institute of Environmental Health Sciences
W.F. Busby	Massachusetts Institute of Technology, Cambridge, MA	Core—Tumorigenicity testing (mice)	National Institute of Environmental Health Sciences
D.R. Bevan	Virginia Polytechnic Institute, Blacksburg, VA	Disposition of benzo(*a*)pyrene *in vivo*	U.S. Department of Agriculture
R.L. Hill	Florida State University, Tallahassee, FL	The impact of energy-related pollutants on chromosome structure	Not specified
N. Hahon	NIOSH DRDS, Morgantown, WV	Polycyclic aromatic hydrocarbons, particulates and defense mechanisms	National Institute of Occupational Safety and Health
M.K. Sanyal	Yale University, New Haven, CT	Abnormal fetal development during to toxic exposure (humans, rats, mice)	National Institute of Environmental Health Sciences
M. Koreeda	University of Michigan, Ann Arbor, MI	Synthesis and reactions of polycyclic aromatic hydrocarbon metabolites	National Institute of Environmental Health Sciences
L.M. Anderson	National Institutes of Health, Bethesda, MD	Metabolic and pharmacological determinants in perinatal carcinogenesis	National Institutes of Health
K. Frenkel	New York University Medical Center, New York, NY	Tumor promoters affecting base modification in DNA (mice)	National Institutes of Health
M.E. Knuckles	Meharry Medical College, Nashville, TN	Acute and subchronic inhalation and oral toxicity testing of benzo(a)pyrene and fluoranthene	Agency for Toxic Substances and Disease Registry

[a]Information obtained from Federal Research in Progress (October, November 1992) and CRISP (October 1992) databases

Attachment C4

National Library of Medicine Hazardous Substance Data Bank Toxicity Data

TOXICOLOGICAL PROFILE FOR STYRENE

Agency for Toxic Substances and Disease Registry
U.S. Public Health Service

September 1992

DISCLAIMER

The use of company or product name(s) is for identification only and does not imply endorsement by the Agency for Toxic Substances and Disease Registry.

FOREWORD

The Superfund Amendments and Reauthorization Act (SARA) of 1986 (Public Law 99-499) extended and amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law directed the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare toxicological profiles for hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List and which pose the most significant potential threat to human health, as determined by ATSDR and the Environmental Protection Agency (EPA). The lists of the 250 most significant hazardous substances were published in the Federal Register on April 17, 1987; on October 20, 1988; on October 26, 1989; and on October 17, 1990. A revised list of 275 substances was published on October 17, 1991.

Section 104(i)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the lists. Each profile must include the following content:

> (A) An examination, summary, and interpretation of available toxicological information and epidemiological evaluations on the hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects.
>
> (B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, and chronic health effects.
>
> (C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

This toxicological profile is prepared in accordance with guidelines developed by ATSDR and EPA. The original guidelines were published in the Federal Register on April 17, 1987. Each profile will be revised and republished as necessary.

The ATSDR toxicological profile is intended to characterize succinctly the toxicological and adverse health effects information for the hazardous substance being described. Each profile identifies and reviews the key literature (that has been peer-reviewed) that describes a hazardous substance's toxicological properties. Other pertinent literature is also presented but described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

Foreword

Each toxicological profile begins with a public health statement, which describes in nontechnical language a substance's relevant toxicological properties. Following the public health statement is information concerning levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Data needs that are of significance to protection of public health will be identified by ATSDR, the National Toxicology Program (NTP) of the Public Health Service, and EPA. The focus of the profiles is on health and toxicological information; therefore, we have included this information in the beginning of the document.

The principal audiences for the toxicological profiles are health professionals at the federal, state, and local levels, interested private sector organizations and groups, and members of the public.

This profile reflects our assessment of all relevant toxicological testing and information that has been peer reviewed. It has been reviewed by scientists from ATSDR, the Centers for Disease Control, the NTP, and other federal agencies. It has also been reviewed by a panel of nongovernment peer reviewers. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.

William L. Roper

William L. Roper, M.D., M.P.H.
Administrator
Agency for Toxic Substances and
Disease Registry

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1. PUBLIC HEALTH STATEMENT

This Statement was prepared to give you information about styrene and to emphasize the human health effects that may result from exposure to it. The Environmental Protection Agency (EPA) has identified 1,177 sites on its National Priorities List (NPL). Styrene has been found in at least 52 of these sites. However, we do not know how many of the 1,177 NPL sites have been evaluated for styrene. As EPA evaluates more sites, the number of sites at which styrene is found may change. This information is important for you to know because styrene may cause harmful health effects and because these sites are potential or actual sources of human exposure to styrene.

When a chemical is released from a large area, such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment as a chemical emission. This emission, which is also called a release, does not always lead to exposure. You can be exposed to a chemical only when you come into contact with the chemical. You may be exposed to it in the environment by breathing, eating, or drinking substances containing the chemical or from skin contact with it.

If you are exposed to a hazardous chemical such as styrene, several factors will determine whether harmful health effects will occur and what the type and severity of those health effects will be. These factors include the dose (how much), the duration (how long), the route or pathway by which you are exposed (breathing, eating, drinking, or skin contact), the other chemicals to which you are exposed, and your individual characteristics such as age, sex, nutritional status, family traits, life style, and state of health.

1.1 WHAT IS STYRENE?

Pure styrene is a colorless liquid that evaporates easily and has a sweet smell. However, styrene often contains other chemicals that give it a sharp, unpleasant smell. Styrene dissolves in some liquids, but dissolves only slightly in water.

Styrene is used mostly to make rubber and plastics. Billions of pounds of styrene are produced for this purpose each year in the United States. Products produced from styrene include packaging, insulation (electrical and thermal), fiberglass, pipes, automobile parts, drinking cups and other "fooduse" items, and carpet backing. These products mainly contain styrene linked together in long chains (polystyrene). However, most of these products also contain a residue of unlinked styrene. Styrene is also present in combustion products such as cigarette smoke and automobile exhaust.

Low levels of styrene occur naturally in a variety of foods, such as fruits, vegetables, nuts, beverages, and meats. Styrene can be found in air, soil, and water after release from the manufacture, use, and disposal of styrene-based products.

Styrene is quickly broken down in the air, usually within 1-2 days. Styrene evaporates from shallow soils and surface water. Styrene that remains in soil or water may be broken down by bacteria. More information about the chemical and physical properties of styrene can be found in Chapter 3. More information about styrene's occurrence and what happens to it in the environment can be found in Chapter 5.

1.2 HOW MIGHT I BE EXPOSED TO STYRENE?

The major way you can be exposed to styrene is by breathing air containing it. Styrene is found in city air and indoor air. Styrene is released into the air from industries that make and use styrene. It is also released from automobile exhaust, cigarette smoke, building materials, and consumer products (polystyrene products such as packaging materials, toys, housewares and appliances that may contain residual amounts of unlinked styrene). Accidental spills and hazardous waste disposal sites are also sources of styrene in air. Usually indoor air that has less movement contains higher levels of styrene than does outdoor air. Rural or suburban air generally contains lower concentrations of styrene than city air.

Styrene is not usually found in drinking water. When it is found in water, the main source is usually industrial waste discharge from factories and coal gasification plants. Also styrene may leach into groundwater around hazardous waste sites. Soil may become contaminated with styrene by spills, landfilling with wastes, and industrial discharges. Styrene can be a natural part of some foods, or can be transferred to food from polystyrene packaging material. For more information on human exposure to styrene see Chapter 5.

1.3 HOW CAN STYRENE ENTER AND LEAVE MY BODY?

Styrene can enter your body through your lungs if you breathe contaminated air or through your stomach and intestines if you eat or drink contaminated food or water. Styrene can also pass through the skin into your body. Studies on humans show that styrene enters the body tissues quickly after it is breathed in or taken in by mouth. Because styrene is not usually found in drinking water, the most common way it will enter your body is if you breathe air containing it. Ingestion of styrene contaminated foods is another way styrene can enter the body. Once styrene is in the body, it changes quickly to other chemical forms and leaves the body through the urine and exhaled air within a few days to a few weeks. Chapter 2 has more information on how styrene enters and leaves the body.

1.4 HOW CAN STYRENE AFFECT MY HEALTH?

Illness or injury has been reported in people, especially workers, who breathe large amounts of styrene for short periods of time. The most common health problems involve the nervous system. These health effects include depression, concentration problems, muscle weakness, tiredness, and nausea. People exposed to styrene may also have irritation of the eyes, nose, and throat. There have been no reports of death as a result of styrene exposure.

Recovery from the ill effects of short-term exposure is rapid after styrene exposure ends. The health effects for people exposed to styrene for longer periods of time are not known except for limited information on the harmful effects on the nervous system in occupationally-exposed workers.

Some studies of female workers exposed to elevated air concentrations of styrene have suggested that styrene may cause lower birth weights and produce an increased risk of spontaneous abortions. However, these studies are not completely reliable because the studies often involved exposure to chemicals other than styrene.

Styrene vapor affects the lungs of animals that breathe it. Animal studies have shown that inhalation of styrene can result in changes in the lining of the nose that can last up to 12 weeks after exposure ceases. Longterm animal exposure t.o high levels of styrene results in damage to the liver but this effect has not been seen in people.

There is little or no information regarding adverse effects in humans following oral or dermal exposure to styrene. However, animal studies indicate that ingestion of styrene can produce effects on the liver, kidney, blood, immune system and nervous system. Dermal exposure has resulted in irritation to the skin and eyes of rabbits. The International Agency for Research on Cancer has determined that styrene is possibly carcinogenic to humans.

Further information on the health effects of styrene in humans and animals can be found in Chapter 2.

1.5 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO STYRENE?

Styrene and its breakdown products can be found in your blood, urine, and body tissues for a short time following exposure to moderate-to-high levels. Because urine samples are easily obtained, urine is often analyzed for the common breakdown products to determine whether a person has been exposed to styrene. However,, the breakdown products can also be found in the urine of persons who have been exposed to chemicals other than styrene. The tests for styrene and its breakdown products in urine require specific methods and equipment and are not usually available at a doctor's office. Because styrene is cleared quickly from the body, the above methods are useful only for detecting exposures that have occurred within 1 day. Testing within 1 day after moderate-to-high exposures allows us to estimate the actual exposure level. Testing urine for styrene and its breakdown products usually does not help predict how severe the resulting health effects may be, Information about tests for detecting styrene in the body is given in Chapters 2 and 6.

1.6 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

The Environmental Protection Agency (EPA) has determined that 0.1 ppm is the maximum amount of styrene that may be present in drinking water. This level is believed to be low enough to protect an adult from the noncancer effects of styrene, even if exposure occurs for a lifetime. The EPA is currently reviewing the cancer studies on styrene to decide if this chemical is likely to cause cancer in humans.

The Occupational Safety and Health Administration (OSHA) has set a time weighted average (TWA) of 50 ppm styrene as a permissible exposure limit (PEL) and a short-term exposure limit (STEL) of 100 ppm styrene to protect workers during an 8-hour shift over a 40-hour workweek.

More information on governmental regulations for styrene can be found in Chapter 7.

1.7 WHERE CAN I GET MORE INFORMATION?

If you have any more questions or concerns not covered here, please contact your state health or environmental department or:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road, E-29
Atlanta, Georgia 30333

This agency can also provide you with information on the location of the nearest occupational and environmental health clinic. Such clinics specialize in recognizing, evaluating, and treating illnesses that result from exposure to hazardous substances.

2. HEALTH EFFECTS

2.1 INTRODUCTION

The primary purpose of this chapter is to provide public health officials, physicians, toxicologists, and other interested individuals and groups with an overall perspective of the toxicology of styrene and a depiction of significant exposure levels associated with various adverse health effects. It contains descriptions and evaluations of studies and presents levels of significant exposure for styrene based on toxicological studies and epidemiological investigations.

2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

To help public health professionals address the needs of persons living or working near hazardous waste sites, the information in this section is organized first by route of exposure--inhalation, oral, and dermal--and then by health effect--death, systemic, immunological, neurological, developmental, reproductive, genotoxic, and carcinogenic effects. These data are discussed in terms of three exposure periods--acute (less than 15 days), intermediate (15-364 days), and chronic (365 days or more).

Levels of significant exposure for each route and duration are presented in this chapter in tables and illustrated in figures. The points in the figures showing no-observed-adverse-effect levels (NOAELs) or lowest-observed-adverse-effect levels (LOAELS) reflect the actual doses (levels of exposure)used in the studies. LOAELs have been classified into "less serious" or "serious" effects. These distinctions are intended to help the users of the document to identify the levels of exposure at which adverse health effects start to appear. They should also help to determine whether or not the effects vary with dose and/or duration, and place into perspective the possible significance of these effects to human health.

The significance of the exposure levels shown in the tables and figures may differ depending on the user's perspective. For example, physicians concerned with the interpretation of clinical findings in exposed persons may be interested in levels of exposure associated with "serious" effects. Public heal,th officials and project managers concerned with appropriate actions to take at hazardous waste sites may want information on levels of exposure associated with more subtle effects in humans or animals (LOAEL) or exposure levels below which no adverse effects (NOAEL) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels, MRLs) may be of interest to health professionals and citizens alike.

Levels of exposure associated with the carcinogenic effects of styrene in animals are indicated in Figures 2-1 and 2-2.

Estimates of exposure levels posing minimal risk to humans (MRLs) have been made, where data were believed reliable, for the most sensitive noncancer effect for each exposure duration. MRLs include adjustments to reflect human variability from laboratory animal data to humans.

Although methods have been established to derive these levels (Barnes et al. 1988; EPA 1989d), uncertainties are associated with these techniques. Furthermore, ATSDR acknowledges additional uncertainties inherent in the application of the procedures to derive less than lifetime MRLs. As an example, acute inhalation MRLs may not be protective for health effects that are delayed in development or are acquired following repeated acute insults, such as hypersensitivity reactions, asthma, or chronic bronchitis. As these kinds of health effects data become available and methods to assess levels of significant human exposure improve, these MRLs will be revised.

2.2.1 Inhalation Exposure

Most information on the effects of inhalation exposure to styrene in humans comes from studies of workers exposed to styrene vapors in the production and use of plastics and resins, especially polystyrene resins. In most cases, the studies involve workplace exposures such as fiberglass boat building factories where the actual levels of styrene are reported as a range of styrene air concentrations. However, there are a few human clinical studies in which exposures are better quantified. Provided below are descriptions of the known effects of inhalation exposure of humans and animals to styrene.

2.2.1.1 Death

There have been no reports of deaths in humans directly associated with exposure to styrene in the workplace (EPA 1988b; Gosselin et al. 1984; NIOSH 1983).

In animals, inhalation studies indicate that the acute toxicity of styrene is low to moderate. An LC_{50} of 2,770 ppm after 2 hours of exposure was reported in rats, and the LC_{50} for mice after exposure for 4 hours was 4,940 ppm (Shugaev 1969). All rats and guinea pigs survived after exposure to 1,300 ppm styrene for 30 hours and 16 hours, respectively (Spencer et al. 1942). However, all animals died after 40 hours of exposure.

All reliable LOAEL values and LC_{50} values for lethality in each species and duration category are recorded in Table 2-1 and plotted in Figure 2-1.

2.2.1.2 Systemic Effects

No studies were located regarding cardiovascular and musculoskeletal effects in humans or animals after inhalation exposure to styrene.

For the following systemic effects resulting from inhalation exposure to styrene, the highest NOAEL values and all reliable LOAEL values in each species and duration category are recorded in Table 2-1 and plotted in Figure 2-1.

TABLE 2-1. Levels of Significant Exposure to Styrene - Inhalation

Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect) Less serious (ppm)	LOAEL (effect) Serious (ppm)	Reference
ACUTE EXPOSURE							
Death							
1	Rat	3-40+ hr				1300 (LC100)	Spencer et al. 1942
2	Rat	4 hr				2770 (LC50)	Shugaev 1969
3	Gn pig	16-40 hr				1300 (LC100)	Spencer et al. 1942
4	Mouse	2 hr				4940 (LC50)	Shugaev 1969
Systemic							
5	Human	1 d (occup)	Renal		212 (increased urinary levels of alanine aminopeptidase)		Aliberti and Severini 1987
6	Human	15-45 min	Resp Derm/oc	216	216 (nasal irritation) 376 (eye and skin irritation)		Stewart et al. 1968
7	Mouse	3 min	Resp		156 (irritation of upper respiratory tract)		Alarie 1973
Neurological							
8	Human	1 d (occup)			55 (slowed reaction time)		Gamberale et al. 1976
9	Human	1 hr			87 (inhibition of vestibular-oculomotor system)		Odkvist et al. 1982
10	Human	7 hr			99 (impaired balance)		Stewart et al. 1968

TABLE 2-1 (Continued)

Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect) Less serious (ppm)	LOAEL (effect) Serious (ppm)	Reference
11	Human	1 d (occup)			92 (tiredness, slow reaction times, mood changes)		Cherry et al. 1980
12	Mouse	4 hr			413 (behavioral changes)		DeCeaurriz et al. 1983
Developmental							
13	Rat	10 d 7hr/d		600			Murray et al. 1978
14	Rabbit	13 d 7hr/d		600			Murray et al. 1978
15	Hamster	12 d 6hr/d		750		1000 (fetal deaths or resorptions)	Kankaanpaa et al. 1980
Reproductive							
16	Mouse	5 d 6hr/d		300			Salomaa et al. 1985
INTERMEDIATE EXPOSURE							
Systemic							
17	Rat	21 d 5d/wk 4hr/d	Resp	150	1000 (nasal mucosa effects)		Ohashi et al. 1986
18	Rat	11 wk 5d/wk 6hr/d	Hepatic		300 (enzyme alterations, liver morphology)		Vainio et al. 1979
			Renal	300			
19	Rat	13 wk 5d/wk 7hr/d	Renal	133			Viau et al. 1987

TABLE 2-1 (Continued)

Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect) Less serious (ppm)	LOAEL (effect) Serious (ppm)	Reference
20	Gn pig	26 wk 5d/wk 7-8hr/d	Derm/oc			1300 (nasal irritation, severe lung irritation after a few exposures)	Spencer et al. 1942
21	Pig	3 wk 5d/wk 6hr/d	Hemato	360			Johnston et al. 1983
Neurological							
22	Rat	3 mo (cont)		90	320 (astroglial alterations)		Rosengren and Haglid 1989
23	Rat	18 wk 5d/wk 16hr/d		1400			Kulig 1988
24	Rat	21 d 14hr/d			800 (ototoxicity)		Pryor et al. 1987
CHRONIC EXPOSURE							
Systemic							
25	Human	5.1 yr (occup)	Hepatic	120			Harkonen et al. 1984
26	Human	ND (occup)	Hemato		44 (lowered red blood cell count)		Checkoway and Williams 1982
27	Human	1-20 yr (occup)	Hepatic		100 (increased serum levels of OCT and ALAT)		Hotz et al. 1980
28	Human	6 yr (mean)	Renal	24			Viau et al. 1987

TABLE 2-1 (Continued)

Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect) Less serious (ppm)	LOAEL (effect) Serious (ppm)	Reference
29	Human	11 yr (mean) (occup)	Renal	53			Vyskocil et al. 1989
30	Human	>1 yr (occup)	Hepatic		100 (elevated serum amino-transferase levels)		Axelson and Gustavson 1978
31	Rat	18-21 mo 5d/wk 6hr/d	Hepatic		600 (increased liver weight)		Jersey et al. 1978
Neurological							
32	Human	5.1 yr (mean) (occup)			31 (EEG abnormalities)	55 (visuomotor accuracy and psychomotor performance decline)	Harkonen et al. 1978
33	Human	8.6 yr (mean) (occup)			25[b] (decreased verbal learning skills)		Mutti et al. 1984a
34	Human	6.2 yr (mean) (occup)			130 (neuroendocrine effects)		Mutti et al. 1984b
Cancer							
35	Rat	52 wk 5d/wk 4hr/d				100[c] CEL (mammary tumors)	Conti et al. 1988

TABLE 2-1 (Continued)

Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect) Less serious (ppm)	LOAEL (effect) Serious (ppm)	Reference
36	Rat	18-21 mo 5d/wk 6hr/d				600[c] CEL (mammary adenocarcinomas - females)	Jersey et al. 1978

[a]The number corresponds to entries in Figure 2-1.
[b]Used to derive a chronic inhalation MRL of 0.06 ppm: exposure level adjusted by 5/7 and 8/24 to account for intermittent exposure, and divided by an uncertainty factor of 100 (10 for use of a LOAEL, and 10 for human variability).
[c]There is significant uncertainty in this CEL value for styrene; see text for discussion of study limitations.

ALAT = alanine aminotransferase; CEL = cancer effect level; cont = continuous; d = day(s); Derm/oc = dermal/ocular; EEG = electroencephalograph; Gn pig = guinea pig; Hemato = hematological; hr = hour(s); LC50 = lethal concentration, 50% kill; LC100 = lethal concentration, 100% kill; LOAEL = lowest-observed-adverse-effect level; min = minute(s); mo = month(s); Musc/skel = musculoskeletal; ND = no data; NOAEL = no-observed-adverse-effect level; occup = occupational (typically 5 d/wk, 8 hr/d); OCT = ornithine carbamyl transferase; Resp = respiratory; wk = week(s); yr = year(s)

FIGURE 2-1. Levels of Significant Exposure to Styrene – Inhalation

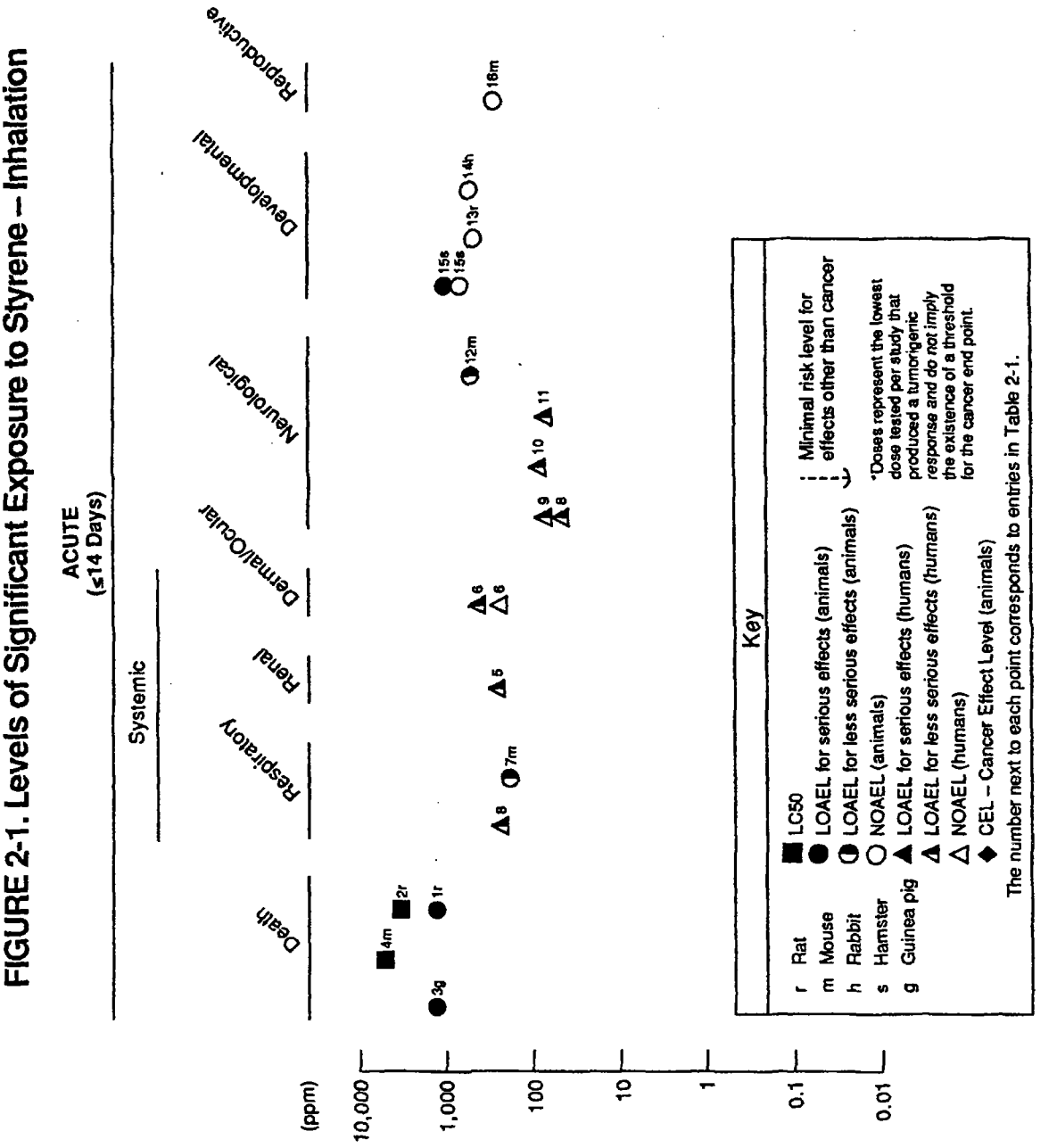
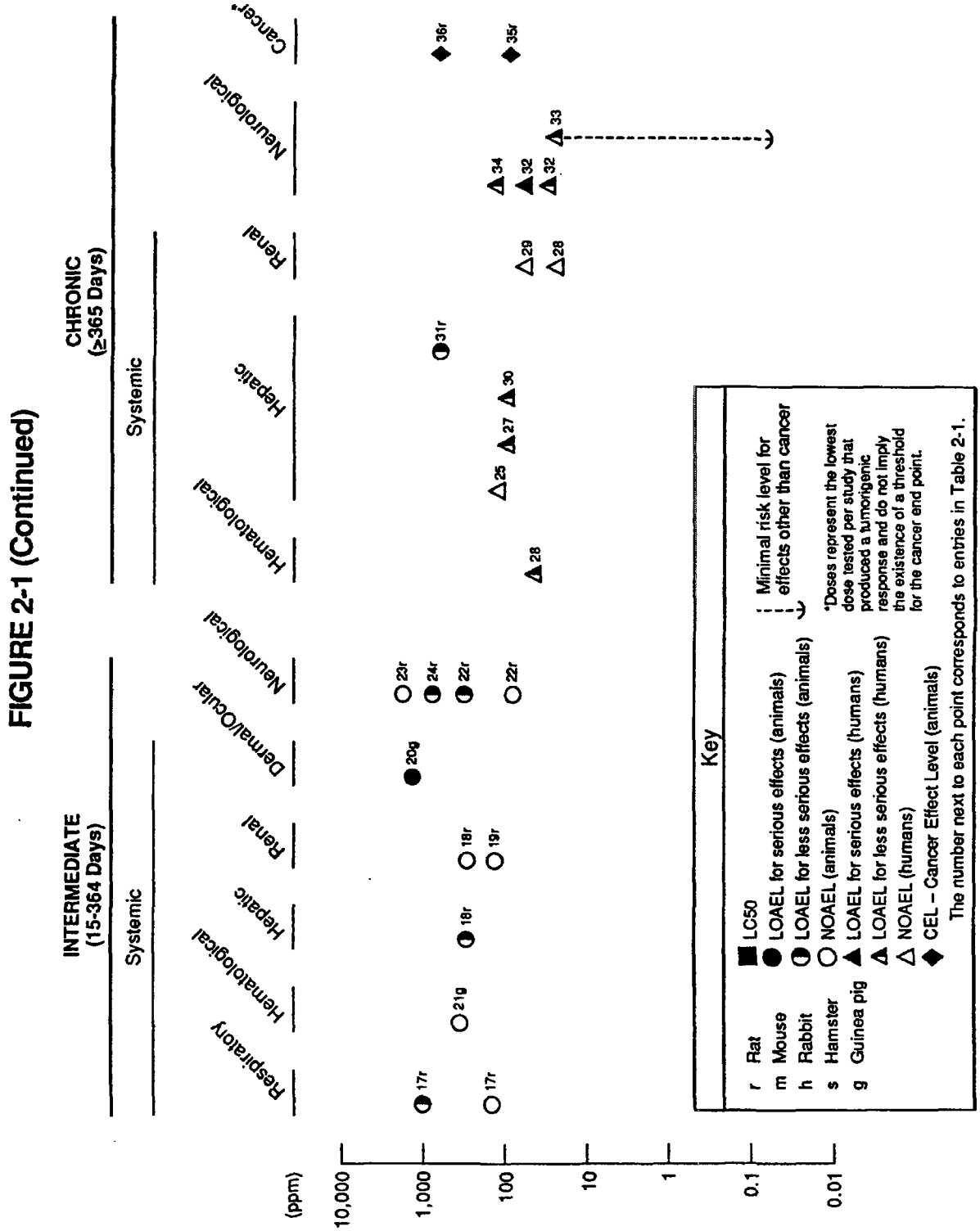


FIGURE 2-1 (Continued)



2. HEALTH EFFECTS

Respiratory Effects. Several human studies have examined the respiratory effects caused by inhalation exposure to styrene. The most commonly reported general symptom is mucous membrane irritation. Irritation of the upper respiratory tract (i.e., nose and throat) has occurred in human volunteers (Carpenter et al. 1944; Stewart et al. 1968) and workers (NIOSH 1983). Throat irritation and increased nasal secretion occurred following exposure of two male subjects to 800 ppm for 4 hours (Carpenter et al. 1944). Nasal irritation was observed in all volunteers after exposure to 376 ppm styrene for 60 minutes (Stewart et al. 1968). Obstructive lung changes were observed in 4 of 21 workers exposed to styrene for about 10 years (Chmielewski and Renke 1975; Chmielewski et al. 1977). However, exposure levels were not defined.

Similar effects have been reported in animals following exposure to styrene vapor. In rats, pathological changes in the respiratory mucosa were found following exposure to 1,000 ppm styrene for 4 hours/day, 5 days/week for 3 weeks. The upper nasal mucosa demonstrated decreased ciliary activity and abnormal morphology. Also, vacuolization and increased numbers of dense bodies of respiratory epithelial cells and sporadic rupture of the cytoplasmic membrane were observed in the rats exposed to 1,000 ppm for 21 days (Ohashi et al. 1986).

Rats and guinea pigs exposed to styrene at a level of 1,300 ppm for 7-8 hours/day, 5 days/week for 6 months showed nasal irritation, but rabbits and monkeys did not (Spencer et al. 1942). Histopathological examinations revealed no changes between test and control rats, but pronounced lung irritation was seen in guinea pigs that died after a few exposures. The irritation, which included congestion, hemorrhages, edema, exudation, and a general acute inflammatory reaction, was not seen in the guinea pigs, rabbits, and monkeys that survived the 6-month exposure period (Spencer et al. 1942). In another study, sensory irritation of the upper respiratory tract in mice was observed following exposure to a styrene aerosol of 666 mg/m^3 (156 ppm) (Alarie 1973). This effect was determined by measuring the decrease in respiratory rate during the exposure of the mice to the aerosol. β-Nitrostyrene, which was also tested in this study, exhibited much greater activity than styrene. No pathological data were available.

These well conducted human and animal studies (see Table 2-1 and Figure 2-1) demonstrate the characteristic irritant properties of styrene on the upper respiratory tract.

Gastrointestinal Effects. Nausea was observed in humans exposed to 376 ppm styrene after 1 hour exposure (Stewart et al. 1968). This effect is probably secondary to effect on the central nervous system, although mucociliary transport of styrene aerosol droplets from the upper respiratory tract to the gastrointestinal tract might also contribute to gastrointestinal irritation. A Russian study (Basirov 1975) reviewed by the World Health Organization (WHO 1983) investigated the effects of styrene on digestive function by testing the secretory, excretory, motor, and pepsinogen-generating functions of the stomach in 20 unexposed and 80 exposed workers. The authors

reported that some workers in the styrene-butadiene synthetic rubber manufacture exposed to 60-130 mg/m^3 (14-31 ppm) styrene for less than 5 to more than 10 years had decreased digestive function and decreased stomach acidity.

No studies were located regarding gastrointestinal effects in animals after inhalation exposure to styrene.

Hematological Effects. Several studies indicate that inhalation exposure of humans to styrene cause mild or no effects on the blood. In one study, the incidence of abnormal values for hematological parameters including erythrocyte, leukocyte, and platelet counts, and hemoglobin levels for 84 styrene workers generally exposed to less than 1 ppm styrene for 1-36 years was investigated. However, these workers were also exposed to intermittent high levels of styrene as well as to other chemicals. The percentages of the exposed group with abnormally low hemoglobin and erythrocyte values or abnormally high leukocyte values were less than those percentages in the 62 person control group. There were no abnormal thrombocyte values reported in either the exposed or control groups (Thiess and Friedheim 1978). Findings from a group of 93 workers engaged in the manufacture of styrene polymers and exposed to generally less than 1 ppm styrene for 1-38 years were also presented in this study; only the incidence of abnormally low erythrocyte counts (in the group exposed to styrene) was found to be statistically significant ($p \leq 0.05$). However, because exposures could not be determined accurately and because there were concomitant exposures to other chemicals, the results of these studies are difficult to interpret.

Lowered erythrocyte counts, hemoglobin, platelets, and neutrophils and slightly higher mean corpuscular red cell volumes and neutrophil band counts were observed in workers in a styrene-butadiene rubber manufacturing plant (Checkoway and Williams 1982). The highest mean styrene level was 13.67 ppm. However, interpretation of this study is limited because multiple-chemical exposures were involved and exposure and clinical signs were measured at the same time and only once. An earlier study of styrene workers showed no definite pattern of hematological changes (Lorimer et al. 1978). In these studies, exposure levels were uncertain and multiple chemicals were involved.

In an animal inhalation study, no adverse hematological effects were noted in Jersey pigs exposed to 72 or 360 ppm styrene for 3 weeks (Johnston et al. 1983). In rats exposed to 49 ppm styrene, erythrocyte-aminolevulinate dehydratase (ALA-D) was depressed markedly. The decrease in enzyme activity was accompanied by a decrease in the enzyme content in bone marrow cells (Fujita et al. 1987). The author's suggestion that the changes may have been a result of styrene oxide reducing the enzyme protein is based on in vitro data.

The well-conducted Thiess and Friedheim (1978) study as well as the more limited studies indicate that few adverse hematological effects occurred in styrene-exposed workers. However, the full meaning of the findings is not clear because of poor characterization of the exposure level and concurrent

exposures to other chemicals. The animal data do not permit a characterization of hematological effects in animals after inhalation exposure to styrene. However, oral animal data support the suggestive evidence in humans that styrene may affect hematological parameters (Section 2.2.2.2).

Hepatic Effects. Human studies on the hepatic effects of styrene inhalation frequently used serum levels of enzymes as indicators of liver dysfunction. In general, human studies have resulted in negative or equivocal results (Harkonen et al. 1984; Hotz et al. 1980; Lorimer et al. 1978; Thiess and Friedheim 1978). The effects of styrene, at exposure levels generally less than 1 ppm, were evaluated in 84 styrene workers exposed for 1-36 years (Thiess and Friedheim 1978). In this study, serum glutamate-oxalacetate transaminase (SGOT), serum glutamate-pyruvate transaminase (SGPT) and gammaglutamyl transferase (GGT) were measured in exposed workers and a reference population. Within the styrene-exposed group the incidence of high SGOT or SGPT values was less than the reference group. The number in the exposed group having abnormally high GGT values was twice as high as the control group. However, only a small number of exposed workers and controls were included in this study and the results were not statistically significant. In another study, workers exposed to styrene in the range of 100-300 ppm as an 8-hour time-weighted average in small manufacturing operations showed elevated levels of liver amino transferase (Axelson and Gustavson 1978). However, the cause of the increased levels and effects on liver function are uncertain. In another exposed population of 93 workers exposed to less than 1 ppm styrene for 1-38 years, hepatic enzyme levels (SGOT, SGPT, and GGT) were measured (Thiess and Friedheim 1978). There were no statistically significant differences in the hepatic enzyme levels of the exposed and reference population.

Liver enzyme levels were also measured in 57 workers exposed to styrene in the polyester industry for 1-20 years (Hotz et al. 1980). The styrene exposure concentrations were from 1 to 100 ppm. The hepatic enzymes, ornithine carbamyl transferase (OCT), aspartate amino transferase (ASAT), alanine amino transferase (ALAT), and GGT were measured and showed increased activity compared to control values. The OCT and ALAT levels correlated better than the GGT and ASAT levels with the degree of styrene exposure. These study results suggest hepatic injury at 100 ppm and less. In another study, the effect of styrene exposure in 34 styrene-exposed and 34 control female workers was evaluated (Harkonen et al. 1984). These workers were exposed to approximately 50-120 ppm styrene for a mean duration of 5.1 years in the breathing zone with the highest levels temporarily exceeding 200 ppm. Liver function was assessed by measurement of ASAT, ALAT, and GGT. Bile acid concentrations were also measured. The styrene-exposed group did not have higher activity levels of either liver enzymes or bile acids when compared to the control group values. A few abnormal values in both the exposed and control groups were associated with the use of drugs or alcohol and the study results indicated no hepatic effects associated with exposure to styrene. In

a different study, workers exposed to approximately 5-20 ppm styrene for up to 20 years or more were found to have high GGT values even when the use of alcohol was taken into consideration (Lorimer et al. 1978). However, no other hepatic parameters were affected.

In animal studies, rats were exposed to 300 ppm styrene intermittently for 11 weeks (Vainio et al. 1979). Free glutathione in rat liver significantly decreased (approximately 59%) after an exposure period of 2 weeks. The glutathione depression continued throughout the intermittent 11-week exposure. The cytochrome P-450 content of hepatic microsomes was doubled during the first 2 weeks of exposure to 300 ppm. The epoxide hydratase and UDP glucuronosyltransferase activity in rat liver increased upon exposure to 300 ppm over 11 weeks of intermittent exposure. Degenerative morphologic alterations were also observed in the parenchymal cells of the liver 2 weeks after exposure to 300 ppm (Vainio et al. 1979). In another study by the same author, a 4-day exposure at even lower styrene levels (less than 200 ppm) resulted in decreased free glutathione in rat liver. In this case the decrease was reversible as evidenced by a slight elevation of hepatic glutathione concentrations in styrene exposed animals 18 hours after exposure.

In a 24 month study of rats exposed to 600 or 1,000 ppm styrene, increased absolute and relative liver weights were observed in females at both exposure levels at 6 months (Jersey et al. 1978). At 12 months and terminal necropsy, these effects were inconsistent and not dose-related. Histopathological findings were similar for exposed and control females at the 6 and 12 month intervals. For males, there was evidence of a nutritional state associated with decreased body weight gain. At termination, alveolar histiocytosis was observed in the lungs of females exposed to 1,000 ppm only. Excessive mortality and chronic mucosa pneumonia prevented an appropriate evaluation of the male rat histopathology.

Although the well-conducted studies on workers generally gave negative results, the animal studies involving higher exposures suggest that styrene inhalation may affect liver function.

Renal Effects. Human studies generally confirm the importance of urinary enzymes as indicators of kidney damage due to exposure to styrene (Aliberti and Severini 1987; Viau et al. 1987; Vyskocil et al. 1989) and other chemicals. The urine of 15 subjects exposed to styrene (900 mg/m^3 or 212 ppm) for an 8-hour workshift and 20 unexposed control subjects was evaluated for urinary enzyme effects (Aliberti and Severini 1987). The subjects exposed to styrene demonstrated higher levels of alanine-aminopeptidase (AAP) at the end of the workshift compared to unexposed controls ($p<0.001$). The N-acetylglucosaminidase(NAG) was increased much less than AAP but the increase over the control group was statistically significant ($p<0.01$). These results are considered to represent an early biochemical indication of adverse renal effects. Viau et al. (1987) measured urinary excretion of β-microglobulin, retinol-binding protein and albumin in 65 workers exposed to styrene (24 ppm) for a mean duration of 6 years. No significant difference was observed in the urinary excretion of proteins when compared to controls. No significant

difference was found by Vyskocil et al. (1989) in the urinary excretion of albumin β-microglobulin, retinol-binding protein, total protein, glucose, lysozyme, lactate dehydrogenase, and β-N-acetyl-D-glucosaminidase in workers exposed to an average of 53 ppm styrene when compared to a control group. The minor kidney effects noted in these well-conducted human studies indicate that styrene may exert a minor effect on some kidney enzyme functions.

Minor changes in renal enzyme activities and no effects on morphology (Vainio et al. 1979; Viau et al. 1987) have also been observed in animals after exposure to styrene. Intermittent 11-week exposure to styrene by inhalation (300 ppm) induced the activities of the drug hydroxylating enzymes ethoxycoumarin 0-deethylase, and cytochrome P-450. Activities of the conjugating enzymes, epoxide hydratase, and UDP glucuronosyltransferase were also induced in the exposed rats (Vainio et al. 1979). Since there were no degenerative morphologic alterations observed in the kidney, this is not a clear adverse effect. In another study, no functional or morphological renal changes could be detected in rats exposed to 133 ppm styrene (5 days/week) for 13 weeks (Viau et al. 1987).

Dermal/Ocular Effects. Eye irritation in humans has been reported at high styrene concentrations (Carpenter et al. 1944; Stewart et al. 1968). Immediate eye irritation was reported in two human subjects exposed to 800 ppm styrene for 4 hours (Carpenter et al. 1944). Eye irritation was also noted by Stewart et al. (1968) in two of five volunteers exposed to 376 ppm styrene for 1 hour. Also, 345 styrene-exposed workers (98% male) were evaluated for ocular toxicity due to exposure to styrene (5-200 ppm) for 7-20 years. No evidence of optic neuritis, central retinal vein occlusion, or retrobulbar neuritis was found. Conjunctival irritation was a complaint of 22% of the 345 workers exposed to styrene levels above 50 ppm (Kohn 1978). Eye and nasal irritation was observed in rats and guinea pigs exposed to 1,300 or 2,000 ppm styrene, 7-8 hours/day, from 21 to 30 weeks (Wolf et al. 1956). 5 days/week for durations ranging Rabbits and monkeys were exposed for up to 360 days with no effects.

Other Effects. Exposure to styrene vapors has been found to increase the levels of several pituitary hormones (prolactin, growth hormone) in female workers (Mutti et al. 1984b). This effect is probably mediated through the nervous system, and so is discussed in Section 2.2.1.4.

2.2.1.3 Immunological Effects

No dose-related differences in the concentrations of serum alpha, beta and gamma globulins were found in workers exposed to different concentrations of styrene (Chmielewski et al. 1977). However, exposure levels and durations were not specified. In patch-testing studies of cross-reactors to styrene, styrene epoxide was more sensitizing than styrene itself (Sjoberg et al. 1984). The authors interpreted this as evidence that styrene requires metabolism by skin aryl hydrocarbon hydroxylase to styrene epoxide for its sensitizing activity.

No other studies were located regarding immunological effects in humans or animals after inhalation exposure to styrene.

2.2.1.4 Neurological Effects

Several epidemiological and clinical studies have shown that styrene exposure causes alterations of central nervous system functions in humans. Men exposed to levels of 52-117 ppm (mean = 92 ppm) in a boat-building factory were more subject to mood changes, were more likely to report feeling tired, and had slower reaction times than unexposed workers (Cherry et al. 1980). A similar decrease in reaction time was observed in four groups of workers exposed to styrene at levels of 17-101 ppm (mean = 55 ppm) (Gamberale et al. 1976). Workers exposed to styrene in several industries at mean concentrations of 5-125 ppm had mild sensory neuropathy characterized by decreased sensory conduction amplitude and increased duration, but there were too few people to define no-adverse-effect levels (Rosen et al. 1978). An increased occurrence of fast activity in central and precentral areas of the brain was also noted in styrene workers. These effects were clearly visible in workers exposed to an average of 47 ppm or more. In a study by Stewart et al. (1968), no toxicity was noted following 1- or 2-hour exposure to 51 ppm (3 subjects) or 117 ppm (1 subject) styrene, respectively. In the same study, 6 subjects were exposed to 99 ppm styrene vapor for 7 hours. Three of these subjects reported that they were having difficulty performing the modified Romberg test which measures balance and coordination. Also, 1-hour exposure to 376 ppm styrene vapor resulted in abnormal neurological findings and complaints of nausea and inebriation. In another study, immediate muscular weakness, listlessness, drowsiness and impaired balance was observed in two human subjects exposed to 800 ppm styrene (Carpenter et al. 1944). Odkvist et al. (1982) investigated the inhibition of the vestibular-oculomotor system in ten human subjects experimentally exposed to 87-139 ppm styrene for 1 hour. Visual suppression was disturbed and the authors concluded that styrene acts, along with other organic solvents, to block cerebellar inhibition of the vestibula-oculomotor system.

Chronic exposure of workers to styrene results in increased incidence of abnormal electroencephalograms (EEGs) (Harkonen et al. 1978). In this study, exposure levels were estimated from an empirical relationship that was established between workplace air concentrations and urinary levels of mandelic acid (MA) in exposed workers. This relationship is expressed as:

$$\ln(\text{styrene air concentration, ppm}) = -3.4915 + 1.0568 \bullet \ln(\text{urinary MA concentration, mg/L})$$

The authors had previously observed a strong correlation ($r^2 = 0.86$, $p<0.001$) between the time weighted average styrene concentrations in air and urinary mandelic acid concentrations. Thus, exposure estimates derived from urinary metabolite levels are considered to be sufficiently reliable to establish meaningful dose-response relationships. Exposure to an 8 hour time-weighted average of 31 ppm or above resulted in a 30% incidence of altered EEGs, compared to 10% in workers exposed to less than 31 ppm. The abnormalities

included local slow wave activity (14/23), diffuse theta activity (8/23), and bilateral discharges (2/23). Exposure to 55 ppm or higher resulted in decreased visuomotor accuracy and impaired psychomotor performance. As part of the same study, 9 out of 40 workers who displayed subjective symptoms of styrene exposure were found to have abnormal nerve conduction velocities. However, no clear relationship between the altered conduction velocity and styrene exposure could be established. Mutti et al. (1984a) reported verbal learning skills were significantly impaired in workers exposed to mean daily concentrations of styrene greater than 25 ppm (this value is also estimated from levels of urinary metabolites). This exposure level (25 ppm) is the lowest concentration known to have caused significant neurological effects in humans, and so has been selected to calculate a chronic inhalation MRL of 0.06 ppm, as described in the footnote to Table 2-1. Logical memory and visuo-constructive abilities were also significantly affected in workers exposed to greater than 50 ppm styrene.

Inhalation exposure to styrene may also cause peripheral neuropathy. A man exposed to an undetermined concentration of styrene vapor for 5 years (4-10 hours/day, 7 days/week) developed burning sensations in the feet and moderate slowing of nerve conduction velocity in the lower limbs (Behari et al. 1986). Histologic examination revealed demyelination of sural nerve fibers. However, this individual also had a history of prescription drug use and may have been exposed to chemicals other than styrene. Therefore, this report does not contain adequate information to establish an unequivocal cause-effect relationship.

The effects of styrene on the neuroendocrine activity of the tuberoinfundibular dopaminergic system (TIDA) in humans was indirectly investigated with measurements of adenohypophysial hormones, including serum prolactin (PRL), human growth hormone (HGH), thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH) and luteinizing hormone (LH) in 30 female workers exposed to approximately 130 ppm styrene and 30 age-matched controls (Mutti et al. 1984b). The exposed subjects' serum levels of PRL were more than double the reference values and correlated with exposure to styrene. The serum levels of HGH in exposed women were also higher than the reference group. The investigators concluded that the styrene-induced neuroendocrine effects were mostly due to acute exposure and were not influenced by the duration of exposure after control for age and concentration of styrene.

The effect of occupational exposure to styrene on high-frequency hearing loss was evaluated in workers exposed to 35-165 ppm styrene. The studies did not demonstrate an increased age-dependent decrease in hearing high frequencies when compared to controls (Muijser et al. 1988). However, a comparison within the exposed group indicated a statistically significant difference in hearing thresholds for high frequencies in the workers exposed to the highest concentration of styrene (up to 700 mg/m^3

Limited neurobehavioral and neurotoxic effects of styrene have been investigated in animal studies. In rabbits, exposure to 750 or 1,500 ppm of styrene resulted in dose-dependent decreases in striatal and tubero-

infundibular dopamine and homovanillic acid levels. Noradrenalin levels were not significantly changed (Mutti et al. 1984c). Mice exposed to 413-851 ppm styrene for 4 hours exhibited decreased immobility in a confined area swimming test (DeCeaurriz et al. 1983). In another study, groups of rats were exposed to 350, 700, and 1,400 ppm of styrene for 18 weeks (Kulig 1988). Compared to controls, styrene-treated rats exhibited an initial reduction in activity and grip strength, but this effect tended to diminish during the study period. This suggests that some level of tolerance might develop during continuous exposure. Coordinated movement and nerve conduction time were not affected. Initially there were some styrene-related neurobehavioral effects. However, at the end *of* the exposure period the performance of styrene-treated rats was not significantly different from the control group and there were no deficits in performance during the post-exposure period. In another animal study, Rosengren and Haglid (1989) demonstrated that constant styrene exposure of rats to 320 ppm (24 hours/day) for 3 months induced increases in glial fibrillary acidic proteins 4 months after the exposure period. Using this glial cell marker, this study suggests that styrene may induce abnormalities in the central nervous system of rats. Pryor et al. (1987) reported that 800 ppm styrene caused an elevation in behavioral auditory response thresholds ($12kH_z$) in rats exposed for a 3 week period (14 hours/day). No differences were found between exposure groups in the acquisition of multisensory conditioned avoidance response tasks.

The highest NOAEL values and all reliable LOAEL values for neurological effects in each species and duration category are recorded in Table 2-1 and plotted in Figure 2-1.

2.2.1.5 Developmental Effects

Limited information concerning developmental effects of styrene in humans is available from studies of delivery outcome of women employed in the plastics industry (processing styrene or polyurethane plastics). Case-control studies performed in Sweden and Norway did not detect an increase in the odds ratio for developmental effects (stillbirth, infant death, malformations, low birth weight) in women who worked in the plastic industry (Ahlborg et al. 1987). However, actual levels.of styrene exposure were not known for either group of workers. In another study, the birth weights of infants whose mothers worked during pregnancy in the reinforced plastics industry were analyzed by Lemasters et al. (1989). Women who worked in areas with elevated levels of styrene (estimated from industrial hygiene data to average about 82 ppm) had offspring with adjusted birthweights that were 4% less than the offspring of unexposed women. However, this decrease was not statistically significant ($p=0.08$). These studies suggest that developmental effects in exposed workers are not of major concern, but the data are not adequate to exclude this effect. Moreover, interpretation of the results is complicated due to exposure of the workers to other chemicals in the workplace such as toluene, xylene, acetone, methylene chloride, and methyl ketone (Lemasters et al. 1989), as well as thermal degradation products of styrene polymers (Ahlborg et al. 1987). Workers may also be exposed to aerosols containing aldehydes, ketones, alcohols, esters, acids, and anhydrides.

Evaluations of developmental effects of styrene in rats, rabbits, mice, and hamsters have been reported (Kankaanpaa et al. 1980; Murray et al. 1978). Rats were exposed to 0 or 300 ppm styrene on days 6 to 15 of gestation and additional rats were subsequently exposed to 0 or 600 ppm styrene (Murray et al. 1978). The average fetal crown-rump length was significantly reduced in the 300 ppm group, but not in the 600 ppm group. The authors concluded this effect was not treatment-related. The number of live fetuses or resorptions/litter was not affected by exposure to styrene. A few skeletal variants such as lumbar spurs and delayed ossification of sternebrae occurred in the styrene-exposed litters at a higher incidence than the control litters; however, the occurrence of this effect was similar to historical controls. Additionally, it was reported that there were no fetotoxic or teratogenic effects in rabbits exposed to 300 or 600 ppm styrene on days 6-18 of gestation (Murray et al. 1978). Although there was a significant increase in the incidence of unossified sternebrae in the 600 ppm group, it did not exceed that found in historical control data. Embryotoxicity was observed following exposure of pregnant mice to 250 ppm styrene on days 6-16 of gestation (Kankaanpaa et al. 1980). The incidence of dead or resorbed fetuses was higher in the exposed group but was not statistically significant ($p<0.10$). Some minor skeletal malformations (rib fusions, extra ribs) were observed in the mice. In the same study, hamsters were exposed to 300, 500, 750, and 1,000 ppm of styrene on days 6-18 of gestation. Fetotoxicity (dead or resorbed fetuses) was observed only at 1,000 ppm and teratogenicity was not reported at any of the exposure levels. The incidence of dead or resorbed fetuses was 26% in the control group versus 60% in the exposed group. No skeletal malformations were noted in the hamsters.

The highest NOAEL values and all reliable LOAEL values for developmental effects in each species and duration category are recorded in Table 2-1 and plotted in Figure 2-1.

2.2.1.6 Reproductive Effects

Information on the reproductive effects of styrene in humans is available from epidemiological studies of the reproductive outcomes of females employed in the various industrial operations in which styrene is used. However, exposures to styrene were not adequately quantified in any of the studies cited. In one study, spontaneous abortions among 9,000 Finnish chemical workers from 1973 to 1976 were analyzed (Hemminki et al. 1980). The risk of spontaneous abortion (expressed as number of abortions per 100 pregnancies) was significantly higher in women employed in styrene production compared to all women in Finland (15.0 vs. 5.5). However, this increase was not detected in a follow-up study of the same workers (Hemminki et al. 1984). The possible embryotoxic effects of styrene on 67 female lamination workers compared to 67 age-matched controls were evaluated in a second study (Harkonen and Holmberg 1982). The number of births was significantly lower among the workers exposed to styrene. This result was explained in part by a greater number of induced abortions in the styrene-exposed group. The number of spontaneous abortions was not elevated in the exposed women. No increased risk of spontaneous abortions among workers processing polymerized plastics or

heated plastics made of vinyl chloride or styrene was reported (Lindbohm et al. 1985). The authors reported that the statistical power of the study was low due to the small study population. These studies are not conclusive since the workers were exposed to chemicals other than styrene in the workplace and the concentrations of styrene were not adequately reported.

Mice exposed to 150 or 300 ppm styrene by inhalation for 5 days (6 hours/day) did not have a statistically significant increase in the frequency of abnormal sperm heads 3-5 weeks after exposure (Salomaa et al. 1985). These findings suggest that reproductive effects, if they exist, may not be produced through a genotoxic mechanism.

2.2.1.7 Genotoxic Effects

Chromosomal damage in peripheral lymphocytes and other cellular effects have frequently been studied in workers exposed to styrene in the production of reinforced plastic products and styrene/polystyrene production. In general, these studies are limited by the fact that workers in these industries are often exposed to chemicals other than styrene such as methylene chloride and epoxide resins. Confounding factors such as age, sex, and smoking status must also be considered. Studies of this nature may also be limited by small sample sizes and differing cell culture methodologies.

Chromosomal aberrations have been reported in several studies of workers exposed to styrene for 1 to 15 years in reinforced plastic operations (Andersson et al. 1980; Hogstedt et al. 1979; Meretoja et al. 1977, 1978). For example, in an evaluation of lymphocytes from 16 men exposed to styrene (1-140 ppm) and 5 controls, styrene-exposed men showed 11% - 26% aberrant cells versus 3% or less in the control subjects (Meretoja et al. 1977). The aberrations were almost totally chromosome breaks. The frequency of micronuclei and cells connected with nuclear bridges were also increased in exposed workers. In another study, 10 styrene-exposed workers (1-140 ppm) and 5 controls were reexamined. It was reported that the frequencies of aberrant lymphocytes varied from 10% to 26% in the exposed group and from 1% to 4% in the referents (Meretoja et al. 1978). The most frequent class of aberrations was again chromosome breaks or,gaps. The incidence of sister chromatid exchange (SCE) among styrene-exposed workers in this study was not significantly higher in the controls. In another study of 36 exposed workers and 37 controls, Andersson et al. (1980) reported an increase in the incidence of chromosome breaks/gaps and SCEs (21 exposed subjects (2.8-154 ppm) versus 20 control subjects for the SCE subset). Chromosome aberrations in lymphocytes from peripheral blood were more frequent in 6 workers when compared to 6 age- and sex-matched controls (Hogstedt et al. 1979). In this study workroom concentrations were a little lower (12-74 ppm) than in previously reported studies. In another study, negative results were reported for chromosomal aberrations and SCEs in reinforced plastics workers (16 exposed versus 13 controls) in workroom exposures from 33 to less than 70 ppm styrene (Watanabe et al. 1981).

Styrene exposures are generally lower (1-58 ppm) in styrene and polystyrene manufacturing facilities than in reinforced plastic operations, and studies of chromosome damage and other cellular effects in these facilities have been generally negative (Hansteen et al. 1984; Nordenson and Beckman 1984; Thiess et al. 1980). For example, Thiess et al. (1980) reported that 24 employees exposed to styrene in the laboratory (6.0 ppm) and a polyester processing plant (58.1 ppm) showed a nonstatistically significant increase in chromosomal aberration rates compared to controls. In another study, chromosomal aberrations were studied in lymphocytes of 15 workers and 13 controls employed in the manufacture of polyester reinforced windowglass fiber where workroom exposure was 24 ppm styrene. No increased frequency of chromosome breaks/gaps was observed, but the number of micronuclei was significantly increased (Nordenson and Beckman 1984). The authors concluded that the mitotic spindle membranes may be more sensitive to styrene and its metabolites than DNA. Eighteen workers exposed to less than 50 ppm styrene were found to have a significant increase in chromosome gaps (Hansteen et al. 1984). No increase in the number of chromosome breaks and SCE's was found compared to controls. In another study, increased frequency of lymphocyte micronuclei in workers exposed to a mean 13 ppm styrene was reported (Hogstedt et al. 1983). An increase in chromosomal aberrations was observed in workers exposed to a mixture of phenol, styrene, and formaldehyde (levels not specified) (Mierauskiene and Lekevicius 1985). In an evaluation of cytogenic monitoring of industrial populations potentially exposed to genotoxic chemicals including styrene in the Netherlands, DeJong et al. (1988) concluded that the results of chromosome analyses are difficult to interpret due to variable and high background levels of chromosome aberration in control populations.

Male and female rats exposed to styrene vapor (600 and 1,000 ppm) for 1 year did not show an increased incidence of chromosome abnormalities in bone marrow cells collected at the end of the last exposure (Sinha et al. 1983), although detectable chromosomal abnormalities are not likely to endure for such a long period.

In summary, the mutagenicity data from studies of workers exposed to styrene suggest that styrene exposure can produce an increased incidence of chromosomal aberrations (primarily gaps and breaks). However, interpretation of these data are complicated by the possible involvement of concommitant exposures to other chemicals. The data are insufficient to show styrene exposure produces an increased incidence of sister chromatid exchanges or micronuclei formation.

Other genotoxicity studies are discussed in Section 2.4.

2.2.1.8 Cancer

Although there are several epidemiologic studies which suggest there may be an association between styrene exposure and an increased risk of leukemia and lymphoma, the evidence is generally inconclusive due to multiple chemical exposures and inadequate documentation of the levels and durations of exposure

to styrene. In a study of employees who worked in the development or production of styrene-based products, deaths due to malignant neoplasia were fewer than expected in the total study group (2,904 subjects) (Ott et al. 1980). An increase in lymphatic leukemia (4 observed deaths versus 0.5 expected) was observed in a group of employees exposed to polymer extrusion fumes, solvents, and colorants but was not found to be related to duration or level of exposure. A retrospective cohort mortality study was conducted for two styrene-butadiene rubber plants, designated as Plant A and Plant B (Meinhardt et al. 1982). Occupational history records were available from 1943 at Plant A and from 1950 at Plant B to the study end-date of March 31, 1976. No statistically significant excess in total or cause-specific mortality rates was observed for the overall worker population at either plant. Plant A workers had a statistically nonsignificant increase in leukemia and aleukemia. The mean concentrations of styrene, butadiene and benzene in Plant A were 0.94, 1.24, and 0.1 ppm, respectively, and in Plant B styrene and butadiene levels were 1.99. and 13.5 ppm, respectively. The presence of a known leukemogenic agent, benzene, obviously further confounded the study results with regard to styrene carcinogenicity. The authors concluded that the study findings suggested that the production and manufacture of styrene-butadiene rubber may be associated with an excess of lymphatic and hematopoietic neoplasms. In a study of 560 male employees of a styrene-polystyrene manufacturing plant who had at least 5 years of exposure, there were no significant increases in cause-specific mortality (Nicholson et al. 1978). The reported leukemia incidence suggested the need for further study. In another study, a statistically significant excess of lymphoma deaths in an exposed population (662 subjects) was reported, and 2 of the 3 deaths occurred in men less than 40 years of age who,had been exposed for at least a year (Hodgson and Jones 1985). However, the lack of association with actual exposure levels or specific durations and the small number of observed deaths requires cautious interpretation. In a very large epidemiological study of nearly 16,000 workers in the styrene plastic industry, the death rate from leukemia was twice as high in areas of high exposure as in areas of low exposure (Wong 1990). However, there were too few cases for this to be statistically significant. Several other studies in humans have not detected any evidence of leukemia, lymphoma, or other cancers (Coggon et al. 1987; Okun et al. 1985; Matanoski and Schwartz 1987). The International Agency for Research on Cancer (IARC) has concluded that the evidence for carcinogenicity in humans from epidemiological studies is inadequate and classifies styrene in Group 2B, possibly carcinogenic to humans (IARC 1987). EPA agreed that results of epidemiological studies were confounded by multiple chemical exposures and considered the epidemiological evidence inadequate to determine potential human carcinogenicity of styrene (EPA 1988b).

Three chronic animal inhalation studies (Conti et al. 1988; Jersey et al. 1978; Maltoni et al. 1982) have been conducted to evaluate the carcinogenicity of styrene. These studies have produced variable results. Groups of 85 male and 85 female rats were exposed to 600 or 1,200 ppm styrene (99.5% purity) for 6 hours/day, 5 days/week for 18-20 months (Jersey et al. 1978). The concentration in the high-dose group was decreased to 1,000 ppm due to decreased weight gains in male rats. The incidence of mammary

adenocarcinomas in the 600 ppm female group was significantly higher than in controls. However, there was no significant response evident at 1,000 ppm, and the control rats had an unusually low mammary adenocarcinoma incidence when compared with historical controls. In the same study, the incidence of lymphosarcomas and leukemia in females was identical for both exposed groups at 5.27% and 1.04%, respectively. These values were not statistically higher than the respective values of concurrent control animals, but were significant when compared to historical control data. However, there was an absence of dose response. A high incidence of chronic murine pneumonia in these rats makes a complete evaluation of the data difficult and the results uncertain.

In a second study, designed to determine if styrene would induce brain tumors, groups of 40 male and 40 female rats were exposed to 0, 25, 50, 100, 200, and 300 ppm styrene for 52 weeks (Maltoni et al. 1982). There was no increased incidence of brain tumors in any of the exposed groups of rats. In a third study (performed by the same group as the second study), 30 male and 30 female rats were exposed to 25, 50, 100, 200, or 300 ppm styrene for 52 weeks (Conti et al. 1988). A higher incidence of total malignant tumors in the group exposed to 100 ppm styrene was observed. The increased incidence was not due to any specific type of tumor. However, the higher incidence of total malignant tumors in the 100 ppm styrene-exposed group was not dose related since the 200 and 300 ppm groups did not have significantly higher total malignant tumor incidences. A higher incidence of malignant and total (benign plus malignant) mammary tumors was observed in females of all the groups exposed to styrene. Although the authors did not report tests for statistical significance or levels of significance, the data provided in tabular form clearly indicate a dose trend of increased incidence of combined benign and malignant mammary tumors. Although statistical methods are not provided, the data reported indicate that statistical significance may be marginal at the two lower doses (25 and 50 ppm) and significant at 100 ppm and above.

2.2.2 Oral Exposure

No studies were located regarding health effects in humans after oral ingestion of styrene. Based on the animal data that follow, the oral toxicity of styrene in humans would be expected to be low to moderate.

2.2.2.1 Death

No deaths in humans from ingesting styrene have been reported in the evaluations of case studies (EPA 1989c; Gosselin et al. 1984; NIOSH 1983).

The approximate reported oral LD_{50} for male and female rats was 5,000 mg/kg (Wolf et al. 1956). A 100% survival rate and 100% mortality rate were reported in rats exposed to single oral doses of styrene (observation period 2 weeks) at 1,600 and 8,000 mg/kg, respectively (Spencer et al. 1942). Death in this study was mainly due to pronounced irritation of the esophagus and stomach. In another study, female mice were given a single oral dose of 1,350 mg/kg styrene on the 17th day of pregnancy (Ponomarkov and Tomatis

1978). After weaning, the progeny received the same dose once per week. The treatment was suspended after 16 weeks due to high mortality among the progeny (including both males and females). Fifty percent of.the males and 20% of the females had died after 20 weeks, despite the suspension of treatment at week 16. The cause of death was liver necrosis and lung congestion. A high mortality rate (number not specified) was reported in 40 female rats exposed to 250 mg/kg/day styrene for 52 weeks (Conti et al. 1988). Mortality was significantly elevated in male and female rats administered styrene by gavage at a dosage level of 2,000 mg/kg/day for 78 weeks (NCI 1979b). In this study, mortality was unaffected at dosage levels of 500 and 1,000 mg/kg/day in male and female rats. Male mice administered styrene at doses of 150 or 300 mg/kg/day for 78 weeks showed increased mortality; however, the female mice did not.

The highest reliable LOAEL values and LD_{50}'s values in each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2.

2.2.2.2 Systemic Effects

No studies were located regarding cardiovascular, gastrointestinal, musculoskeletal, or dermal/ocular effects in humans or animals after oral exposure to styrene.

For the following systemic effects resulting from oral exposure to styrene, the highest NOAEL values and all reliable LOAEL values for each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2.

Respiratory Effects. No studies were located regarding respiratory effects in humans after oral exposure to styrene.

Severe lung congestion was observed in mice that were the offspring of dams given a single oral dose of styrene at 1,350 mg/kg on the 17th day of gestation and that continued to receive the same dose once per week after weaning (Ponomarkov and Tomatis 1978). The lung congestion was noted following continuous administration of the styrene for 16 weeks.

Hematological Effects. No studies were located regarding hematological effects in humans after oral exposure to styrene.

Male and female purebred beagle dogs were exposed to 0, 200, 400, or 600 mg/kg/day styrene by gavage for up to 561 days (Quast et al. 1979). Treatment with styrene was stopped on day 316 in the 600 mg/kg/day group and resumed on day 470 for 90 additional days to investigate the reversibility of any effects. There were only minimal toxicological changes. Intraerythrocytic Heinz bodies were regularly detected in a dose-related manner in males and females in the 400 and 600 mg/kg/day groups and sporadically in females in the 200 mg/kg/day group. There were occasional decreased red blood

TABLE 2-2. Levels of Significant Exposure to Styrene - Oral

Key to figure[a]	Species	Route	Exposure frequency/ duration	System	NOAEL (mg/kg/day)	LOAEL (effect) Less serious (mg/kg/day)	LOAEL (effect) Serious (mg/kg/day)	Reference
ACUTE EXPOSURE								
Death								
1	Rat	(GO)	1 d		1600		8000 (100% lethality)	Spencer et al. 1942
2	Rat	(GO)	1 d				5000 (LD50)	Wolf et al. 1956
Systemic								
3	Rat	(GO)	7 d 1x/d	Renal		900 (decreased glutathione content)		Das et al. 1983
4	Rat	(GO)	7 d 1x/d	Hepatic		900 (decreased glutathione content)		Das et al. 1981
Neurological								
5	Rat	(GO)	7 d 1x/d		270	450 (inhibition of glutathione-S-transferase, glutathione depletion)		Dixit et al. 1982
6	Rat	(GO)	14 d 1x/d		100	200 (increased serotonin levels in several brain sections)		Husain et al. 1985
Developmental								
7	Rat	(GW)	10 d 1x/d		300			Murray et al. 1978

TABLE 2-2 (Continued)

Key to figure[a]	Species	Route	Exposure frequency/ duration	System	NOAEL (mg/kg/day)	LOAEL (effect) Less serious (mg/kg/day)	LOAEL (effect) Serious (mg/kg/day)	Reference
Reproductive								
8	Rat	(GW)	10 d 1x/d			300 (35% decreased weight gain on days 6-9 of gestation, reduced food consumption)		Murray et al. 1978
INTERMEDIATE EXPOSURE								
Death								
9	Mouse	(GO)	16 wk 1x/wk				1350 (50% of males and 20% of females dead 4 weeks after treatment suspended)	Ponomarkov and Tomatis 1978
Systemic								
10	Rat	(GO)	100 d 6d/wk 1x/d	Hepatic		200[b] (changes in mitochondrial and microsomal enzymes)	400 (small areas of necrosis with degenerated hepatocytes and inflammatory cells)	Srivastava et al. 1982
11	Rat		6 mo 5d/wk	Hepatic	133	400 (increased liver weight)		Wolf et al. 1956
				Renal	133	400 (increased kidney weight)		
12	Mouse	(GO)	16 wk 1d/wk	Resp			1350 (severe lung congestion)	Ponomarkov and Tomatis 1978
Neurological								
13	Rat	(GO)	90 d 1x/d			200 (increased spiroperidol binding to brain membranes)		Agrawal et al. 1982

TABLE 2-2 (Continued)

Key to figure[a]	Species	Route	Exposure frequency/ duration	System	NOAEL (mg/kg/day)	LOAEL (effect) Less serious (mg/kg/day)	LOAEL (effect) Serious (mg/kg/day)	Reference
Reproductive								
14	Rat	(GO)	60 d 6d/wk 1x/d		200		400 (decreased spermatozoa, tubular degeneration)	Srivastava et al. 1989
15	Rat	(W)	90 d (cont)		35			Beliles et al. 1985
Cancer								
16	Mouse	(GO)	16 wk 1d/wk				1350 CEL (lung tumors)	Ponomarkov and Tomatis 1978
CHRONIC EXPOSURE								
Death								
17	Rat	(GO)	78 wk 5d/wk 1x/d				2000 (decreased survival in males and females)	NCI 1979b
Systemic								
18	Rat	(W)	105 wk 7d/wk	Resp	21			Beliles 1985
				Cardio	21			
				Gastro	21			
				Hemato	21			
				Musc/skel	21			
				Hepatic	21			
				Renal	21			
				Derm/oc	21			
				Other	21			
19	Dog	(GO)	561 d 1x/d	Hemato	200	400 (Heinz body formation)		Quast et al. 1979

TABLE 2-2 (Continued)

Key to figure[a]	Species	Route	Exposure frequency/ duration	System	NOAEL (mg/kg/day)	LOAEL (effect) Less serious (mg/kg/day)	LOAEL (effect) Serious (mg/kg/day)	Reference
Cancer								
20	Mouse	(GO)	78 wk 5d/wk 1x/d				300 CEL (lung tumors)	NCI 1979b

[a]The number corresponds to entries in Figure 2-2.
[b]Used to derive an intermediate oral minimal risk level (MRL) of 0.2 mg/kg/day; dose divided by an uncertainty factor of 1,000 (10 for use of a LOAEL, 10 for extrapolation from animals to humans, 10 for human variability and 6/7 for less than continuous exposure).

Cardio = cardiovascular; CEL = cancer effect level; cont = continuous; d = day(s); Derm/oc = dermal/ocular; Gastro = gastrointestinal; (GO) = gavage - oil; (GW) = gavage - water; Hemato = hematological; LD50 = lethal dose, 50% kill; LOAEL = lowest-observed-adverse-effect level; mo = month(s); Musc/skel = musculoskeletal; NOAEL = no-observed-adverse-effect level; Resp = respiratory; (W) = drinking water; wk = week(s); x = time(s)

FIGURE 2-2. Levels of Significant Exposure to Styrene – Oral

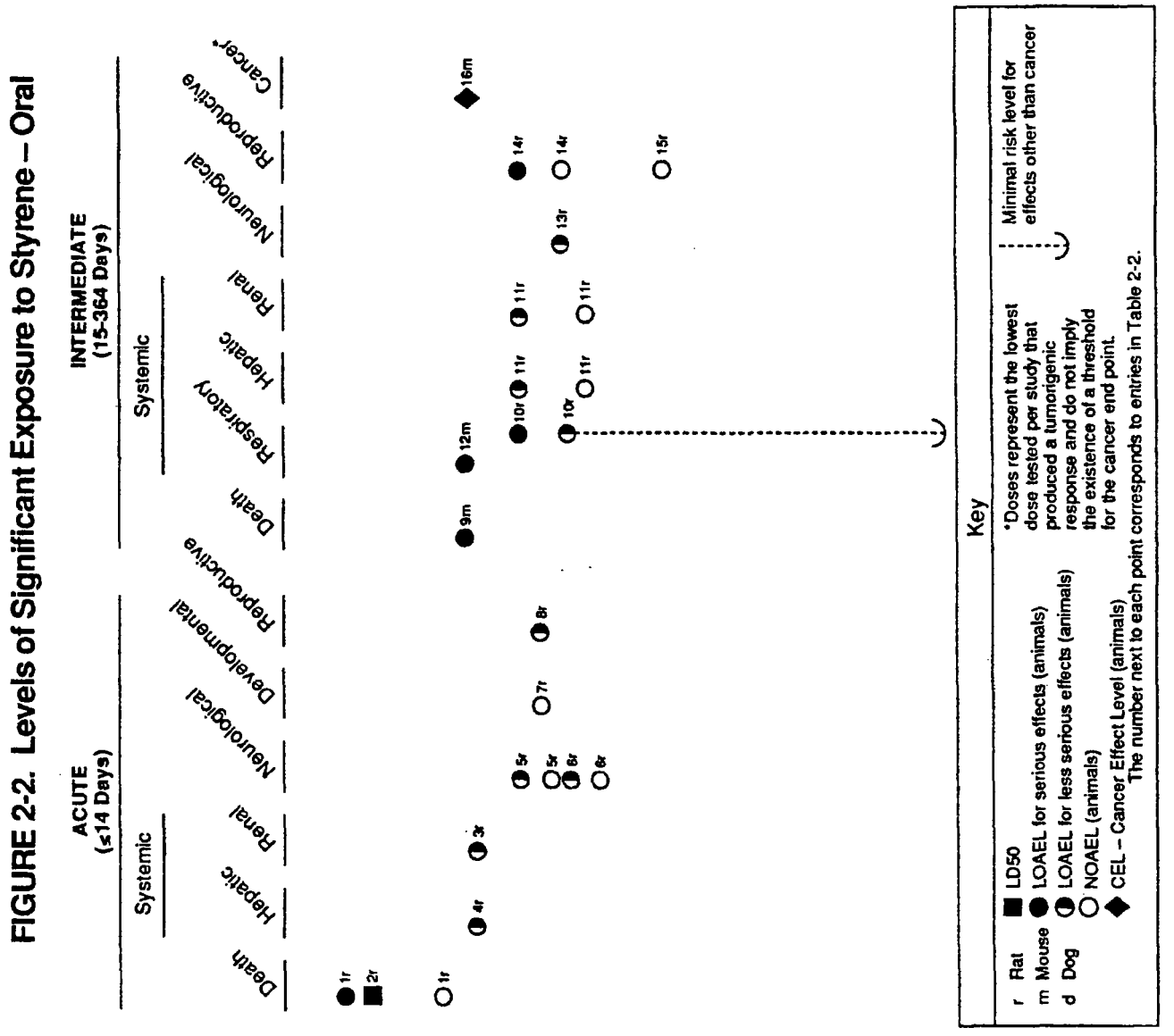
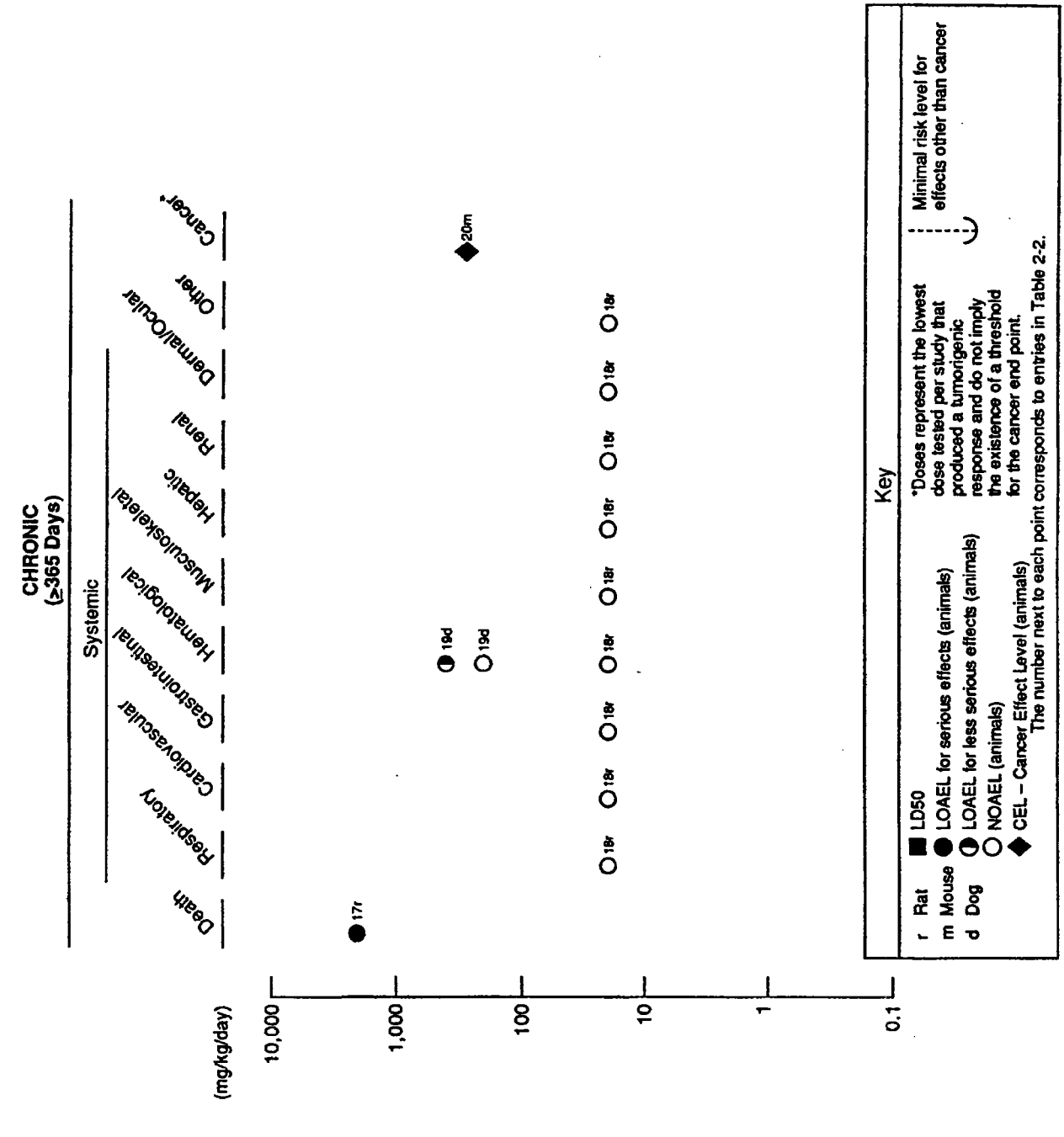


FIGURE 2-2. (Continued)



cell counts, hemoglobin levels and erythrocyte sedimentation rates in males and females in the 600 mg/kg/day groups. Increased hemosiderin deposits and intranuclear inclusions in liver were noted in animals dosed with 600 mg/kg/day. This was probably secondary to the effects on the red blood cells. The formation of intra-erythrocytic Heinz bodies was readily reversible upon discontinuing the administration of styrene in the 600 mg/kg/day group.

Hepatic Effects. No studies were located regarding hepatic effects in humans after oral exposure to styrene.

Hepatic glutathione content was reduced in rats orally administered 900 mg/kg styrene for 7 consecutive days (Das et al. 1981). In male rats that received 200 or 400 mg/kg/day styrene by gavage for 100 days, changes in mitochondrial and microsomal enzymes were observed at both doses. In addition to elevated enzyme activity, small areas of focal necrosis were noted in rats administered 400 mg/kg/day indicating a dose-response trend. In another study, growth depression and increased liver weight (general indicators of toxicity) were noted in rats orally administered 400 and 667 mg/kg/day styrene for 6 months (Wolf et al. 1956). As noted above, increased numbers of hemosiderin deposits and intranuclear crystalline inclusions were reported in the hepatocytes of dogs orally administered 600 mg/kg/day of styrene by gavage for 316 days (Quast et al. 1979). This was presumably secondary to Heinz body formation, and no other hepatic histological effects were in this study. The LOAEL of 200 mg/kg/day for enzyme level changes in rats (Srivastava et al. 1982) was selected as the basis for an oral intermediate MRL of 0.2 mg/kg/day. This MRL value is supported by the study by Wolf et al. (1956) in which a LOAEL of 400 mg/kg/day and a NOAEL of 133 mg/kg/day were reported. Additional support comes from other intermediate oral studies in which renal, neurological, and reproductive effects have been observed at or near the critical LOAEL (Agrawal et al. 1982; Srivastava et al. 1989; Wolf et al. 1956).

Renal Effects. No studies were located regarding renal effects in humans after oral exposure to styrene.

A decrease in renal glutathione content and decreased glutathione-stransferase activity was noted in rats orally administered 900 mg/kg styrene for 7 days (Das et al. 1983). This was similar to a reduction in the activity of these enzymes that was seen in hepatic tissue (Srivastava et al. 1982). Growth depression and increased kidney weight were reported in female rats orally administered 400 and 667 mg/kg/day of styrene for 6 months (Wolf et al. 1956). Histopathological examination of kidney tissue showed no abnormalities. Elevated levels of serum glutamic oxaloacetic transaminase and glutamic pyruvic transaminase were observed at 667 mg/kg/day. Dose-dependent increases of the cytochrome 450-dependent enzymes, benzo[a]pyrene hydroxylase and aminopyrine-N-demethylase were also observed. In another study, female rats and **mice** were exposed to 1,350 mg/kg/day of styrene on the 17th day of gestation. The offspring were also administered styrene, by gavage, at the following doses: rats, 500 mg/kg/day; O_{20} mice, 1,350 mg/kg/day; and C57Bl

mice, 300 mg/kg/day. Treatment was weekly for 120 weeks. Hyperplasia of the kidney pelvis epithelium was frequently reported in the offspring of the rats but not in the mice (Ponomarkov and Tomatis 1978).

2.2.2.3 Immunological Effects

No studies were located regarding immunological effects in humans after oral exposure to styrene.

The World Health Organization (WHO 1983) reviewed a Russian study (Sinitskij 1969) in which styrene was fed to 36 rabbits at doses of 250 mg/kg for 58 days, 5 mg/kg for 216 days, and 0.5 mg/kg for 202 days. Impairment of the immunological defense system was indicated by a nearly total suppression of leukocyte phagocytic activity. Although no statistical analysis was provided, the data showed a dose-response relationship for both the severity of the effect and the time of onset.

2.2.2.4 Neurological Effects

Although it is not clear if oral administration of styrene causes neurological effects in humans, the following animal studies support, in part, a biochemical basis for neurological effects of inhaled styrene.

It has been suggested that exposure of rats to styrene alters the biotransformation capacity of the brain dependent on glutathione content (Dixit et al. 1982). Significant inhibition of aryl hydrocarbon hydroxylase and glutathione-S-transferase activity followed by glutathione depletion was observed in rats exposed to styrene at 450 and 900 mg/kg/day for 7 days (Dixit et al. 1982). Oral intubation of male rats with styrene (94 mg/kg/day) for 15 days resulted in increased serotonin and noradrenalin levels in brain tissue (Husain et al. 1980).

Behavioral effects were observed by Husain et al. (1985) in rats exposed to styrene at 100 or 200 mg/kg/day for 14 days. Styrene significantly increased the mean percent avoidance response (learning) but no definite doseresponse relationship was evident. Conditioned stimuli, consisting of the sound of a buzzer and turning on light in the test chamber were used during an induced pole climbing task. The unconditioned stimulus was electric shock. Serotonin levels in hippocampus, hypothalamus, and mid-brain were raised at the 200 mg/kg/day styrene exposure. The study results indicate that elevated serotonin levels may account for the increased avoidance response.

In another study, styrene was administered to rats at doses of 200 or 400 mg/kg/day for up to 90 days. A significant increase in specific binding of ^{3}H-spiroperidol to the striatal membranes of the brain 24 hours after the last dose was observed (Agrawal et al. 1982). The data suggested that styrene altered the sensitivity of the dopamine receptors. Other neurotoxic chemicals such as acrylamide and manganese also are known to involve the dopaminergic system (Ali et al. 1983; ATSDR 1990).

The highest NOAEL and LOAEL values for neurological effects in each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2.

2.2.2.5 Developmental Effects

No studies were located regarding developmental effects in humans after oral exposure to styrene.

No teratological effects were observed in the offspring of rats given oral doses of either 180 or 300 mg/kg/day styrene during gestation (Murray et al. 1978).

The highest NOAEL value for developmental effects is recorded in Table 2-2 and plotted in Figure 2-2.

2.2.2.6 Reproductive Effects

No studies were located regarding reproductive effects in humans after oral exposure to styrene.

Exposure of pregnant rats to 180 or 300 mg/kg/day of styrene on days 6-15 of gestation resulted in no significant effects on maternal mortality or percent pregnancy (Murray et al. 1978). However, a 35% decrease in maternal weight gain was observed in the 300 mg/kg/day group during days 6-9 of gestation.

A three-generation reproduction study (Beliles et al. 1985) was conducted in which rats were maintained on styrene-treated drinking water for 2 years (7.7-21 mg/kg/day). The styrene-treated rats had no treatment-related changes, including mortality patterns. There was no evidence of adverse reproductive performance related to exposure to styrene. The only finding was that styrene-treated rats exhibited reduced water consumption due to poor palatability. In another study, styrene was administered by gavage to adult male rats for 60 days (Srivastava et al. 1989). At the high dose of 400 mg/kg/day, the activities of some marker enzymes for testicular function were significantly altered and there was a decrease in spermatozoa count. Histopathological examination revealed degeneration of seminiferous tubules and lumina devoid of sperm. The study results indicate that the male reproductive system may be sensitive to styrene exposure.

The highest NOAEL values and all reliable LOAEL values for reproductive effects in rats in the acute and intermediate duration categories are recorded in Table 2-2 and plotted in Figure 2-2.

2.2.2.7 Genotoxic Effects

No studies were located regarding genotoxic effects in humans after oral exposure to styrene.

The capacity for orally administered styrene to induce chromosomal aberrations in animals was studied by Sbrana et al. (1983). No mouse bone marrow cell chromosomal aberrations were detected after a 0-day treatment with 500 mg/kg/day or a 70-day exposure to 200 mg/kg/day. In a 3-generation reproduction study, no cytogenetic effects were noted in the bone marrow of pups born to rats that received styrene in their drinking water at doses of 125 or 250 ppm for approximately 90 days before mating (Beliles et al. 1985).

Other genotoxicity studies are discussed in Section 2.4.

2.2.2.8 Cancer

No studies were located regarding cancer effects in humans after oral exposure to styrene.

Investigations of the carcinogenic potential of styrene in animals after oral exposure have yielded variable results. Studies were conducted in which 29 female O_{20} mice (1,350 mg/kg), 15 female C57Bl mice (300 mg/kg), and 21 female BDIV rats (1,350 mg/kg) received styrene, by gavage administration, on day 17 of gestation (Ponomarkov and Tomatis 1978). The offspring of the C57Bl mice and BDIV rats were treated with styrene for life. The O_{20} mice offspring were only treated for 16 weeks due to excessive mortality from toxic effects. The weekly doses used for offspring were 1,350 mg/kg for O_{20} mice, 300 mg/kg for C57Bl mice, and 500 mg/kg for BDIV rats. After 100 weeks, the oral administration of styrene resulted in an increased incidence of lung tumors in male and female O_{20} mice compared to olive oil controls. An increased incidence of liver tumors was reported in styrene-treated C57Bl mice (12%) as compared to controls (3%), although this was not a statistically significant increase. There were no statistically significant increases in tumor incidences in the styrene-exposed BDIV rats. However, a few rare tumors were observed in styrene-exposed rats including stomach tumors and neurinomas of the heart and intestine. These results provide only weak evidence of the carcinogenicity of styrene in the O_{20} and C57Bl mice.

The carcinogenic potential of styrene was evaluated in male and female Fischer 344 rats (500, 1,000, and 2,000 mg/kg/day) and B6C3F1 mice (300 and 150 mg/kg/day) (NCI 1979b). In male mice, there was a significant positive association between styrene dosage and the combined incidence of adenomas and carcinomas of the lung. However, the statistical significance of this result may have been due to an unusually low tumor incidence in the concurrent controls, since the results were not statistically significant when compared to historical controls from the same laboratory. No association was detected between styrene exposure and tumor incidence in female mice or in rats. The NCI concluded that, while there was suggestive evidence for carcinogenicity in male mice, overall the results were not convincing for carcinogenicity in either rats or mice.

Styrene was also evaluated for its chronic toxicity and carcinogenic potential in male and female Sprague-Dawley and Wistar rats administered the chemical in the drinking water for 105 weeks (Beliles et al. 1985). The doses

were 17.5 and 35 mg/kg/day. There was some difficulty in maintaining the styrene level in the drinking water; the levels averaged 89.8% for the low level and 88.5% for the high level. Although there were incidental findings (e.g. ocular opacity) in both test and control rats, there were no gross pathological findings at the 52-week interim kill or terminal necropsy which were associated with the chronic administration of styrene, Likewise, there were no histopathological findings. The authors concluded that there was no evidence of carcinogenicity under the conditions of the study.

The potential for styrene to induce brain tumors was evaluated in Sprague-Dawley rats exposed for 52 weeks to 50 or 250 mg/kg/day styrene (Maltoni et al. 1982). The tumor incidence was not significantly different in exposed rats versus vehicle or historical controls. Similarly, in a 2-year study, no brain tumors were observed in male or female rats administered styrene at levels of 125 and 250 ppm in their drinking water (Beliles et al. 1985). In another study, the carcinogenic potential of styrene was investigated in Sprague-Dawley rats exposed to 50 or 250 mg/kg styrene for 52 weeks (Conti et al. 1988). The results of this study were also negative. However, due to a higher mortality rate, a lower incidence of total benign and malignant tumors and total mammary tumors was observed in rats at the highest (250 mg/kg/day) dose.

The International Agency for Research on Cancer (IARC) has concluded that evidence for styrene carcinogenicity in humans is inadequate, while evidence for carcinogenicity of styrene in animals is limited (IARC 1987). Using the lung tumor incidence of B6C3F1 mice (NC1 1979b) and appropriate dose conversions, the EPA (1988b) calculated a slope factor (potency factor or q_1^*) of 0.03 $(mg/kg/day)^{-1}$. EPA has requested public comment on the EPA group cancer classification of styrene for regulation under the Safe Drinking Water Act (EPA 1989b). The EPA has proposed the possibility of classification in Group B2 (Probable Human Carcinogen) or Group C (Possible Human Carcinogen).

2.2.3 Dermal Exposure

No studies were located regarding health effects in humans after dermal exposure to styrene.

2.2.3.1 Death

No studies were located regarding lethality in humans or animals after dermal exposure to styrene.

2.2.3.2 Systemic Effects

No studies were located regarding respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, and renal effects in humans or animals after dermal exposure to styrene.

Dermal/Ocular Effects. Marked irritation with denaturation of the skin was noted when styrene was applied in small amounts over a 4 week period to

the shaved abdomen of rabbits at 20,000 mg/kg (total dose) (Spencer et al. 1942). This study is summarized in Table 2-3. In another study, moderate conjunctival irritation and transient corneal injury of the eyes were observed when undiluted styrene was tested in rabbit eyes (Wolf et al. 1956). The effects were produced immediately (within 3 minutes) by a single administration of two drops (about 0.1 mL) and persisted throughout the 7-day observation period.

No studies were located regarding the following health effects in humans or animals after .dermal exposure to styrene:

2.2.3.3 Immunological Effects
2.2.3.4 Neurological Effects
2.2.3.5 Developmental Effects
2.2.3.6 Reproductive Effects
2.2.3.7 Genotoxic Effects

Genotoxicity studies are discussed in Section 2.4.

2.2.3.8 Cancer

No studies were located regarding cancer affects in humans or animals after dermal exposure to styrene.

2.3 TOXICOKINETICS

2.3.1 Absorption

2.3.1.1 Inhalation Exposure

The uptake of styrene following inhalation exposure in humans and animals is rapid (Ramsey and Anderson 1984; Ramsey and Young 1978; Ramsey et al. 1980; Withey and Collins 1979; Withey and Karpinski 1985). Pulmonary retention of inhaled styrene in humans is approximately 2/3 of the administered concentrations (Engstrom et al. 1978a, 1978b). For example, male human subjects were exposed to styrene in inspired air during 30 minute rest and three 30-minute work periods on a bicycle ergometer. The mean uptake was approximately 63% (range was 59%-70%) of the amount of inspired styrene. Exposures of rats to styrene concentrations of from 50 to 2,000 ppm for 5 hours yielded blood uptakes which showed a continued and increasing rapid absorption, proportional to the styrene air level (Withey and Collins 1979). Plateau levels of styrene in rats' blood were reached within 6-8 hours during exposures ranging from 80 to 1,200 ppm styrene for up to 24 hours (Ramsey and Young 1978). Physiologically-based inhalation pharmacokinetic models indicate that styrene metabolism becomes saturated at inhaled levels above 200 ppm in mice, rats, and humans (Ramsey and Andersen 1984). When inhaled concentrations are below 200 ppm, the ratio of styrene concentration in the blood to inhaled air is moderated by perfusion-limited metabolism rather than blood:air partition coefficients.

TABLE 2-3. Levels of Significant Exposure to Styrene - Dermal

Species	Exposure frequency/ duration	System	NOAEL	LOAEL (effect) Less serious	LOAEL (effect) Serious	Reference
ACUTE EXPOSURE						
Systemic						
Rabbit	1 d	Derm/oc		0.1 mL (moderate conjunctival irritation, transient corneal injury)		Wolf et al. 1956
INTERMEDIATE EXPOSURE						
Systemic						
Rabbit	4 wk	Derm/oc		20 g/kg (total) (moderate skin irritation with blistering, hair loss)		Spencer et al. 1942

d = day(s); Derm/oc = dermal/ocular; LOAEL = lowest-observed-adverse-effect level; NOAEL = no-observed-adverse-effect level; wk = week(s)

2.3.1.2 Oral Exposure

No studies were located regarding absorption in humans after oral exposure to styrene.

The absorption of styrene from the gastrointestinal tract was rapid and complete in rats deprived of food overnight and given styrene by gavage at a total dose of 3.147 mg styrene in 10 mL aqueous solution. A peak blood level of 6 µg/mL was reached in a few.minutes. There was a much slower uptake of the styrene administered in vegetable oil (Withey 1976). Styrene administered in vegetable oil at a total dose of 32.61 mg produced *a* peak level of 12 µg /mL. This was reached at about 100 minutes (Withey 1976).

2.3.1.3 Dermal Exposure

Limited data indicate that absorption of styrene via the dermal route is probably low compared to absorption via other routes. When liquid styrene was applied to the forearms of male subjects, the absorption rate was estimated to be 9-15 mg/cm^2/hour (Dutkiewicz and Tyras 1968). By contrast, the rate of absorption through human skin was very low (1±0.5 µg /cm^2/min) in subjects who dipped one hand into liquid styrene (Berode et al. 1985). It is believed that the higher absorption rate reported by Dutkiewicz and Tyras (1968) also included the disappearance rate of the solvent from the surface of the skin (Guillemin and Berode 1988). Riihimaki and Pfaffli (1978) demonstrated that in humans, dermal exposure to moderate concentrations of styrene vapor (300 and 600 ppm) resulted in percutaneous penetration corresponding to approximately 0.1%-2% of the amount estimated to be absorbed from the respiratory tract.

Although absorption of styrene applied to the abdomen of rabbits was reported, there was no information on absorption rates (Spencer et al. 1942).

2.3.2 Distribution

2.3.2.1 Inhalation Exposure

Inhalation studies in both humans and animals resulted in the widespread distribution of styrene with the highest concentration in adipose tissue.

Three humans were exposed to 8-20 ppm styrene which resulted in a mean daily uptake of 193-558 mg styrene (Engstrom et al. 1978b). The concentration of styrene in adipose tissue was 2.8-8.1 mg/kg at the beginning of the week and 4.7-11.6 mg/kg at the end of the week. The authors estimated the half-life of styrene in the subcutaneous fat of man to be about 72 hours. Subsequent studies by this author confirmed this estimate and reported the half-life of styrene in adipose tissue to be 24-96 hours (Engstrom et al. 1978a).

Fiberglass factory workers exposed to greater than 215 mg/m^3 of styrene for 8-hour work shifts had blood styrene levels which ranged from 120-684 µg /L at the end of the shift (Apostoli et al. 1983). The concentrations of urinary MA and phenylglyoxilic acid (PGA) were 133-2,100 and 107-685 mg/L, respectively. These levels were also determined at the end of the work-shift. Distribution of styrene was also studied in adult men exposed to about 300 mg/m^3 of styrene for 2 hours during light physical exercise (Wigaeus et al. 1983). Blood styrene reached a level of approximately 20 µmol/l after 75 minutes. The concentrations of styrene in adipose tissue was about 50 µmol/kg after 30-90 minutes of exposure.

Rats were exposed for 5 hours to styrene at concentrations ranging from 50 to 2,000 ppm (Withey and Collins 1979). Tissue concentrations of styrene in the heart, liver, lung, kidney, spleen, brain, and perirenal fat demonstrated different patterns of distribution as the dose increased. The styrene concentration in perirenal fat was 10 times greater than in other organs. The largest amounts of styrene were found in the subcutaneous fat of male rats exposed to about 45 ppm of radioactively labeled styrene in the inspired air for 1-8 hours (Carlsson 1981). The concentration increased steadily during the first 4 hours of exposure. Styrene concentrations in brain tissue and muscles were about 70% of the arterial blood value. Other investigators (Ramsey and Anderson 1984; Ramsey and Young 1978; Savolainen and Pfaffli 1978; Withey 1976) demonstrated that higher levels of styrene in adipose tissue increase with higher exposures to styrene. Styrene was found to distribute to the fetuses of pregnant rats after inhalation exposure, but at concentrations much lower than those measured in maternal organs and tissues (Withey and Karpinski 1985).

2.3.2.2 Oral Exposure

No studies were located regarding distribution in humans after oral exposure to styrene.

An oral dose of 20 mg/kg of ^{14}C styrene was administered to male and female rats (Plotnick and Weigel 1979). Tissue levels peaked at 4 hours or earlier after dosing. Less than 10% of the administered dose was found in the stomach, small intestine, and large intestine 8 hours after dosing. The kidney had the highest concentration of radioactivity at all time intervals, with decreasing amounts in the liver and pancreas. Fat tissue showed increased levels after 2 hours. All tissue levels were below 1 µg /g at 24 hours and at 48 and 72 hours were below the limit of detection. Excretion data from the Plotnick and Weigel (1979) study are presented in Section 2.3.4.2.

2.3.2.3 Dermal Exposure

No studies were located regarding distribution in humans after dermal exposure to styrene.

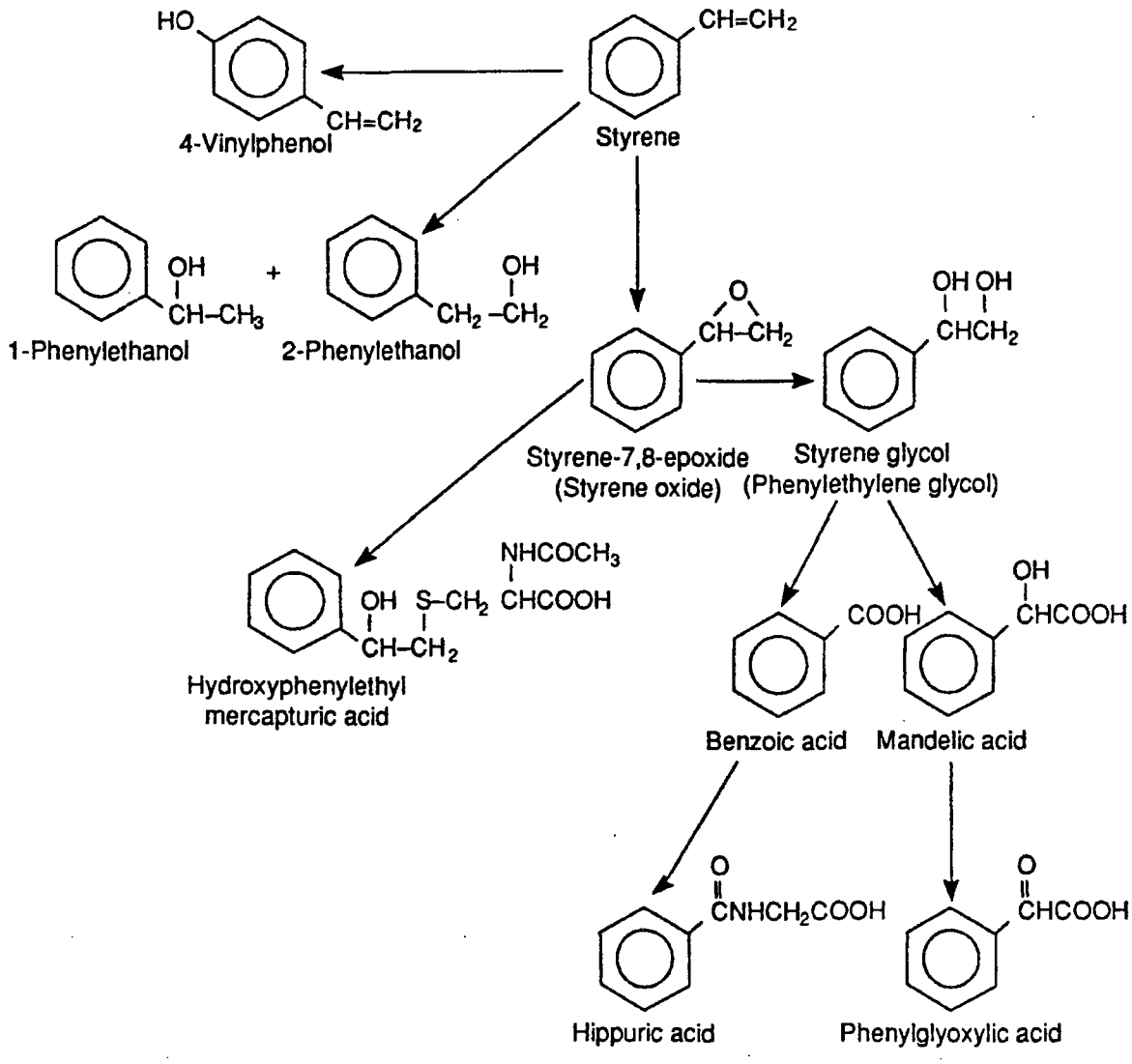
One animal study involved immersion of rats' tails in pure liquid styrene for 1 hour (Shugaev 1969). This procedure resulted in styrene levels in the liver and brain that were estimated to be between 50% and 70% of the concentrations found in the same organs after 4-hour inhalation exposure to a vapor concentration of 11.8 g/m^3.

2.3.3 Metabolism

There have been numerous studies, conducted primarily via inhalation, that address the metabolism of styrene in humans and animals (Drummond et al. 1989; Engstrom et al. 1976; Korn et al. 1984; Korn et *al.* 1987; Leibman 1975; Lof et al. 1983; Withey and Collins 1979; Young et al. 1979). The .proposed pathways of styrene metabolism are shown in Figure 2-3. Styrene is metabolized by the microsomal NADPH-cytochrome P-450 dependent mono-oxygenase to styrene oxide. The styrene oxide is then hydrated to phenylethylene glycol (styrene glycol). This transformation is catalyzed by microsomal epoxide hydratase. The styrene glycol is then metabolized directly to MA or to benzoic acid and then hippuric acid. Mandelic acid is also metabolized to PGA. The MA, hippuric acid and PGA are excreted in the urine. In another pathway, styrene oxide is metabolized by cystolic glutathione-S-transferase to mercapturic acids appearing in the urine as hydroxyphenylethyl mercapturic acid. A minor metabolic pathway of styrene in rats involves the formation of 1- and 2-phenylethanol and ring hydroxlation to form vinyl phenol as urinary metabolites. The presence of 4-vinylphenol has been reported in the urine of workers exposed to styrene, but this may have been due to the contamination of the styrene to which the subjects were exposed (Pfaffli et al. 1981). The urinary metabolites that predominate in humans are MA and PGA. In rats, the predominant urinary metabolites are MA, PGA, hippuric acid and glucuronide. Metabolic conversion to styrene-7,8-epoxide (styrene oxide) by the microsomal mixed function oxidase and epoxide hydratase from the liver and spleen of several rodent species has been demonstrated (Belvedere and Tursi 1981; Cantoni et al. 1978; Leibman 1975; Lof et al. 1984; Vainio et al. 1979). However, styrene oxide has only been found at low concentration, close to detection levels (0.02 µmol/L), in the blood of workers exposed to styrene (Lof et al. 1986a). Mendrala et al. (1991) investigated the species differences in the in vitro hepatic metabolism of styrene. The results indicated that mice had the greatest capacity to produce styrene oxide, (highest styrene epoxidase activity), followed by rats and then humans. In addition, humans may have the highest capacity to metabolize styrene oxide to styrene glycol, since the human form of styrene oxide hydratase had the highest affinity (lowest Km) for styrene oxide. Assuming that styrene oxide is the metabolite responsible for styrene-induced toxicity (see,below), the results of this study indicate that care must be taken in extrapolation of data from animal studies to humans for risk assessment.

The formation of styrene oxide may be a key step in the carcinogenicity of styrene. Several studies indicate that styrene oxide is genotoxic (DeMeester et al. 1981; Vainio et al. 1976), and three studies in animals indicate that ingestion of styrene oxide leads to hyperplasia and neoplasia of

FIGURE 2-3. Metabolic Pathways of Styrene*



*Adapted from Bond 1989; EPA 1988b; Leibman 1975

the stomach (Conti et al. 1988; Lijinsky 1986; Ponomarkov et al. 1984). The fact that tumors occurred in the stomach and were not detected in other tissues suggests that styrene oxide acts mainly at the point of contact. Thus, tissues most active in metabolizing styrene to styrene oxide might be most susceptible to the carcinogenic potential of styrene. Direct dermal application of styrene oxide did not cause a statistically significant increase in skin tumors in mice (Van Duuren et al. 1983).

2.3.4 Excretion

2.3.4.1 Inhalation Exposure

Several studies have demonstrated that styrene is almost totally excreted as urinary metabolites in humans, and at higher doses, the elimination profile indicates saturation of metabolic excretion or processes (Ramsey and Young 1978; Ramsey et al. 1980). Most of the inhaled styrene is excreted in urine as MA and PGA. In a study of the excretion of styrene and its metabolites resulting from a 100-ppm/8-hour inhalation exposure, 2.6% of the total uptake was excreted as unchanged styrene in exhaled air (Guillemin and Berode 1988). The metabolites MA, PGA, and hippuric acid were excreted in the urine at 56.9%, 33% and 7.5% of the absorbed dose, respectively. In human volunteers exposed to 80 ppm styrene, it is cleared from the blood in a bi-phasic manner, indicating a two-compartment pharmacokinetic model. The half-lives for the rapid and slow clearance phases are 0.58 and 13.0 hours, respectively. The half-life of styrene in subcutaneous adipose tissue of humans is 2-4 days (Engstrom et al. 1978a). The quantities of the major metabolites of styrene in urine compared with the quantity of styrene eliminated unchanged in expired air indicated that approximately 97% is cleared by the metabolic route (Ramsey et al. 1980).

Another human inhalation study determined that between 59%-66% of inhaled styrene (50-200 ppm) was retained after a 4-8 hour exposure (Guillemin and Bauer 1979). Urinary elimination of MA was biphasic with a half-life for the first phase of 4 hours and for the second phase, 25 hours. These findings were comparable to those reported by Engstrom et al. (1976). The half-life of urinary elimination of PGA was determined to be 11 hours. This was regarded by the authors as being the first phase of elimination since MA is a precursor of PGA.

Styrene is almost totally excreted as urinary metabolites in animals. The blood elimination curve for rats is biphasic exponential at 80 and 200 ppm styrene over 6 hours. For exposures greater than 600 ppm exposure levels for (6 hours duration), a nonlinear blood elimination curve following Michaelis-Menten kinetics was observed. In going from 80 to 1,200 ppm (a 15-fold increase) the area under the blood concentration curves increases by 112-fold (Ramsey and Young 1978; Young et al. 1979). Rats exposed to 50-2,000 ppm styrene by inhalation for 5 hours exhibited a dose dependent biphasic pattern of elimination (Withey and Collins 1979).

2.3.4.2 Oral Exposure

No studies were located regarding excretion in humans after oral exposure to styrene.

Excretion of styrene was studied in the same rats for which there was good distribution data (Plotnick and Weigel 1979). Styrene was rapidly excreted in the urine with 90% of the dose detected in the urine within 24 hours of administration, Less than 2% of the dose was found in the feces. Detectable tissue levels were not found 48 and 72 hours after administration.

2.3.4.3 Dermal Exposure

In a study of the absorption of liquid styrene applied to the forearms of male volunteers, about 13% of the absorbed dose was excreted as MA (Dutkiewicz and Tyras 1968).

No studies were located regarding excretion in animals after dermal exposure to styrene.

2.4 RELEVANCE TO PUBLIC HEALTH

Illness or injury from exposure to styrene is most commonly reported among workers using styrene in the production of polystyrene plastics, protective coatings, polyester resins, and other products. Exposure of the general public to high levels of styrene in air from the home, in the urban environment, or around hazardous waste sites is unlikely, based on occurrence data. The most commonly reported adverse health effects from exposure to styrene include subjective symptoms of central nervous system depression and irritation of the eyes and upper respiratory tract. Oral or dermal exposure to styrene in significant amounts has not been commonly reported in the workplace or the general environment.

Studies in workers exposed to styrene in workplace air suggest that neurological effects are probably the most sensitive indicator of styrene toxicity. Available data do not.provide a clear picture of the NOAEL for neurological effects following acute- or intermediate-duration inhalation exposure, but two chronic studies in workers identify LOAELs of 25 ppm (Mutti et al. 1984a) and 31 ppm (Harkonen et al. 1978). Based on the lower LOAEL (25 ppm), a chronic inhalation MRL of 0.06 ppm has been derived using factors of 8/24 and 5/7 to account for exposure 8 hours/day, 5 days/week, and an uncertainty factor of 100 (10 to account for human variability, and 10 to account for use of a LOAEL). Oral studies in animals suggest that hepatic effects may be the most sensitive indicator of toxicity (Srivastava et al. 1982). Based on a LOAEL of 200 mg/kg/day, an intermediate oral MRL of 0.2 mg/kg/day was derived. The LOAEL was multiplied by 6/7 to account for exposure occurring 6 days/week, and was then divided by an uncertainty factor of 1,000 (100 to account for intraspecies and interspecies extrapolation, and 10 to account for use of a LOAEL). Available data do not permit for the derivation of acute or chronic oral MRLs. Dermal MRLs were not derived for

styrene due to lack of dose-response data and lack of an appropriate methodology for the development of dermal MRLs.

Death. No deaths of humans have been reported after inhalation, oral or dermal exposure to styrene (EPA 1989c; NIOSH 1983). Although no deaths were reported in humans exposed to styrene by inhalation at concentrations in workplace air that exceeded 1,000 ppm (NIOSH 1983) or in laboratory studies at 800 ppm (Carpenter et al. 1944), these levels are severely irritating to the eyes, nose, and throat. Animal studies confirmed the relatively low to moderate acute toxicity following inhalation (Jaeger et al. 1974; Shugaev 1969; Spencer et al. 1942), oral (Ponomarkov and Tomatis 1978; Spencer et *al.* 1942; Wolf et al. 1956), and dermal (Spencer et al. 1942) exposures. Levels of styrene at hazardous waste sites (1-6 mg/m3) are orders of magnitude below the workplace levels, and oral exposure to significant levels from food or water is unlikely. However, the potential effects on human longevity of longterm inhalation or dermal exposure of humans to low levels of styrene at waste sites, in industrial neighborhoods, or in the environment have not been evaluated.

Systemic Effects.

Respiratory Effects. Occupational and laboratory studies of humans have demonstrated that the most commonly reported immediate symptom after exposure to styrene is irritation of the mucous membranes of the nose and throat. The symptoms appeared when workers were exposed to styrene below 300 ppm for short-time periods (NIOSH 1983). Similarly, human volunteers exposed to 216 ppm for 20 minutes or 376 ppm for 1 hour developed the characteristic nasal irritation (Stewart et al. 1968). The effect has been confirmed in animal studies in which the styrene exposures were high (1,000 ppm) over a period of 3 weeks (Ohashi et al. 1986). Pathological changes of the respiratory mucosa of the rats were also observed. No respiratory effects have been seen in humans after oral exposure to styrene. Mice that were administered styrene one time per week at a dosage of 1,350 mg/kg/week for 6 weeks developed severe lung congestion. This single observation is difficult to correlate with other aspects of styrene toxicity. There are no reports of respiratory effects.associated with dermal exposure of humans or animals to styrene. It appears that the respiratory system and the central nervous system are important target organs of styrene. However, the potential effects of long-term human exposure to low levels of styrene at waste sites, in industrial neighborhoods, or in the environment have not been evaluated.

Hematological Effects. No significant hematological effects have been reported in humans exposed to styrene. However, effects or erythrocytes were reported in dogs exposed to high doses of styrene (Quast et al. 1979). Increased numbers of Heinz bodies in the erythrocytes, decreased packed cell values and sporadic decreases in hemoglobin and erythrocyte counts were seen in dogs that received oral doses of 400 or 600 mg/kg/day by gavage for *560* days. No such effects were seen in dogs administered 200 mg/kg/day. The EPA has used the NOAEL of 200 mg/kg/day identified in this study to derive a chronic oral RfD of 0.2 mg/kg/day (IRIS 1991). However, the NOAEL for this

effect (200 mg/kg/day) is quite close to a chronic LOAEL for increased mortality (Conti et al. 1988), and is also close to doses that caused biochemical changes in the brain in several acute oral exposure studies in animals (Agrawal et al. 1982; Husain et al. 1985; Srivastava et al. 1982). Therefore, the true chronic oral NOAEL is judged to be sufficiently uncertain and no chronic oral MRL is derived. No studies were located that relate dermal exposure of humans or animals and hematological effects. However, based on experimental data that demonstrated eye, nose, and throat irritation are principal effects of styrene, it is unlikely that sufficient concentrations would be tolerated on the skin for a long enough time to accumulate and cause hematological effects. However, the potential effects on the blood and blood-forming organs of the body from long-term exposure of humans to low levels of styrene at waste sites, in industrial neighborhoods, or in the environment have not been evaluated.

Hepatic Effects. Evaluation of the potential adverse effects of styrene on the liver has resulted in mixed results in human and animal studies. The studies either involved occupational exposures of workers or inhalation and oral studies in animals. There are no studies relating dermal exposure and hepatic effects in humans or animals. Measurements to identify elevated serum enzyme levels in styrene-exposed workers have been inconclusive in determining if styrene causes a decrement in liver function (Harkonen et al. 1984; Hotz et al. 1980; Thiess and Friedheim 1978). Rodent inhalation studies have demonstrated that exposure to 300 ppm styrene for 11 weeks results in depletion of glutathione levels and an increase in the cytochrome P-450 content of liver cells (Vainio et al. 1979). A reduction in glutathione content was also seen in rats orally administered 900 mg/kg/day styrene for 7 days (Das et al. 1981). Similarly, increases in liver weights were noted in rats orally administered 400 and 667 mg/kg/day for 6 months (Wolf et al. 1956). Although the results of both human and animal studies are difficult to interpret, and their findings may be nonspecific, the enzyme and organ weight changes reported in these studies suggest that the liver must be regarded as an end point for the inhalation and oral routes of exposure. No changes in microsomal and mitochondrial liver enzymes were observed in rats receiving 200 or 400 mg/kg/day styrene by oral gavage (Srivastava et al. 1982). In addition, areas of focal necrosis were noted in animals administered the high dose, indicating a dose-response trend. Based on the LOAEL of 200 mg/kg/day (Srivastava et al. 1982) an intermediate oral MRL of 0.2 mg/kg/day has been derived. This MRL value is supported by the study by Wolfe et al. (1956) in which a LOAEL of 400 mg/kg/day and a NOAEL of 133 mg/kg/day were identified for hepatic effects. In addition, inhalation studies serve to indicate the liver as a target of styrene toxicity (Axelson and Gustavson 1978; Hotz et al. 1980; Jersey et al. 1978; Vaino et al. 1979). Other studies in the intermediate oral data base have reported renal, neurological, and reproductive effects at doses at or near the critical LOAEL (Agrawal et al. 1982; Srivastava et al. 1989; Wolf et al. 1956). The potential hepatic effects of long-term human exposure to low levels of styrene at waste sites, in industrial neighborhoods, or in the environment, have not been evaluated.

Renal Effects. The potential for styrene to cause kidney toxicity has been evaluated in both humans and animals following inhalation exposures. There are no studies relating oral or dermal exposure and renal effects in humans or animals. Human studies generally confirm the importance of urinary enzymes as indicators of kidney damage due to occupational exposure to styrene (Aliberti and Severini 1987; Viau et al. 1987; Vyskocil et al. 1989). However, findings indicate only minor effects of styrene on some kidney enzyme functions. Similar evidence for styrene causing minor effects on the kidney is provided by animal studies involving both inhalation (Vainio et al. 1979; Viau et al. 1987) and oral (Das et al. 1983) exposures. The induction reported in the activity of these enzymes is similar to that seen in hepatic tissue. This may mean that the kidney is a potential end point for evaluation of the inhalation and oral routes of exposure. As with the liver, histopathological findings are lacking. The potential renal effects of long-term human exposure to low levels of styrene at waste sites, in industrial neighborhoods, or in the environment have not been evaluated.

Immunological Effects. Systemic immunological studies of styrene have not been conducted in humans or animals by the inhalation, oral, or dermal routes of exposure. However, there is limited information that suggests immunotoxicological concerns. For example, styrene has produced sensitizing reactions in humans. It has also been shown that styrene is apparently metabolized in the skin by aryl hydrocarbon hydroxylase to the more sensitizing epoxide (Sjoborg et al. 1984). Effects of styrene on lymphocyte chromosomes are discussed under "Genotoxic Effects" (below). Because of the association of dermal exposure and immunological reactions, the lack of data on styrene or its metabolites makes it difficult to reach conclusions about potential immunotoxicological concerns. Also, potential immunological effects of long-term human exposure to low levels of styrene at waste sites, in industrial neighborhoods, or in the environment have not been evaluated.

Neurological Effects. Epidemiological and clinical studies on workers have demonstrated that inhalation exposure to styrene may cause alterations of central nervous system function. The symptoms are typical of central nervous system depression, and appear to be the most sensitive end point for styrene exposure via the inhalation route (Kulig 1988; Pryor et al. 1987). High levels (800 ppm) produced immediate muscular weakness, listlessness, drowsiness, and impaired balance within minutes of exposure (Carpenter et al. 1944). Exposures to levels in the range of 50-200 ppm have resulted in a number of signs and symptoms, including impairment of balance and coordination, altered reaction times, sensory neuropathy, impaired manual dexterity, headaches, nausea, mood swings, malaise, and decrement in concentration (Cherry et al. 1980; Lindstrom et al. 1976; Mutti et al. 1984a; Rosen et al. 1978; Stewart et al. 1968). Exposure levels above 50 ppm were frequently encountered in the workplace in the past, but current regulations restrict workplace concentrations to less than 50 ppm (see Chapter 7). However, the study of Harkonen et al. (1978) indicates that some neurological effects, as evidenced by altered EEGs, occur at exposure levels as low as 31 ppm, and the study of Mutti et al. (1984a) indicates effects may occur at a

level of 25 ppm. Based on a LOAEL of 25 ppm from the Mutti et al. study, a chronic inhalation MEL of 0.06 ppm has been derived.

Less information is available on neurological effects following oral exposure to styrene. No data were located for humans, but studies in animals reveal that repeated oral exposure can lead to altered enzyme levels in brain (Dixit et al. 1982), increased brain levels of several neurotransmitters (serotonin, norepinephrine) (Husain et al. 1980), increased binding of spiroperidal to brain membranes (Agrawal et al. 1982), and increased avoidance response learning (Husain et al. 1985). Some of these responses are similar to those seen following inhalation exposure. For example, the increased spiroperidal binding noted in the oral study of Agrawal et al. (1982) might be due to the decreased dopamine levels noted in the inhalation study by Mutti et al. (1984). However, other effects do not always agree between oral and inhalation studies. For example, the increased levels of norepinephrine in brain reported by Husain et al. (1980) following oral exposure were not observed in rabbits following inhalation exposure (Mutti et al. 1984c). Similarly, the increased conditional response reported by Husain et al. (1985) following oral exposure was not observed in a study of rats exposed by inhalation (Pryor et al. 1987). These apparent differences in effect between routes might be the result of toxicokinetic differences between exposure routes, or might simply be the result of differing experimental designs (different species, doses, durations, end points).

The potential neurological effects of long-term human exposure to low levels of styrene at waste sites, in industrial neighborhoods, or in the environment have not been evaluated. No data are available concerning the neurological effects following dermal exposure to styrene in either humans or animals.

Developmental Effects. Evaluation of the potential developmental effects in occupationally exposed styrene workers suggests that styrene is not teratogenic in humans (Ahlborg et al. 1987). However, a single study (Lemasters et al. 1989) reported that women who work in'high styrene exposure settings, such as laminators in fiberglass boat manufacturing companies, had offspring with a 4% lower birthweight than unexposed women. However, this effect was not statistically significant. The actual levels of styrene exposure were not adequately determined for the workers in either the Ahlborg or Lemasters studies. Further, interpretation of the data is complicated by the fact that the women were exposed to other chemicals in the workplace including thermal degradation products of styrene polymers. There are no studies of developmental effects in humans after oral or dermal exposure. Animal studies have produced mixed results. No fetotoxicity or teratogenicity was observed in rats or rabbits exposed via inhalation to either 300 or 600 ppm styrene (Murray et al. 1978). However, an increase in dead or resorbed fetuses was observed in mice exposed to 250 ppm and hamsters exposed to 1,000 ppm (Kankaanpaa et al. 1980). No teratogenic effects were observed in the mice and hamsters. Limited oral studies in rats and rabbits revealed no fetotoxicity or teratogenicity (Murray et al. 1978). There are no reports

of developmental effects after dermal exposure of animals to styrene. Based on the human and animal data and the low concentrations of styrene in air (1-6 $\mu g/m^3$) that have been reported at hazardous wastes sites, developmental effects should not be expected. However, potential developmental effects associated with long-term human exposure to the low levels of styrene at waste sites, in industrial neighborhoods, or in the environment have not been evaluated.

Reproductive Effects. The results of some studies of occupationally exposed female workers in the plastics industry in which styrene is used have suggested an increased risk of spontaneous abortion (Hemminki et al. 1980). Other studies suggest no such increased risk (Lindbohm et al. 1985). Interpretation of these studies is difficult because small study populations were used and there were multiple chemical exposures in the workplace environment. There are no studies of reproductive effects in humans after oral or dermal exposure. Animal studies, either by the inhalation (Salomaa et al. 1985) or the oral route (Beliles et al. 1985; Murray et al. 1978), indicate that styrene is not a reproductive toxicant. However, male rats administered styrene by gavage for 60 days had altered testicular function at the high dose of 400 mg/kg/day (Srivastava et al. 1989). There are no reports of reproductive effects after dermal exposure of animals to styrene. The potential reproductive effects associated with long-term human exposure to low levels of styrene at waste sites, in industrial neighborhoods, or in the environment have not been evaluated.

Genotoxic Effects. Styrene has been tested for genotoxic potential in a variety of systems, and the results have been mixed. Bacterial assays for gene mutation in the absence of activation have been negative, while studies with activation were positive in two out of six cases (see Table 2-4). The lack of evidence for styrene genotoxicity in bacteria may be due in part to volatilization of styrene from the test systems, or possibly to metabolism of styrene to nongenotoxic forms (Dunkel et al. 1985; Yoshikawa et al. 1980). Styrene has induced genotoxic effects in animals following intraperitoneal injection. Male mice were injected with single doses of styrene at levels of 250, 500, 1,000 or 1,500 mg/kg b.w. Significant increases in micronuclei of polychromatic erythrocytes were observed only at the 250 and 1,000 mg/kg levels, and nonsignificant increases were noted at the other two doses. In another study, styrene administered intraperitoneally to male mice at single doses of 177-1,051 mg/kg b.w. induced increases in single-strand breaks in DNA. This genotoxic effect observed in the kidney, liver, lung, testes, and brain 1 hour after administration and in all organs except the liver after 24 hours (Walles and Orsen 1983).

Styrene production of chromosomal aberrations (breaks and gaps) in peripheral lymphocytes of workers in the styrene industry has been reported (Andersson et al. 1980; Hogstedt et al. 1979; Meretoja et al. 1977, 1978) (see Table 2-5). However, positive findings are limited by the fact that workers are often exposed to other chemicals besides styrene, and that aberrations also depend upon parameters such as age and smoking. On the other hand, negative studies (e.g., Thiess et al. 1980; Watanabe et al. 1981) may also be

TABLE 2-4. Genotoxicity of Styrene *In Vitro*

Species (test system)	End point	Results: With activation	Results: Without activation	Reference
Prokaryotic organisms:				
Salmonella typhimurium (2 strains, plate incorporation method)	Gene mutation	+	-	Vainio et al. 1976
S. typhimurium (3 strains, plate incorporation method)	Gene mutation	-	-	Vainio et al. 1976
S. typhimurium (3 strains, vapor exposure - desiccator test)	Gene mutation	+	-	DeMeester et al. 1981
S. typhimurium (4 strains, vapor exposure - desiccator test)	Gene mutation	-	-	DeMeester et al. 1981
S. typhimurium (5 strains, preincubation method)	Gene mutation	-	-	Dunkel et al. 1985
Escherichia coli (1 strain, preincubation method)	Gene mutation	-	-	Dunkel et al. 1985
Mammalian cells:				
Human lymphocytes	Sister chromatid exchange	No data	+	Norppa et al. 1983
Human lymphocytes	Chromosomal aberrations	No data	+	Jantunen et al. 1986

+ = positive result; - = negative result

TABLE 2-5. Genotoxicity of Styrene In Vivo

Species (test system)	End point	Results	Reference
Mammalian cells:			
Human lymphocytes	Chromosomal aberrations	+	Meretoja et al. 1977
Human lymphocytes	Chromosomal aberrations	+	Meretoja et al. 1978
Human lymphocytes	Chromosomal aberrations	+	Hogstedt et al. 1979
Human lymphocytes	Chromosomal aberrations	-	Thiess et al. 1980
Mouse bone marrow, liver cells, and alveolar macrophages	Sister chromatid exchange	+	Conner et al. 1980
Human lymphocytes	Chromosomal aberrations	-	Andersson et al. 1980
	Sister chromatid exchange	+	
Human lymphocytes	Chromosomal aberrations	-	Watanabe et al. 1981
	Sister chromatid exchange	-	
Mouse bone marrow, polychromatic erythrocytes	Micronuclei	±	Norppa 1981
Mouse kidney, liver, lung, testes, and brain	DNA	+	Walles and Orsen 1983
Human lymphoctyes	Unscheduled DNA synthesis	+	Pero et al. 1982
Mouse bone marrow	Chromosomal aberrations	-	Sbrana et al. 1983
Rat bone marrow	Chromosomal aberrations	-	Sinha et al. 1983
Human lymphocytes	Chromosomal aberrations	-	Nordenson and Beckman 1984
	Micronuclei	+	
Human lymphocytes	Chromosomal aberrations	-	Hansteen et al. 1984
	Sister chromatid exchange	-	
Human lymphocytes	Micronuclei	+	Hogstedt et al. 1983
Human lymphocytes	Chromosomal aberrations	-	Maki-Paakkanen 1987
	Sister chromatid exchange	-	
	Micronuclei	-	
Human lymphocytes	Chromosomal aberrations	-	Jablonicka et al. 1988

+ = positive result; - = negative result; DNA = deoxyribonucleic acid

due to the wide variability in aberration levels. Thus, evidence for styrene-induced chromosomal aberrations in humans is suggestive, but not conclusive. One inhalation study has been conducted in order to evaluate chromosome changes, and this was negative (Sinha et al. 1983). The results were also negative in two studies in which styrene was orally administered to mice (Sbrana et al. 1983) and rats (Beliles et al. 1985). Levels of styrene in air at hazardous waste sites (1-6 μg /m^3) are not likely to cause genotoxicity regardless of the route or duration of exposure. However, potential genotoxic effects of long-term human exposure to low levels of styrene at waste sites, in industrial neighborhoods, or in the environment have not been evaluated.

Cancer. There are several epidemiologic studies of styrene workers that suggest an association between occupational exposure and an increased incidence of leukemia (Meinhardt et al. 1982; Nicholson et al. 1978; Ott et al. 1980) and lymphoma (Hodgson and Jones 1985). However, the reported studies are inconclusive due to exposure to multiple chemicals (including benzene) and the small size of the cohorts. Other studies have reported negative results (Coggon et al. 1987; Matanoski and Schwartz 1987; Okun et al. 1985). There are no reports of cancer resulting from styrene exposure by the oral or dermal routes in humans. It is, therefore, unknown if styrene causes cancer in humans.

Although animal evidence is limited, the results suggest that styrene is weakly carcinogenic in some strains of rats and mice. Overall, human and animal studies suggest that styrene may be a weak human carcinogen. This conclusion is supported by the presence of small amounts of the metabolite styrene oxide (a carcinogen and mutagen) in the blood of styrene industry workers (Lof et al. 1986a).

Three chronic inhalation studies have been conducted in which rats were exposed to styrene vapor (Conti et al. 1988; Jersey et al. 1978; Maltoni et al. 1982). In one study, there was an increased incidence of mammary adenocarcinomas in female rats at the low dose (600 ppm), but a significant response was not evident at the higher dose (1,200 ppm reduced to 1,000 ppm due to growth retardation) (Jersey et al. 1978). In another rat study, designed to detect an elevated incidence of brain tumors, the results were negative (Maltoni et al. 1982). The third inhalation study in rats reported a higher incidence of total (benign and malignant) mammary tumors and malignant mammary tumors in females (Conti et al. 1988).

Other studies have investigated the effects of styrene in animals after long-term oral exposure. In one study, styrene was administered to BD IV rats (500 mg/kg/day) and mice (1,350 mg/kg/day for O_{20} strain and 300 mg/kg/day for C57Bl strain) for 100 days. There was an increased incidence of lung tumors in the O_{20} strain of mice (Ponomarkov and Tomatis 1978). In another study (NCI 1979b), rats and mice were given styrene for a lifetime. In male mice, there was a significant increase in the combined incidences of adenomas and carcinomas of the lung. However, this was significant only when compared to concurrent controls but not compared to historical controls from the same laboratory. Another study (Maltoni et al. 1982) did not detect an increased

incidence of brain tumors in rats. A more recent study to evaluate the carcinogenicity of styrene via the oral route in rats was negative (Conti et al. 1988).

There are no reports of cancer effects associated with dermal exposure of animals to styrene.

Based on the information obtained from human and animal studies, it is not known if styrene causes cancer in humans, and the EPA has not yet assigned styrene to a cancer weight of evidence category (IRIS 1991). The IARC has assigned styrene to Group 2B, possibly carcinogenic to humans (IARC 1988). However, cancer effects associated with long-term human exposure to low levels of styrene at waste sites, in industrial neighborhoods, or in the environment have not been evaluated.

2.5 BIOMARXERS OF EXPOSURE AND EFFECT

Biomarkers are broadly defined as indicators signaling events in biologic systems or samples. They have been classified as markers of exposure, markers of effect, and markers of susceptibility (NAS/NRC 1989).

A biomarker of exposure is a xenobiotic substance or its metabolite(s) or the product of an interaction between a xenobiotic agent and some target molecule(s) or cell(s) that is measured within a compartment.of ,an organism (NAS/NRC 1989). The preferred biomarkers of exposure are generally the substance itself or substance-specific metabolites in readily obtainable body fluid(s) or excreta. However, several factors can confound the use and interpretation of biomarkers of exposure. The body burden of a substance may be the result of exposures from more than one source. The substance being measured may be a metabolite of another xenobiotic substance (e.g., high urinary levels of phenol can result from exposure to several different aromatic compounds). Depending on the properties of the substance (e.g., biologic half-life) and environmental conditions (e.g., duration and route of exposure), the substance and all of its metabolites may have left the body by the time biologic samples can be taken. It may be difficult to identify individuals exposed to hazardous substances that are commonly found in body tissues and fluids (e.g., essential mineral nutrients such as copper, zinc, and selenium). Biomarkers of exposure to styrene are discussed in Section 2.5.1.

Biomarkers of effect are defined as any measurable biochemical, physiologic, or other alteration within an organism that, depending on magnitude, can be recognized as an established or potential health impairment or disease (NAS/NRC 1989). This definition encompasses biochemical or cellular signals of tissue dysfunction (e.g., increased liver enzyme activity or pathologic changes in female genital epithelial cells), as well physiologic signs of dysfunction such as increased blood pressure or decreased lung capacity. Note that these markers are often not substance specific. They also may not be directly adverse, but can indicate potential health impairment

(e.g., DNA adducts). Biomarkers of effects caused by styrene are discussed in Section 2.5.2.

A biomarker of susceptibility is an indicator of an inherent or acquired limitation of an organism's ability to respond to the challenge of exposure to a specific xenobiotic substance. It can be an intrinsic genetic or other characteristic or a preexisting disease that results in an increase in absorbed dose, biologically effective dose, or target tissue response. If biomarkers of susceptibility exist, they are discussed in Section 2.7, "POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE."

2.5.1 Biomarkers Used to Identify and/or Quantify Exposure to Styrene

The elimination of styrene via expired air may be used to identify exposure to styrene (Guillemin and Berode 1988; Stewart et al. 1968). Only a small percentage of unchanged styrene is expired after cessation of exposure. There are no adequate studies correlating post-exposure exhaled styrene with previous exposure levels. Assessment of occupational exposure involving measurement of unchanged styrene in urine has been reported (Dolara et al. 1984). In this study of workers, the styrene air concentrations were 16-61 mg/m^3 and the urinary concentrations of styrene were 0-7-4.1 µg/L. Urinary mutagenic activity was also evaluated in this study and was not a good indication of exposure to styrene. Only a small fraction of unchanged styrene is recovered in the urine. However, measurement of styrene in urine is a reliable indicator of styrene exposure if the exposure is recent (Dolara et al. 1984; Guillemin and Berode 1988; Pezzagno et al. 1985).

Analysis of unchanged styrene in blood may be used as a qualitative indicator of styrene exposure (Antoine et al. 1986). In one study, styrene was detected in the blood of humans exposed to 80 ppm (Ramsey et al. 1980). The maximum blood concentration at the end of exposure was 0.92±0.26 µg/mL. The half-life values for rapid and slow clearance curves were 0.58 and 13 hours, respectively. In another study, the concentration of styrene in blood (0.2-3.7 mg/L) increased with the level and duration of styrene exposure (Baselt 1988a).

The presence of styrene in adipose tissue is also an indicator of exposure. The concentration of styrene in the adipose tissue of two workers exposed to 32-85 mg/m^3 of styrene during a work week suggested a half-life of 5.2 days for one worker and 2.8 days for the other worker. The elimination time was estimated to be 5 weeks (Engstrom et al. 1978b).

Levels of occupational exposure to styrene may also be estimated by measurement of styrene metabolites such as MA and PGA in urine (Bartolucci et al. 1986; Elia et al. 1980; Engstrom et al. 1976; Sedivec et al. 1984; Sollenberg et al. 1988). It should be noted that large intra-individual differences in MA and PGA urinary concentrations have been reported. Some studies found a good correlation between the time-weighted styrene exposure and urinary MA concentrations (Engstrom et al. 1976; Harkonen et al. 1979), while other studies found a better correlation with the sum of urinary MA and

PGA at the end of the work period (Elia et al. 1980; Sollenberg et al. 1988). Total MA and PGA measured the morning after exposure may be a more reliable biological indicator of styrene exposure in factories where there is high variability in the environmental styrene concentration (Bartolucci et al. 1986).

Reference levels of styrene likely to be observed in workers exposed to the TWA concentrations by inhalation have been reported. These are called biological exposure indices (ACGIH 1988-1989). Values recommended are: MA in urine, 1 g/L; PGA in urine, 250 µg/L, styrene in mixed-exhaled air (before shift) 40 ppb; styrene in mixed-exhaled air (during shift), 18 ppm; styrene in blood (before shift), 0.02 mg/L; and styrene in blood (end of shift), 1 mg/L.

2.5.2 Biomarkers Used to Characterize Effects Caused by Styrene

The most common symptom of styrene exposure is depression of the central nervous system. Other organic solvent vapors cause similar effects. However, neurological symptoms can be used with caution to estimate styrene exposure and adverse effects. Central nervous system depression induced by styrene has been correlated with a urinary MA concentration in excess of 800 mg/L. A measured decrement in psychomotor performance has been associated with urinary MA concentrations of greater than 1,200 mg/L (Harkonen et al. 1978).

Logic, memory, and visuo-constructive abilities were significantly affected in 50 workers with MA and PGA levels corresponding to greater than 50 ppm of styrene in air (Mutti et al. 1984a). Reaction time to a sequence of light stimuli in two female workers resulted in marked impairment in workers with the highest MA excretion. The correlation coefficient for reaction time versus urinary MA (measured as mmol/mmol creatinine) was 0.86 (Mackay and Kelman 1986).

Cytogenetic monitoring of peripheral lymphocytes as a biomarker of effect has been proposed (DeJong et al. 1988; Pero et al. 1982). Future biomarkers may include hemoglobin adducts. Using unscheduled DNA synthesis (UDS) as an indicator of DNA damage, the lymphocytes of 38 individuals occupationally exposed to styrene were evaluated. The induced UDS was significantly increased for the group exposed to 1-40 ppm styrene (Pero et al. 1982). Measurement of chromosome aberration in peripheral blood lymphocyte has been used for many years to monitor the biologic effects of genotoxic chemicals. However, due to high background levels of chromosomal aberration and exposures to other genotoxic workplace chemicals, the sensitivity of this biomarker for the effects of styrene is probably not adequate (DeJong et al. 1988). The role of hepatic glutathione in the toxicity of styrene has been proposed as inhibiting the covalent binding of styrene. This has been confirmed in animal studies by decreased glutathione in styrene-exposed animals (Parkki 1978). However, its use as a biomarker of effect in humans remains to be demonstrated since data on the adverse effects of styrene on the human liver are insufficient.

Levels of styrene oxide may also be a useful biomarker of effect, since this metabolic intermediate may be responsible for many of styrene's toxic effects. However, no data were located regarding a correlation between styrene oxide and any adverse health effect.

2.6 INTERACTIONS WITH OTHER CHEMICALS

Styrene metabolism is known to be inhibited by the presence of other chemicals such as toluene, trichloromethylene, and ethyl benzene. The biotransformation of styrene in rats to PGA, MA, and hippuric acid was suppressed by coadministration of toluene (Ikeda et al. 1972). This may be due to competitive inhibition of oxidative mechanisms. Similar results were reported by Ikeda and Hirayama (1978) in rats when styrene metabolism was inhibited by the administration of trichloroethylene. Urinary metabolites of styrene may be markedly reduced when humans or animals are concurrently exposed to organic solvents that inhibit styrene metabolism.

2.7 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

Styrene is a hazardous substance found in the workplace with much lower levels found in the environment. Therefore, the populations at risk are workers in industries making polystyrene plastics, coating, polyester resins, and other products'. Persons with pre-existing respiratory or neurological problems would be at risk for the irritant action and central nervous system depressant effects of styrene, respectively. Individuals deficient in glucose-6-phosphate dehydrogenase (G6PD) may be at increased risk since Heinz bodies, which are readily formed in the blood of G6PD-deficient humans (Wintrobe et al. 1970), have been found in the red blood cells of dogs orally exposed to styrene. Women from families pre-disposed to mammary gland tumors may also be at increased risk since this type of tumor was observed in some animal studies. Some studies suggest that the incidence of adverse reproductive outcome (low birth weight, spontaneous abortions) may be elevated in styrene-exposed female workers (see Section 2.2.1.6), therefore, pregnant women may be susceptible. Individuals with liver dysfunction might also be somewhat more susceptible, since this liver is affected by styrene.

2.8 MITIGATION OF EFFECTS

This section will describe clinical practice and research concerning methods for reducing toxic effects of exposure to styrene. However, because some of the treatments discussed may be experimental and unproven, this section should not be used as a guide for treatment of exposures to styrene. When specific exposures have occurred, poison control centers and medical toxicologists should be consulted for medical advice.

Human exposure to styrene may occur by inhalation, ingestion, or by dermal contact. General recommendations for reducing absorption of styrene following exposure include removing the exposed individual from the contaminated area and removing the contaminated clothing. If the eyes and skin were exposed, they are flushed with water. There are some disagreements

regarding appropriate procedures for mitigation of absorption of styrene following oral exposure. Since aspiration of styrene into the lung can cause pulmonary edema and hemorrhage, some authors advise against the use of emetics, but recommend administration of water for dilution of gastric lavage (Bronstein and Currance 1988; Haddad and Winchester 1990). Others suggest administration of syrup of ipecac to induce vomiting, but consider the usefulness of activated charcoal to bind the styrene and cathartics to speed fecal excretion as questionable (Ellenhorn and Barceloux 1988). Following acute inhalation exposure, administration of oxygen and use of mechanical ventilation to support respiration have been suggested (Bronstein and Currance 1988; Ellenhorn and Barceloux 1988; Haddad and Winchester 1990). Administration of aminophylline and inhaled bronchodilators may be required to treat bronchospasm (Ellenhorn and Barceloux 1988). Furthermore, cardiac monitoring has been suggested. Supportive treatment may be needed for neurological effects of styrene exposure (Haddad and Winchester 1990).

Styrene is metabolized by the body, and most styrene that is absorbed is excreted in the urine as metabolites of the parent compound. Styrene is cleared rapidly from the human body. Its half-life is several hours in the blood and about 2-4 days in subcutaneous adipose tissue (see Section 2.3). No method is commonly used to enhance the elimination of the absorbed dose of styrene.

In humans, central nervous system depression and upper respiratory tract irritation were reported following acute exposure to higher styrene concentrations (see Section 2.2). Studies in animals indicate that chronic styrene exposure causes liver and kidney effects and may induce cancer. Styrene oxide was found to be the active mutagenic metabolite of styrene in several studies (de Raat 1978; Donner et al. 1979; Norppa et al. 1979, 1980a, 1980b, 1981, 1984, 1988; Pohlova et al. 1985; Vainio et al. 1976). Based on these studies, it can be concluded that styrene is a typical indirect mutagen that needs metabolic activation to be able to bind covalently to macromolecules (e.g., nucleic acids). In one of the possible metabolic pathways, styrene oxide is further metabolized to hydroxyphenylethyl mercapturic acid. The reaction utilizes glutathione (Bond 1989). It has been demonstrated that mutagenic activity of styrene oxide was decreased in the presence of glutathione in S. typhimurium TA 100 (Yoshikawa et al. 1980). This experiment, therefore, suggests that glutathione may reduce the mutagenic effects of styrene oxide.

The formation of styrene oxide may also contribute to other effects following styrene exposure. It is well established that glutathione decreases the cytotoxicity of many reactive chemicals by acting as a scavenger of toxic metabolites. It was found that exposure of rodents to high levels of styrene caused depletion of glutathione content in the liver cells of these animals (Das et al. 1978; Vainio et al. 1979). It was suggested that glutathione decreases the hepatoxicity by preventing styrene oxide reaction with other endogenous macromolecules. Similarly, depletion of glutathione was found in all regions of rat brain following exposure to styrene oxide (Dixit .et al. 1982; Trenga et al. 1990). The authors speculated that the depletion of brain glutathione may lead to an increased concentration of free styrene oxide with

increased binding to cellular nucleophiles. This process would contribute to oxidative injury to neuronal and glial cells and may be a part of styreneinduced neurotoxicity. It should be noted, however, that styrene itself, being a lipophilic compound, may disrupt the nerve membrane function in a manner similar to anesthetic agents.

Although results from in vitro studies in bacteria and in vivo animal studies demonstrate that exogenous glutathione precursors may decrease the effects of styrene toxicity, it is not known whether this treatment would be beneficial in humans. For low level exposure cases it is unlikely that endogenous glutathione levels would be decreased to a significant extent. Therefore, it is unlikely that exogenous glutathione precursors such as N-acetylcysteine may be effective in mitigating the toxic effects of styrene. Exogenous doses of reducing agents may be useful following acute high dose exposure to styrene. In this case, a significant depletion of glutathione may occur as a result of the presence of high levels of styrene oxide. However, there is no clinical data available to date which supports the use of this treatment.

2.9 ADEQUACY OF THE DATABASE

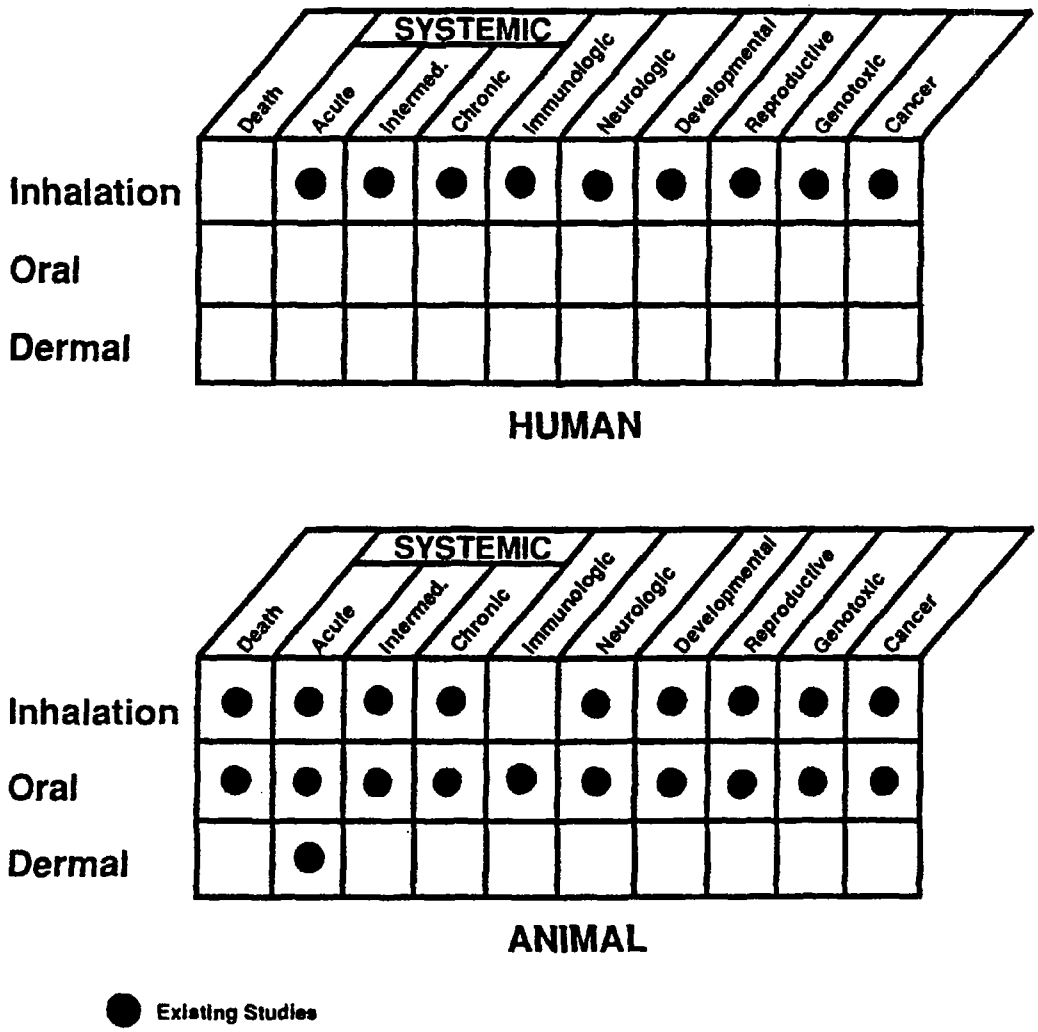
Section 104(i)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of styrene is available. Where adequate information is not available, ATSDR, in conjunction with the National Toxicology Program (NTP), is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of styrene.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA, They are defined as substance-specific informational needs that, if met, would reduce or eliminate the uncertainties of human health assessment. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

2.9.1 Existing Information on Health Effects of Styrene

The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to styrene are summarized in Figure 2-4. The purpose of this figure is to illustrate the existing information concerning the health effects of styrene. Each dot in the figure indicates that one or more studies provide information associated with that particular effect. The dot does not imply anything about the quality of the study or studies. Gaps in this figure should not be interpreted as "data needs" information (i.e., data gaps that must necessarily be filled).

FIGURE 2-4. Existing Information on Health Effects of Styrene



There is information on most categories of human toxicity via the inhalation route from occupational studies. However, data are not available on humans exposed to styrene by the oral or dermal routes. Data from animal studies are more extensive, with studies available for most areas of toxicity resulting from exposure via the oral and inhalation routes; however, there are no data on immunologic effects via inhalation. Little is known about the effects of dermal exposure to styrene in animals.

2.9.2 Data Needs

Acute-Duration Exposure. The possibility for brief human exposure to high concentrations of styrene exists in occupational settings, and might also exist near major spills. Exposure of the general public to episodic high concentrations of styrene at hazardous waste sites, in the home, or in the general environment is unlikely. The respiratory tract and central nervous system are the likely target organ systems for inhaled styrene (Alarie 1973; Carpenter et al. 1944; DeCeaurriz et al. 1983; Kankaanpaa et al. 1980; Murray et al. 1978; Spencer et al. 1942; Stewart et al. 1968). The data are not considered sufficient to establish an inhalation acute-duration MRL. Episodic high-level exposures to styrene from contaminated food or water are unlikely. There are no data on humans orally exposed to styrene, and the animal data are not considered sufficient to derive an oral acute-duration MRL. Thus, additional single-dose oral and inhalation studies are needed to better define toxicity thresholds. However, the potential carcinogenicity of styrene prevents the design of controlled laboratory exposures in humans. Dermal exposure to styrene at significant levels is unlikely except in the case of workplace spills and dermal absorption is probably low based on limited human studies. However, the almost complete lack of dermal toxicity data in animals and humans creates a degree of uncertainty on this issue. Therefore, single dose dermal studies would be useful in determining target organs and thresholds for dermal exposure. In designing these types of studies, precautions should be taken to avoid concomitant inhalation exposure.

Intermediate-Duration Exposure. Intermediate-duration exposure studies in animals and humans confirm that the upper respiratory tract and central nervous system are the target organ systems for inhaled styrene (Kulig 1988; Ohashi et al. 1986; Pryor et al. 1987; Rosengren and Haglid 1989; Spencer et al. 1942). However, additional studies are needed, as the data are not considered sufficient to derive an intermediate-duration inhalation MRL. Oral exposure studies of intermediate-duration are limited. Animal studies indicate that renal and neurological end points need further evaluation (Johnston et al. 1983; Vainio et al. 1979; Viau et al. 1987). The data are considered sufficient to derive an oral intermediate-duration RfD of 0.2 mg/kg/day based on liver enzyme changes in rats (Srivastava et al. 1982). However, additional data would be valuable since the critical study does not define a NOAEL. Basic information on the adverse effects of intermediateduration dermal exposure to styrene in animals is also needed due to the sparsity of available data.

Chronic-Duration Exposure and Cancer. Chronic studies are available that investigated the adverse health effects of styrene on workers in the plastics industry (Harkonen et al. 1978, 1984; Hotz et al. 1980; Lemasters et al. 1989; Lorimer et al. 1978; Mutti et al. 1984a,b; Thiess and Friedheim 1978). Although the lung and liver are both affected by chronic exposure, neurological effects such as decreased short term memory or impaired visuomotor performance seem to be the most sensitive indicators of toxicity (Harkonen et al. 1984; Mutti et al. 1984a). Based on a LOAEL of 25 ppm identified by Mutti et al., a chronic inhalation MRL of 0.06 ppm has been derived. Further research to define the dose-response curve more fully and to identify a chronic inhalation NOAEL for neurological effects would be valuable and would help reduce uncertainty in the MRL. Data on chronic oral exposure to styrene is only available through animal studies (Beliles et al. 1985; Conti et al. 1988; NCI 1979b; Quast et al. 1979). In these studies, the most sensitive indicator of toxicity appears to be Heinz body formation in red blood cells (Quast et al. 1979), and the EPA has calculated a chronic oral RFD based on this study (IRIS 1991). However, as discussed above (Section 2.4), there is some doubt regarding the chronic oral NOAEL, and whether hematological effects are really more sensitive than neurological effects. Moreover, decreased survival has been noted in rats at exposure levels only slightly higher than the no-effect level for hematological effects (Conti et al. 1988). Therefore, no chronic oral MRL has been derived. Further studies on the effects of oral exposure, with special emphasis on neurological or neurobehavioral effects, would be valuable. Although chronic dermal exposure by the general public is not likely, there may be some potential for dermal contact with soil at hazardous waste sites. Therefore, data on longterm effects of dermal contact with styrene would be useful.

Taken together, the animal and human data indicate that styrene may possibly be a weak human carcinogen. Although data from epidemiological studies are limited due *to* concurrent chemical exposures and small *cohorts,* the data are suggestive of some carcinogenic potential in humans (Coggon et al. 1987; Hodgeson and Jones 1985; Matanoski and Schwartz 1987; Meinhardt et al. 1982; Nicholson et al. 1978; Okun et al. 1985; Ott et al. 1980; Wong 1990). Studies in rats and mice have indicated that styrene may be *a* weak animal carcinogen via the oral.and inhalation routes. Clarification of the data is needed in several areas. Interpretation of existing animal bioassays is complicated by the marginal statistical significance of elevated tumor incidences and by the lack of adequate dose response data. Almost all of the available epidemiological studies involve concurrent exposures to other chemicals. Additional studies that account for these issues would be valuable. Finally, the role of the metabolism of styrene to styrene oxide in humans and animals needs to be clarified. This might best be accomplished by studies of industrially exposed (worker) populations.

Genotoxicity. On-going studies by Perera (Columbia University) and Rappaport (University of California) will address links between styrene exposure and cytogenic response. The results of genotoxicity tests for styrene both in vivo and in vitro are frequently conflicting, and the genotoxic potential of styrene is not clear (Andersson et al. 1980; Beliles

et al. 1985; Hogstedt et al. 1979; Meretoja et al. 1977, 1978; Watanabe et al. 1981). The reasons for the mixed or conflicting genotoxicity results may be differences in the metabolism or detoxification of styrene in the various test systems employed. The role of the metabolite styrene oxide in genotoxicity assays on styrene should be fully evaluated, preferably in mammalian in vivo systems. Toxicokinetic studies evaluating the presence, level, and activity of styrene oxide in humans will influence the interpretation of genotoxicity studies on styrene and their relevance to public health.

Reproductive Toxicity. Additional studies are needed to determine the potential effects of styrene exposure on spontaneous abortion rates in female workers in the styrene industry. The exposures in existing studies were not quantified and therefore, interpretation of results is difficult (Harkonen and Holmberg 1982; Hemminki et al. 1980; Lindbohm et al. 1985). A single threegeneration study showed no styrene-related reproductive effects; however, one reproductive study in animals indicated altered testicular function (Beliles et al. 1985; Salomaa et al. 1985). Additional reproductive data on occupationally-exposed males would be useful in evaluating the existing animal data that indicates altered testicular function.

Developmental Toxicity. Data on the developmental effects of inhalation exposure to styrene are available in humans and animals. Developmental effects were not generally observed in animal studies, but some fetal- and embryo-toxicity was observed (Kankaanpaa et al. 1980). This information, in combination with observations of reduced birth weight in the offspring of female workers in the styrene industry (Lemasters et al. 1989), indicates that additional repeated dose animal studies and epidemiological studies would be useful. Little information is available on the potential developmental effects of oral exposure to styrene. The single negative study in rats (Murray et al. 1978) should be supplemented by confirmatory studies in other species.

Immunotoxicity. Immunotoxicity data in humans are limited to one study in which styrene exposure had no effect on serum alpha, beta and gamma globulin concentrations in workers (Chmielewski et al. 1977). In another study, it was found that styrene epoxide was more sensitizing to humans than styrene itself (Sjoberg et al. 1984). Limited data in animals indicate that oral exposure to styrene has some immunotoxic potential (Sinitskij 1969). It would be useful to investigate the potential for styrene-induced immunotoxicity in future studies.

Neurotoxicity. Central nervous system depressant effects in humans from inhalation exposure to styrene are well known (Carpenter et al. 1944; Harkonen et al. 1978; Mutti et al. 1984a,b; Stewart et al. 1968). Although the threshold for neurologic effects is not well defined, the studies of Harkonen et al. (1979) and Mutti et al. (1984a) provide sufficient dose-response data to permit derivation of a chronic inhalation MRL. Since this is based on a LOAEL, further studies which define the chronic NOAEL, as well as acute- and intermediate-duration NOAELs, would be valuable especially at levels of styrene causing problems with coordination and psychological function. These

and other neurological effects may play a role in the rate of workplace accidents and the level of performance. Additional studies in mammalian animal models are needed to determine if styrene causes chronic damage to the central and/or peripheral nervous systems and to determine the associated mechanism of toxicity. Also, information is needed to determine if neurotoxicity can result from exposure to styrene via the oral route.

Epidemiological and Human Dosimetry Studies. Since acute effects such as upper respiratory tract irritation and eye irritation have been frequently noted in occupational health studies and in laboratory experiments, additional epidemiological studies of workers are needed *to* determine the chronic respiratory effects of styrene. Since liver function evaluation of workers exposed to styrene has resulted in equivocal results (Harkonen et al. 1984; Hotz et al. 1980; Lorimer et al. 1978; Thiess and Friedheim 1978), additional studies are necessary and should include complete profiles of serum hepatic enzymes of exposed workers. Further epidemiological information is needed to determine if exposure to styrene causes reproductive effects, developmental effects, or cancer.

Biomarkers of Exposure and Effect. Available studies indicate that there are good quantitative relationships between styrene metabolites (MA and PGA) in the urine and styrene exposure levels in humans (Harkonen et al. 1978; Mutti et al. 1984a). Efforts to establish styrene oxide as a biomarker would also be valuable, since this metabolite may underlie many of styrene's toxic effects. However, methods which focus on these metabolites are mainly useful for determining exposure within 1 day of exposure. Efforts to identify biomarkers of prior exposures would also be valuable.

There are currently no biomarkers specific for the effects of styrene that are not also typical of other central nervous system depressants. Further research is needed to evaluate potential biomarkers of effect in the areas of chromosome aberrations, psychomotor decrement, hepatic glutathione depletion, and adipose tissue retention of styrene. These potential biomarkers should be evaluated in terms of long-term or chronic exposure periods, and their specificity for exposure to styrene.

Absorption, Distribution, Metabolism, and Excretion. Styrene oxide (styrene epoxide) has been identified as an intermediate metabolite of styrene (Drummond et al. 1989; Engstrom et al. 1976; Korn et al. 1984, 1987; Leibman 1975; Lof et al. 1983; Withey and Collins 1979; Young et al. 1979). However, styrene oxide has only been found in minute amounts in human studies (Lof et al. 1986a). The presence of styrene oxide, a mutagen and carcinogen, may account for some conflicting results and/or interspecies variation in mutagenicity tests and cancer bioassays. The role, if any, of styrene oxide in the overall toxicity of styrene needs to be evaluated by additional metabolism studies to confirm its presence, level, and duration in human tissues. The toxicokinetics of styrene exposure via inhalation are reasonably well defined. However, oral and dermal exposure data are needed to better characterize absorption rates and the elimination ratios of the metabolites (MA and PGA).

Comparative Toxicokinetics. Interspecies variations in styrene metabolism have been established by noting, for example, different ratios of MA and PGA in different species (Ramsey et al. 1980; Ramsey and Young 1978; Young et al. 1979). Mendrala et al. (1991) reported species differences in the in vitro metabolism of styrene and styrene oxide which indicated that mice and rats had a higher capacity to produce styrene oxide from than humans. Efforts should continue to identify which animal model best approximates human metabolism of styrene. Although urinary metabolites of styrene in man are known, the occurrence and significance of styrene oxide needs to be evaluated.

Mitigation of Effects. Recommended methods for the mitigation of acute effects of styrene intoxication include mechanical ventilatory support, administration of oxygen, and drug therapy for bronchospasm, if exposure is by inhalation (Bronstein and Currance 1988; Ellenhorn and Barceloux 1988). Thorough washing or flushing with water is recommended for dermal/ocular exposure. There is disagreement concerning the use of emetics to prevent absorption of styrene following ingestion due to potential of aspiration into the lung (Bronstein and Currance 1988; Ellenhorn and Barceloux 1988; Haddad and Winchester 1990). Supportive treatment is indicated for neurological effects of styrene exposure (Haddad and Winchester 1990). No information was located concerning mitigation of effects of lower-level or longer-term exposure to styrene. Further information on techniques to mitigate such effects would be useful in determining the safety and effectiveness of possible methods for treating styrene-exposed populations in the vicinity of hazardous waste sites. This includes further studies on the mechanism(s) of styrene toxicity, so that methods may be developed to interfer with or block styrene's toxic actions in the body.

2.9.3 On-going Studies

A number of research projects are in progress investigating styrene. These projects are summarized in Table 2-6.

TABLE 2-6. On-going Studies on the Health Effects of Styrene

Investigator	Affiliation	Research description	Sponsoring agency
S. M. Rappaport	University of California	Occupational health study	NIOSH
W. J. Nicholson	Mt. Sinai School of Medicine	Epidemiological study	NIEHS
F. P. Perera	Columbia University	Biological markers	NCI
A. M. Jeffrey	Columbia University	Biologically effective doses in humans and mice	NCI
J. Roycroft	NTP	Two-year inhalation bioassays in rats and mice	NCI
M. Kogevinas	IARC	Epidemiological study on 20,000 styrene workers	IARC
R. Nolan	Dow	Metabolism/Kinetics	SIRC
J. Mattson	Dow	Ototoxicity studies	SIRC
J. Filser	GSF Toxicology Institute, Munich	Metabolism/Kinetics	ECETOC
W. Lutz	Institute of Toxicology, Zurich	DNA-binding	ECETOC

DNA = Deoxyribonucleic acid; ECETOC = European Chemical Industry Ecology and Toxicology Center; IARC = International Agency for Research on Cancer; NCI = National Cancer Institute; NIEHS = National Institute of Environmental Health Sciences; NIOSH = National Institute for Occupational Health and Safety; NTP = National Toxicology Progam; SIRC = Styrene Information and Research Center

3. CHEMICAL AND PHYSICAL INFORMATION

3.1 CHEMICAL IDENTITY

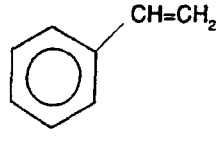
Table 3-1 lists common synonyms, trade names and other pertinent identification information for styrene.

3.2 PHYSICAL AND CHEMICAL PROPERTIES

Table 3-2 lists important physical and chemical properties of styrene.

3. CHEMICAL AND PHYSICAL INFORMATION

TABLE 3-1. Chemical Identity of Styrene

Characteristic	Information	Reference
Chemical name	Styrene	Verschueren 1983
Synonyms	Vinylbenzene; ethenylbenzene; cinnamene; phenylethylene	Verschueren 1983
Trade names	No data	
Chemical formula	C_8H_8	Windholz 1983
Chemical structure		
Identification numbers:		
CAS registry	100-42-5	Sax and Lewis 1987
NIOSH RTECS	WL3675000	HSDB 1989
EPA hazardous waste	No data	
OHM/TADS	7216911	HSDB 1989
DOT/UN/NA/IMCO shipping	UN 2055	NLM 1989
	IMCO 3.3	HSDB 1989
HSDB	171	HSDB 1989
NCI	C02200	NLM 1989

CAS = Chemical Abstracts Service; DOT/UN/NA/IMCO = Department of Transportation/United Nations/North America/International Maritime Dangerous Goods Code; EPA = Environmental Protection Agency; HSDB = Hazardous Substances Data Bank; NCI = National Cancer Institute; NIOSH = National Institute for Occupational Safety and Health; OHM/TADS = Oil and Hazardous Materials/Technical Assistance Data System; RTECS = Registry of Toxic Effects of Chemical Substances

TABLE 3-2. Physical and Chemical Properties of Styrene

Property	Information	Reference
Molecular weight	104.16	Weast 1985
Color	Colorless to yellowish	Windholz 1983
Physical state	Liquid	Sax and Lewis 1987
Melting point	-30.6°C	Weast 1985
Boiling point	145.2°C	Weast 1985
Density at 20°C	0.906	Weast 1985
Odor	Sweet, sharp	Verschueren 1983
Odor threshold:		
Water	0.73 mg/L	HSDB 1989
	0.011 mg/L	Amoore and Hautala 1983
Air	1.36 mg/m^3	Amoore and Hautala 1983
Solubility:		
Water at 20°C	300 mg/L	Verschueren 1983
Organic solvents	Soluble in alcohol, ether, acetone, carbon disulfide	Windholz 1983
Partition coefficients:		
Log octanol/water	2.95	EPA 1984a
Log K_{oc}	No data	
Vapor pressure at 20°C	5 mmHg	Verschueren 1983
Henry's law constant:		
at 25°C	2.61 x 10^{-3} atm-m^3/mol (calculated)	EPA 1983
Autoignition temperature	914°F (490°C)	Sax and Lewis 1987
Flashpoint	87°F (31°C) (closed cup)	Windholz 1983
Flammability limits	No data	
Conversion factors	1 mg/m^3 = 0.23 ppm	Verschueren 1983
	1 ppm = 4.33 mg/m^3	Verschueren 1983
Explosive limits	1.1-6.1%	Sax and Lewis 1987

4. PRODUCTION, IMPORT, USE, AND DISPOSAL

4.1 PRODUCTION

In the United States, styrene is produced principally by the catalytic dehydrogenation of ethylbenzene. Hence, ethylbenzene is a common contaminant. It is also produced by oxidation of ethylbenzene to its peroxide which is then reacted with propylene to produce propylene oxide and alpha-methylphenyl carbinol. The carbinol is then further dehydrated to produce styrene (Dickson et al. 1983; HSDB 1989; IARC 1979).

Styrene has been manufactured in the United States since 1938. Its production has increased 1.8% in the decade between 1978 and 1988 with a 4.8% increase in production during the 5-year period between 1983 and 1988. Production of styrene for 1987 was over 8 billion pounds, and 1989 production is predicted to be almost 9 billion pounds (Dickson et al. 1983; Heylin 1989; SRI 1988a, 1989; USITC 1987, 1988).

Information regarding the locations of the numerous styrene production facilities and the amounts of styrene which may be present on-site is presented in Table 4-1.

4.2 IMPORT/EXPORT

Imports of styrene have generally been less than 1% of United States domestic production volumes with imports reported to be 26.4 million pounds for 1976, 28.6 million pounds for 1981, and 21 million pounds for 1982. Data regarding current styrene imports were not located. Styrene exports were over 1 billion pounds in 1981 and over 1 billion pounds in 1982, which represents a steady increase in styrene exports since the early years of styrene production (Dickson et al. 1983; IARC 1979).

4.3 USE

Styrene is used predominantly in the production of polystyrene plastics and resins (62%). Some of these resins are used for construction purposes such as in insulation or in the fabrication of fiberglass boats. Styrene is also used as an intermediate.in the synthesis of materials used for ion exchange resins and to produce copolymers such as styrene-acrylonitrile (SAN), acrylonitrile-butadiene-styrene (ABS), and styrene-butadiene rubber (SBR).

Consumer products made from styrene-containing compounds include packaging, electrical, and thermal insulation materials, pipes, automotive components, drinking tumblers, other food-use utensils, and carpet backing, The Food and Drug Administration (FDA) permits styrene to be used as a direct additive for synthetic flavoring and an indirect additive in polyester resins, ion-exchange membranes, and in rubber articles (5% by weight maximum) intended for use with foods (HSDB 1989; IARC 1979; NIOSH 1983).

4. PRODUCTION, IMPORT, USE AND DISPOSAL

TABLE 4-1. Facilities That Manufacture or Process Styrene[a]

State[b]	No. of facilities	Range of maximum amounts on site in thousands of pounds[c]	Activities and uses[d]
AL	10	1-9,999	1, 4, 7, 8, 9, 11, 13
AR	14	0.1-9,999	2, 3, 7, 8, 9
AZ	8 (1)[e]	1-99	3, 7, 8, 9
CA	81 (6)[e]	0.1-49,999	2, 3, 7, 8, 9, 10, 11, 13
CO	5	1-9,999	3, 6, 7, 8, 9
CT	5	0.1-49,999	3, 7, 10, 12
DE	3	10-999	7, 8, 9
FL	44	1-9,999	1, 2, 3, 7, 8, 9, 11, 12, 13
GA	24	0.1-9,999	3, 4, 7, 8, 9
IA	16	0.1-9,999	2, 3, 4, 7, 8, 9, 12, 13
ID	2	10-99	9
IL	49 (4)[e]	0.1-99,999	2, 3, 5, 7, 8, 9, 10, 11, 12
IN	50 (4)[e]	0-49,999	2, 3, 4, 5, 7, 8, 9, 11, 12, 13
KS	13	0.1-999	2, 7, 8, 9, 12, 13
KY	21 (1)[e]	1-49,999	1, 5, 6, 7, 8, 9
LA	16 (1)[e]	0.1-99,999	1, 2, 4, 5, 6, 7, 8, 9, 10, 11
MA	13 (2)[e]	1-9,999	7, 8, 9, 10
MD	14 (1)[e]	1-99	3, 4, 5, 7, 8, 9
ME	5	1-99	7, 8, 9
MI	32 (1)[e]	0.1-49,999	2, 5, 7, 8, 9, 10, 11, 12, 13
MN	10 (1)[e]	10-999	1, 3, 6, 7, 8, 9, 12
MO	17 (1)[e]	0.1-999	2, 3, 7, 8, 9, 11, 13
MS	10 (1)[e]	1-9,999	2, 3, 7, 8, 9, 11
MT	2	1-9,999	3, 6, 7, 8, 11
NC	39	0.1-49,999	2, 3, 5, 7, 8, 9, 10, 11, 12, 13
ND	1 (1)[e]	No Data	7
NE	5	0-99	3, 8, 9, 12
NH	5	10-999	3, 5, 7, 8, 9
NJ	32 (3)[e]	1-49,999	2, 3, 6, 7, 8, 9, 10, 13
NM	1	1-9	8
NV	3	10-99	9, 12

TABLE 4-1 (Continued)

State[b]	No. of facilities	Range of maximum amounts on site in thousands of pounds[c]	Activities and uses[d]
NY	13 (2)[e]	1-999	1, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13
OH	70 (6)[e]	0-49,999	1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 13
OK	6 (1)[e]	10-49,999	3, 6, 7, 8, 9, 11
OR	11	1-999	7, 8, 9
PA	47 (2)[e]	0-49,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13
PR	3	1-99	3, 7, 8, 9
RI	5	10-999	2, 4, 7, 8, 9, 13
SC	25 (5)[e]	1-999	2, 3, 7, 8, 9, 11, 12, 13
SD	2	1-99	7, 9
TN	36 (3)[e]	0-9,999	2, 3, 5, 6, 7, 8, 9, 12, 13
TX	78 (4)[e]	0-499,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13
UT	2	1-9	4, 8, 9
VA	17 (2)[e]	1-49,999	2, 3, 7, 8, 9, 10, 12
WA	26 (1)[e]	0.1-9,999	1, 3, 6, 7, 8, 9, 11, 12
WI	23	0.1-499,999	2, 7, 8, 9, 13
WV	9 (3)[e]	10-9,999	3, 7, 8, 9, 10, 12
WY	1	1-9	7

[a]TRI 1989
[b]Post office state abbreviations
[c]Data in TRI are maximum amounts on site at each facility.
[d]Activities/Uses:

1. produce
2. import
3. for on-site use/processing
4. for sale/distribution
5. as a byproduct
6. as an impurity
7. as a reactant
8. as a formulation component
9. as an article component
10. for repackaging only
11. as a chemical processing aid
12. as a manufacturing aid
13. ancillary or other use

[e]Number of facilities reporting "no data" regarding maximum amount of the substance on site.

4.4 DISPOSAL

Typical means of styrene disposal include absorption on vermiculite or similar material, followed by disposal in an EPA-permitted landfill. Incineration is also a useful disposal method, but this must be carefully controlled since pure styrene is highly flammable. No data were located regarding the quantities of styrene disposed by these means (HSDB 1989).

5. POTENTIAL FOR HUMAN EXPOSURE

5.1 OVERVIEW

Styrene is a widely used industrial chemical with reported atmospheric emissions of more than 30 million pounds annually in the United States. Styrene photodegrades in the atmosphere, usually with a half-life of less than 12 hours, depending on the levels of hydroxyl radical and ozone. Styrene is moderately mobile in soil and volatilizes from water to the atmosphere. Styrene may also undergo biodegradation in soil and water. Bioconcentration does not appear to be significant.

The principal route of styrene exposure for the general population is probably by inhalation of contaminated indoor air. Mean indoor air levels of styrene have been reported in the range of 1-9 $\mu g/m^3$, attributable to emissions from building materials, consumer products, and tobacco smoke. Occupational exposure to styrene by inhalation is the most likely means of significant exposure. The highest potential exposure is probably in the reinforced plastics industry and polystyrene factories. Exposure may also be high in areas near major spills. Exposure to styrene from hazardous waste sites is potentially important but the magnitude of the problem is unknown.

Styrene has been identified in 52 of the 1,177 NPL hazardous waste sites in the United States (View 1989). The frequency of these sites within the United States can be seen in Figure 5-1.

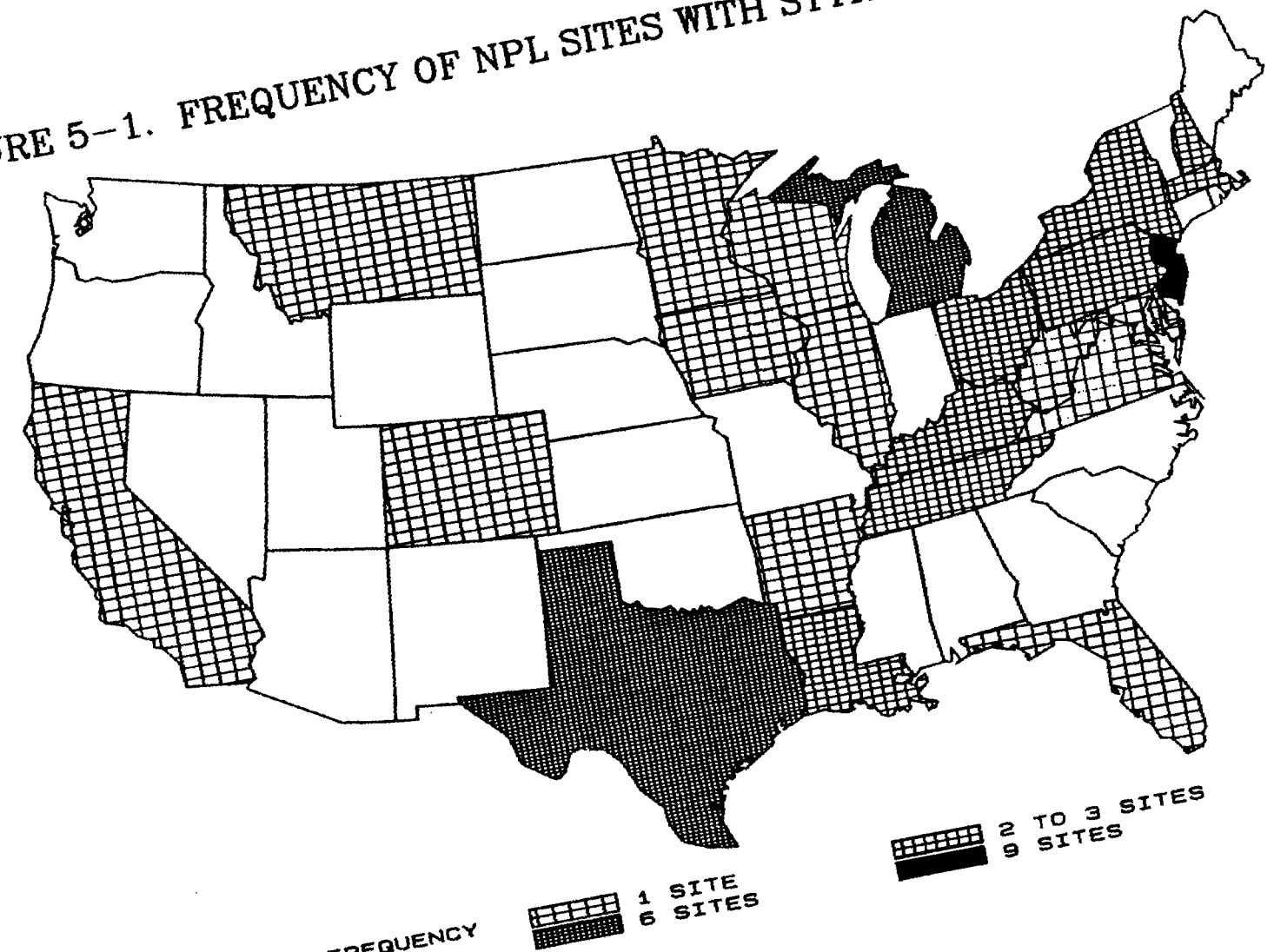
5.2 RELEASES TO THE ENVIRONMENT

Manufacturers, processors, and users of styrene are required to report the quantities of styrene released to environmental media annually (EPA 1988a). The data currently available, compiled in the Toxic Chemical Release Inventory (TRI 1989), are for releases in 1987 and are summarized in Table 5-1. Data relevant to specific media are discussed below.

5.2.1 Air

Styrene may be emitted to the atmosphere from industrial production and usage processes, motor vehicle.operation, combustion processes, building materials, and consumer products. Estimated industrial styrene emissions reported to EPA for the 1987 Toxics Release Inventory (TRI) totaled over 30 million pounds, 18 million pounds from point sources and more than 12 million pounds as fugitive emissions (EPA 1989c). Styrene ranked 20th among air emissions chemicals in the United States in 1987. Since EPA regulations which require reporting of toxic chemical emissions apply only to selected facilities producing and/or using substantial quantities of the chemical (EPA 1988a), the total air emissions of styrene are probably greater than those reported. Typical sources of industrial styrene emissions are those facilities producing styrene, polystyrene, other plastics, synthetic rubber, and resins (Abrams et al. 19.75; EPA 1987d; Graedel 1978; IARC 1979; NIOSH 1983). Facilities reporting styrene emissions for the TRI are listed in Table 5-1.

FIGURE 5-1. FREQUENCY OF NPL SITES WITH STYRENE CONTAMINATION *



* Derived from View 1989

TABLE 5-1. Releases to the Environment from Facilities That Manufacture or Process Styrene[a]

State[a]	No. of facilities	Range of reported amounts released in thousands of pounds[b]						
		Air	Underground injection	Water	Land	Total Environment[a]	POTW[c] transfer	Off-site waste transfer
AL	10	0.1-77	0-0	0-0.3	0-0	0.1-77	0-0	0-4.6
AR	14	0-641.2	0-0	0-0.8	0-0.3	0-641.2	0-2	0-25.3
AZ	8	3.8-273	0-0	0-0	0-0	3.8-273	0-0	0-0.8
CA	81	0-240	0-0	0-0.1	0-0.8	0-240	0-28.2	0-86.1
CO	5	0-4.3	0-0	0-0.5	0-7.8	0-12.1	0-0	0-7.8
CT	5	0-11.8	0-0	0-0.3	0-0	0-11.8	0-0.3	0-291.4
DE	3	8-51.3	0-0	0-0	0-0	8-51.3	0-0.1	0-22.6
FL	44	0-1,000	0-0	0-0	0-20	0-1,000	0-0.1	0-107.3
GA	24	0-248	0-0	0-0.1	0-45	0-248	0-0.3	0-526
IA	16	0-643	0-0	0-0.1	0-0.3	0-643	0-16	0-8.4
ID	2	20-26	0-0	0-0	0-0	20-26	0-0	0-0.8
IL	49	0-856	0-0	0-0.3	0-6.6	0-856	0-0.3	0-899.6
IN	50	0-525	0-0	0-0	0-3.9	0-525	0-0	0-216.7
KS	13	0-39.9	0-0	0-0	0-0.8	0.3-39.9	0-0.1	0-6.6
KY	21	0.1-184.7	0-0	0-0.1	0-18	0.1-184.7	0-15.9	0-70.2
LA	16	0.1-199	0-0	0-1.1	0-0	0-199	0-0	0-26.5
MA	13	0-120	0-0	0-0.3	0-0	0-120	0-0.3	0-404.9
MD	14	0-57.6	0-0	0-0.3	0-0.3	0-57.6	0-0.3	0-0.8
ME	5	0.5-41	0-0	0-0	0-0	0.5-41	0-0.3	0-0
MI	32	0-337	0-0	0-0.3	0-0.3	0-337	0-3.8	0-257
MN	10	0.2-355.2	0-0	0-0.1	0-0	0.2-355.2	0-0	0-7.2
MO	17	0-40	0-0	0-0	0-0.3	0-40	0-0	0-1,258
MS	10	0.3-121.9	0-0	0-0.3	0-0	0.3-121.9	0-0	0-13.7
MT	2	2.4-2.6	0-0	0-0.3	0-0	2.4-2.8	0-0	0-0.3
NC	39	0-222.8	0-0	0-0	0-0	0-222.8	0-1.2	0-22
ND	1	8.2-8.2	0-0	0-0	0-0	8.2-8.2	0-0	0-0
NE	5	0-36	0-0	0-0	0-11.7	0-36	0-0	0-11.7
NH	5	0.5-22.5	0-0	0-0	0-0	0.5-22.5	0-0.3	0-3.2
NJ	32	0.1-85	0-0	0-0.2	0-0	0-85	0-0.3	0-87
NM	1	5.2-5.2	No Data	0-0	0-0	5.2-5.2	0-0	0-0
NV	3	1.4-24.6	0-0	0-0	0-0	1.4-24.6	0-0	0-0.8
NY	13	0-46.3	0-0	0-0.7	0-27.8	0-46.3	0-0.3	0-73.6
OH	70	0-299	0-0	0-9.6	0-25	0-299.3	0-42.7	0-680
OK	6	4.8-164.1	0-0	0-0.3	0-0.3	5.3-164.1	0-0.3	0-20
OR	11	0.5-188	0-0	0-0	0-0	0.5-188	0-0	0-9.6
PA	47	0-230	0-0	0-2	0-5	0-230	0-39.2	0-117.5
PR	3	0.1-0.3	0-0	0-0	0-0	0.1-0.3	0-0.1	0-0.1
RI	5	9.1-87.5	0-0	0-0	0-0	9.1-87.5	0-0	0-6.8
SC	25	0-258.6	0-0	0-1.5	0-0.3	0-258.8	0-3.1	0-176.4
SD	2	14.4-37.1	0-0	0-0	0-0	14.4-37.1	0-0	0-0

TABLE 5-1 (Continued)

State[a]	No. of facilities	Range of reported amounts released in thousands of pounds[b]						
		Air	Underground injection	Water	Land	Total Environment[e]	POTW[c] transfer	Off-site waste transfer
TN	36	0.5-222.4	0-0	0-0.1	0-0.1	0.5-222.4	0-68.5	0-39.5
TX	78	0-1,188	0-0.3	0-18	0-18.8	0-1,188	0-5.9	0-18,099
UT	2	0.3-0.9	0-0	0-0	0-0	0.3-0.9	0-0	0-0
VA	17	0.1-305.8	0-0	0-0.3	0-0.8	0.1-305.8	0-0.3	0-5.2
WA	26	0.7-213.6	0-0	0-0	0-0	0.7-213.6	0-0	0-13.1
WI	23	0-200.8	0-0	0-0.3	0-0.3	0-200.8	0-0.3	0-44.7
WV	9	0.1-760	0-0	0-1.1	0-100	1.2-760	0-190	0-158.8
WY	1	0.5-0.5	No Data	0-0	0-0	0.5-0.5	0-0	0-0

[a]TRI 1989
[b]Data in TRI are maximum amounts released by each facility. Quantities reported here have been rounded to the nearest hundred pounds, except those quantities > 1 million pounds which have been rounded to the nearest thousand pounds.
[c]Publicly owned treatment works
[d]Post office state abbreviation
[e]The sum of all releases of the chemical to air, land, water, and underground injection wells by a given facility.

5. POTENTIAL FOR HUMAN EXPOSURE

Styrene has been identified as a component of motor vehicle emissions from both gasoline- and diesel-powered engines (Hampton et al. 1982, 1983). Styrene emission rates ranging from 6.2 to 7.0 mg/km distance for gasoline powered vehicles and 1.4-2.1 mg/km for diesel trucks have been reported (Hampton et al. 1983).

Styrene may also be emitted into the air by various combustion processes. Styrene has been identified in the stack emissions from waste incineration (Junk and Ford 1980) and Kleindienst et al. (1986) reported the presence of styrene in wood smoke emissions, but no quantitative data were reported.

Emissions of styrene from various building materials and consumer products may contribute significantly to indoor air pollution. A styrene emission rate from glued carpet of 98 ng/min/m^2 was calculated by Wallace et al. (1987b) and Girman et al. (1986) identified styrene as a major emittant from adhesives used in the constructing and finishing of buildings. Polystyrene products such as packaging materials, toys, housewares, and appliances that may contain small amounts of the monomer also contribute to air levels. Styrene was also detected in sidestream smoke emitted from cigarettes but concentrations were not reported (IARC 1979).

5.2.2 Water

The principal sources of styrene releases to water are industrial effluents. Styrene has been detected in effluents from chemical, textile, latex, and coal gasification plants (Pellizzari et al. 1979; Shackelford and Keith 1976). Styrene was also identified in one of 63 industrial effluents at a concentration of <10 µg/L (Perry et al. 1979). Styrene occurred at concentrations up to 83 µg /L in coal gasification effluents (Pellizzari et al. 1979) and King and Sherbin (1986) reported styrene concentrations up to 970 µg /L in chemical plant effluents. The daily styrene loading from a single chemical plant into the St. Clair River (just south of Lake Huron on the Michigan/Ontario border) was estimated at 133 kg (King and Sherbin 1986). Styrene was detected (but not quantified) in the leachate from an industrial landfill in a study of 58 municipal and industrial landfill leachates (Brown and Donnelly 1988).

Styrene has been detected in both surface and groundwater at hazardous waste sites. Data from the Contract Laboratory Program (CLP) Statistical Database indicate styrene occurred at about 2% of the sites sampled at geometric mean concentrations in positive samples of 9.3 µg/L and 5.3 µg/L in surface water and groundwater, respectively (CLPSD 1986). Note that the CLPSD includes data from both NPL and non-NPL sites.

5.2.3 Soil

Soil and sediments may become contaminated with styrene by chemical spills, landfill disposal of styrene-containing wastes or discharge of styrene-contaminated water. Styrene was detected in soil samples at 3.5% of

455 hazardous waste sites at a geometric mean concentration in positive samples of 0.530 mg/kg (CLPSD 1986).

5.3 ENVIRONMENTAL FATE

5.3.1 Transport and Partitioning

In the atmosphere, styrene exists as a vapor. Styrene is an oily liquid that is slightly volatile; its vapor pressure has been determined to be approximately 5 mmHg at 20°C (Verschueren 1983). A small fraction of the styrene released to the atmosphere may dissolve into condensed water vapor such as clouds and raindrops. A Henry's law constant (H) is a measure of the tendency of a chemical to partition between its gas phase and water. A value for H has not been experimentally measured for styrene, but it may be estimated by dividing the vapor pressure of styrene by its solubility in water at the same temperature (Mabey et al. 1982). In this case, the value of H is approximately 2.61×10^{-3} atm-m^3/mole at 25°C. Analogous air-water partition coefficients were measured for styrene at 37°C, yielding a value of approximately 5.4×10^{-1} atm-m^3/mole (Sato and Nakajima 1979). The magnitude of the values suggest that only a small fraction of vapor-phase styrene would dissolve into water. Physical processes such as precipitation and dry deposition would not be significant mechanisms for removing styrene from the atmosphere because of its high photochemical reactivity (EPA 1984b).

The magnitude of the estimated Henry's law constant (2.61×10^{-3} atm-m^3/mole, assuming a water solubility of 300 mg/L at 25°C) suggests that a large fraction of the chemical dissolved in water will volatilize into the atmosphere, depending on temperature gradients, relative humidity, air currents, and the extent of mixing of the solution. The rate of styrene volatilization from water has not been experimentally measured, but its half-life in moving water that is 1 meter in depth may be on the order of 6 hours, based on the empirical relationship reported by Dilling (1977) for the volatilization of chlorinated hydrocarbons from water. The half-life of styrene in the Rhine River was estimated from field measurements at about 14 hours, but it was not certain whether styrene volatilized, biodegraded, and/or photodegraded (Zoeteman et al. 1980). Volatilization from ponds and lakes would be slower; half-life estimates range from 3 to 13 days (EPA 1984b).

Styrene is only sparingly soluble in water, but its exact solubility is uncertain. Values reported for the solubility of styrene range from 160 mg/L at 23°C to 310 mg/L at 20°C (Banerjee et al. 1980; Valvani et al. 1981; Verschueren 1983).

Styrene in water may also partition to soils and sediments. The extent of adsorption of sparingly water-soluble compounds is often correlated with the organic carbon content of the adsorbent (Hassett et al. 1983). When adsorption is expressed as a function of organic-carbon content, an organic carbon/water partition coefficient (K_{oc}) is generated, and may be used to rank the relative mobility of the chemical in soil. A K_{oc} value for styrene has

not been experimentally measured, but may be estimated from its solubility in water, using the empirical regression of Hassett et al. (1983). Assuming that the solubility of styrene is 300 mg/L, a calculated K_{oc} value for styrene is 260. The magnitude of this estimated K_{oc} suggests that styrene is "moderately mobile" in soil (Roy and Griffin 1985). In surface soils, where the amount of organic carbon will be highest, the movement of styrene will be retarded by adsorption. In deeper subsurface environments where the amount of organic carbon may be low, adsorption may not be as significant. Based on field measurements, the rate of movement of styrene in an aquifer was about 80 times slower than that of the groundwater, (Roberts et al. 1980) which is attributed to adsorption. No information was located to corroborate the estimated K_{oc} value, and apparently there are no studies in which the adsorption-desorption characteristics of styrene by soils and sediments have been measured.

The octanol/water partition coefficient (K_{ow}), which reflects the partitioning of a chemical between octanol and water, is believed to be a good indication of the tendency for a chemical to accumulate in the fatty structures in plants and animal tissues (Kenaga and Goring 1980). The K_{ow} of styrene has been measured to be 1,445 (Banerjee et al. 1980) and 891 (Valvani et al. 1981), suggesting that styrene will partition to fat tissues. This is shown to be the case by the work of Engstrom et al. (1978a) and by Stanley (1986).

Even though styrene does tend to partition into fat, it does not tend to bioaccumulate to high levels, mainly because of its metabolism and excretion. A bioconcentration factor (BCF) relates the concentration of a chemical in an organism to the concentration of the chemical in the medium in which it is exposed. Based on the empirical regression of Kenaga (1980), the BCF for styrene is about 25. An experimentally-measured BCF for goldfish was 13.5 (Ogata et al. 1984). These low BCFs suggest that bioconcentration is not a significant fate of styrene released into the environment (EPA 1984b). No other measured BCFs were located to corroborate these reported values.

5.3.2 Transformation and Degradation

5.3.2.1 Air

The major fate of atmospheric styrene is determined by the rate of photooxidation. Styrene may be transformed by direct photolysis, but the half-life of this process may be on the order of 50 years (EPA 1984b). Kopczynski et al. (1972) found that styrene was not degraded by photolysis after 6 hours of exposure.

Styrene is more quickly photooxidized by ozone and hydroxyl radicals. The rate constant for the reaction of styrene with ozone at ambient temperatures (about 25°C) has been measured and is approximately 0.17 to 2.16×10^{-19} cm^3/molecule-sec (Atkinson et al. 1982; Hendry and Kenley 1979). Assuming that the mean concentration of ozone in the troposphere is 1012 molecules/cm^3 (Cupitt 1980), then the half-life of styrene would be approximately 13 hours. The rate constant for the reaction of styrene with

hydroxyl radicals has been measured as 5.3×10^{-11} cm^3/molecule-sec (Bignozzi et al. 1981). Assuming that the concentration of tropospheric hydroxyl radicals varies from 3×10^5 to 1×10^7 molecules/cm^3 (Mac Leod et al. 1984), it follows that the atmospheric half-life of styrene would be between 0.5 and 17 hours. Consequently, because of the combined effect of ozone- and hydroxyl radical-initiated decay, it appears likely that styrene is labile in the troposphere. Transformation products include various oxygen-containing and saturated hydrocarbons (Sloane and Brudzynski 1979).

5.3.2.2 Water

Little is known about abiotic transformations of styrene in water. The reaction of styrene with peroxy radicals appears to be too slow to be significant (EPA 1984b), and no relevant information regarding photochemical reactions in water was located. There is no information that styrene will hydrolyze in water, nor would its chemical structure suggest such potential.

Styrene biodegrades in various aquatic systems. Styrene was only slightly biodegraded in the presence of one type of sewage (Pahren and Bloodgood 1961), but Bridie et al. (1979) found that 42% of the styrene initially present degraded in 5 days when unadapted sewage was used as the source of microorganisms. Very low concentrations of styrene (less than 10 µg/L) were almost completely degraded in 20 minutes in an aerobic biofilm reactor after acclimation, but the chemical was persistent in a methanogenic biofilm column (Bouwer and McCarty 1984). It was found that the rate of styrene biodegradation in groundwater was slow (Wilson et al. 1983). The half-life of styrene in groundwater was estimated to be between 6 weeks and 7.5 months. Although these studies have demonstrated the potential for styrene to biodegrade in water, no information was located about styrene degradation in ambient surface waters.

5.3.2.3 Soil

Styrene may also biodegrade in soils. Microorganisms were isolated from soil that were capable of using,styrene as a sole-carbon source (Sielicki et al. 1978). Biodegradation products included phenylethanol and phenylacetic acid. Cultures of propane-utilizing bacteria isolated from soil and lake samples were able to degrade styrene (Hou et al. 1983). No information was located on the biodegradation of styrene in field soils.

5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

5.4.1 Air

Styrene is a common contaminant of ambient urban air. Concentrations of styrene greater than rural air concentrations have been identified in urban and industrial source areas, near hazardous waste sites, in motor vehicle tunnels, in indoor air, and in workplace environments. A summary of monitoring data for these locations is presented in Table 5-2. The data suggest that indoor air concentrations of styrene may be considerably higher

than outdoor concentrations. Cigarette smoke has been implicated as a significant source of styrene in indoor air (Wallace 1987; Wallace et al. 1986a).

5.4.2 Water

Styrene is not frequently found in United States water supplies. Styrene was not detected in any of the more than 1,000 samples of drinking water analyzed during three federal surveys (EPA 1988b), but has been reported occasionally in drinking water supplies in several states (Abrams et al. 1975; Coleman et al. 1984; Kleopfer and Fairless 1972; Kool et al. 1982; Sanjivamurthy 1978; Shackelford and Keith 1976) well water (Kelley 1985; Krill and Sonzogni 1986), river water (Shackelford and Keith 1976; Sheldon and Hites 1978) and Lake Erie (Konasewich et al. 1978). Quantitative data were not available in these reports. Styrene concentrations in raw and treated waters ranged from 0.1 to ≥1.0 µg/L in an evaluation of organic compounds in Canadian water supplies at nine municipalities along the Great Lakes (Otson 1987).

5.4.3 Soil

Limited data were located regarding estimation of styrene in soils or sediments (see Section 5.2.3).

5.4.4 Other Environmental Media

Styrene has been detected among the natural volatile components of roasted filberts, dried legumes, fried chicken, nectarines, and Beaufort cheese (Dumont and Adda 1978; Kinlin et al. 1972; Lovegren et al. 1979; Takeoko et al. 1988; Tang et al. 1983). Styrene may also enter foods by migration from polystyrene food containers and packaging materials (EPA 1988b). Concentrations of styrene measured in yogurt packaged in polystyrene containers ranged from 5.5 to 150 µg /L (Withey 1976). Mean levels of styrene in foods packaged in plastic in the United Kingdom ranged from <1 to 180 µg /kg (Gilbert and Startin 1983). Similar concentrations of styrene were detected in other dairy products packaged in polystyrene containers (IARC 1979). The rate of styrene migration into food is mainly a function of the diffusion coefficient of the monomer in the polymer and of the lipophilicity of the food (Till et al. 1987). For example, 4%-6% of the free monomer in polystyrene packaging migrated into corn oil or sunflower oil within 10 days, while only 0.3%-0.6% migrated into milk, beef or water. Similarly, migration of styrene from foam cups into liquids such as water, tea or coffee was about 8 ng/cm^2, while migration into 8% ethanol (as might be encountered in wine or other alcoholic drinks) was 36 ng/cm^2 (Varner and Breder 1981). However, Withey and Collins (1978) found no clear relationship between the styrene monomer content of packaging material (which varied widely) and the amount leached into food after comparable residence times. Styrene was detected, but not quantified, in samples of mother's milk from four urban areas (Pellizzari et al. 1982).

TABLE 5-2. Styrene Concentrations in Representative Air Samples in the United States

Location	Concentration ($\mu g/m^3$) Maximum	Mean	Reference
Rural/ suburban	No data	0.28-0.34[a]	Shah and Heyerdahl 1988; Graedel 1978
Urban	0.63-21	0.29-3.8	Grosjean and Fung 1984; Harkov et al. 1985; Hunt et al. 1986; Shah and Heyerdahl 1988; Wallace et al. 1986b; Wallace 1987
Industrial source areas	25	1.3[a]-2.1	Brodinzky and Singh 1983; Pellizzari et al. 1978; Shah and Heyerdahl 1988
Hazardous waste sites	65	1.1-6.4	Harkov et al. 1985; La Regina and Bozzelli 1986
Tunnel	6.6	1.1-6.6[b]	Hampton et al. 1983
Indoors	6,500	0.8-8.9	Shah and Heyerdahl 1988; Wallace et al. 1986a; Wallace 1987
Workplace	4.5×10^6	<1-1.5×10^6	Bartolucci et al. 1986; Cocheo et al. 1983; NIOSH 1983

[a]Median value
[b]Range of values, no mean given

5. POTENTIAL FOR HUMAN EXPOSURE

Styrene has been identified as a component of cigarette smoke (EPA 1984b) and has been detected in concentrations of 18 µg /cigarette in the smoke of cigarettes made in the United States (IARC 1979). Indoor air concentrations of styrene may be significantly higher in homes of smokers than nonsmokers (Wallace 1987).

5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

Exposure to styrene may occur by inhalation, ingestion, or dermal absorption. The most likely mode of exposure of the general population to styrene is by inhalation of indoor air (EPA 1988b). Based on the EPA (1989e) estimate that the average person spends 20.4 hours/day indoors (inhaling about 17 m^3 of air during that time based on an air inhalation rate of 20 m^3/day) and the range of mean indoor air concentrations presented in Table 5-2, typical indoor exposure levels to styrene may range from 14 to 151 µg /day. Additional exposures may occur from inhalation of outdoor air and ingestion of food which was stored in polystyrene containers. Outdoor air concentrations are likely to be lower in rural than urban areas and are likely to be small compared to indoor air concentrations. Exposure from municipal drinking water is probably insignificant. However, groundwater at hazardous waste sites where styrene has been detected may provide significant exposure to styrene if used as local water supply.

Worst-case exposure estimates for styrene of 0-0.5 µg /day from drinking water, 30 µg day from food, and 65,000 µg /day from air were calculated by EPA (1988b). These estimates are based on the highest levels estimated or monitored and, therefore, reflect the highest potential exposure rather than typical exposure for the general population.

Exposure of the general population to styrene is confirmed by human monitoring data. Styrene has been identified in adipose tissue at concentrations of 8-350 ng/g (Stanley 1986), in blood at a mean concentration of 0.4 µg /L (Antoine et al. 1986) and in exhaled breath at mean concentrations of 0.7-1.6 µg /m^3 (Wallace 1987).

A large number of workers are potentially exposed to styrene. NIOSH estimates that approximately 300,000 workers at 22,000 facilities may be exposed to styrene (NOES 1989), about 30,000 of these on a full-time basis (NIOSH 1983). The highest potential exposure occurs in the reinforcedplastics industry, where workers may be exposed to high air concentrations and also have dermal exposure to liquid styrene or resins (Lemasters et al. 1985; NIOSH 1983). Hemminki and Vainio (1984) estimated that heavily exposed workers in this industry in Finland might be exposed to up to 3 g of styrene per day. Significant occupational exposures may also occur in other industrial settings, including styrene polymerization, rubber manufacturing, and styrene-polyester resin facilities (Engstrom et al. 1978b; NIOSH 1983; Rappaport and Fraser 1977).

5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

People working in various styrene industries are likely to have the highest exposures to styrene. Lower levels may be encountered near industrial facilities or hazardous waste sites emitting styrene to outdoor air. High indoor styrene concentrations in the home may be due to emissions from building materials, consumer products, and tobacco smoke. Smokers and those eating a high proportion of foods packaged in polystyrene may also have above average exposure to styrene.

5.7 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of styrene is available. Where adequate information is not available, ATSDR, in conjunction with the NTP, is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of styrene.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that, if met, would reduce or eliminate the uncertainties of human health assessment. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

5.7.1 Data Needs

Physical and Chemical Properties. The solubility of an organic compound in water is indicative of how that chemical will partition between water, soil, and organisms (Banerjee et al. 1980; Hassett et al. 1983; Valvani et al. 1981). Clarification of the exact solubility of styrene in water would be helpful because currently a range of values is reported. The Henry's law constant and K_{oc} value for styrene need to be verified experimentally to provide more accurate predictions of air-water and soil-water partitioning.

Production, Import/Export, Use, and Disposal. Substantial quantities of styrene are currently produced and used in the United States (Heylin 1989; HSDB 1989; SRI 1989; USITC 1988). Production and import quantities, producers, and uses are well documented. There has been an increase in production volume over the past decade and further increases are projected. However, data on current styrene imports were not available. Quantities of styrene disposed of by various disposal methods are not known. Styrene releases into water are regulated by EPA, but styrene is not listed as a hazardous waste constituent and, therefore, land disposal restrictions do not apply to this compound. Additional information on disposal methods used for styrene and styrene-containing products and the quantities disposed of by each

method would help to better characterize the potential for human exposure to this compound from disposal at waste sites or other locations.

According to the Emergency Planning and Community Right-to-Know Act of 1986, 42 U.S.C. Section 11023, industries are required to submit chemical release and off-site transfer information to the EPA. The Toxic Release Inventory (TRI), which contains this information for 1987, became available in May of 1989. This database will be updated yearly and should provide a list of industrial production facilities and emissions. It is likely that styrene will continue to be a high volume production chemical.

Environmental Fate. Styrene will partition among the environmental media, with a tendency to volatilize from water to air and to adsorb to soils (EPA 1984b; Roberts et al. 1980; Sato and Nakajima 1978). However, data on styrene volatilization from water and confirmation of the estimated K_{oc} value by adsorption/desorption data would be useful to estimate more accurately the tendency of styrene to partition to air and soil. Confirmation of the K_{oc} would also provide a more reliable basis for estimating the mobility of styrene in the various types of soil.

Although the reaction mechanisms of styrene transformations in the atmosphere are fairly well understood (Atkinson et al. 1982; Bignozzi et al. 1981; Hendry and Kenley 1979; Sloane and Brudzynski 1979), more information regarding the environmental fates of the transformation products would allow a more accurate prediction of the atmospheric fate of this compound. Data on biodegradation of styrene would be useful in predicting the fate and persistence of the compound in water and soil.

Bioavailability from Environmental Media. Styrene is known to be absorbed following inhalation, oral and dermal contact (Dutkiewicz and Tyras 1968; Engstrom et al. 1978a, 1978b; Ramsey and Anderson 1984; Ramsey and Young 1978; Withey 1976; Withey and Collins 1979). Absorption rates via inhalation are known (Withey and Collins 1978). Additional data are needed to evaluate absorption rates following oral and dermal exposure. It is believed that absorption of styrene from the.gut is generally rapid and therefore contact with styrene contaminated food, soil, or water will probably also result in significant absorption. However, this may depend on the medium in which it is contained. However, actual absorption rates associated with ingestion are unknown and should be investigated.

Food Chain Bioaccumulation. Bioconcentration of styrene in aquatic organisms is not likely to be significant, based on both a measured BCF for a single species and an estimated BCF (EPA 1984b; Kenaga 1980; Ogata et al. 1984). No data on biomagnification of styrene in the food chain were located. Since significant bioaccumulation is unlikely, this lack of data may not be a major limitation. However, additional information on bioconcentration in several species would confirm this prediction.

Exposure Levels in Environmental Media. Monitoring data for styrene in air are extensive and recent data are available (Shah and Heyerdahl 1988; Wallace 1987). However, monitoring data in other environmental media using current, sensitive analytical methods are sparse. Additional data on styrene levels in water and soil, especially in the vicinity of hazardous waste sites would be useful in assessing the potential for human exposure. Quantification of styrene in cigarette smoke would also help in assessing exposure from smoking and passive smoke inhalation. Estimates of human intake from air, water, and soil have been made (EPA 1988b) and will undoubtedly be revised as additional data become available.

Exposure Levels in Humans. Styrene has been detected in human blood, breath, milk, and adipose tissue of the general population (Antoine et al. 1986; Pellizzari et al. 1982; Stanley 1986; Wallace.1987) and metabolites of styrene have been detected in urine of workers exposed to styrene (Elia et al. 1980; Sollenberg et al. 1988). Additional data on blood levels of styrene will be generated by the on-going study described in Section 5.7.2. However, data generated by biological monitoring of populations in the vicinity of waste sites with the most sensitive methods (Section 6.1) would be useful in assessing the magnitude of human exposures from this source.

Exposure Registries. No exposure registries for styrene were located. This compound is not currently one of the compounds for which a subregistry has been established in the National Exposure Registry. The compound will be considered in the future when chemical selection is made for subregistries to be established. The information that is amassed in the National Exposure Registry facilitates the epidemiological research needed to assess adverse health outcomes that may be related to the exposure to this compound.

5.7.2 On-going Studies

As part of the Third National Health and Nutrition Evaluation Survey (NHANES III), the Environmental Health Laboratory Sciences Division of the Center for Environmental Health and Injury Control, Centers for Disease Control, will be analyzing human.blood samples for styrene and other volatile organic compounds (NCHS 1988; Needham 1989). These data will give an indication of the frequency of occurrence and background levels of these compounds in the general population.

No other on-going studies on the fate, transport, or exposure potential of styrene were located.

6. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting and/or measuring and monitoring styrene in environmental media and in biological samples. The intent is not to provide an exhaustive list of analytical methods that could be used to detect and quantify styrene. Rather, the intention is to identify well-established methods that are used as the standard methods of analysis. Many of the analytical methods used to detect styrene in environmental samples are the methods approved by federal agencies such as EPA and the National Institute for Occupational Safety and Health (NIOSH). Other methods presented in this chapter are those that are approved by groups such as the Association of Official Analytical Chemists (AOAC) and the American Public Health Association (APHA). Additionally, analytical methods are included that refine previously used methods to obtain lower detection limits, and/or to improve accuracy and precision.

As a volatile material, styrene is readily determined by gas chromatographic (GC) analysis. As a hydrocarbon, styrene is detected very sensitively by flame ionization detection (FID); its aromatic nature enables some selectivity by photoionization detection (PID); and it can be specifically identified by mass spectrometry. Styrene is usually collected from the gas phase or from vapor evolved from the sample matrix on a column of solid sorbent, such as Tenax@. Cryogenic (low temperature) collection and sorption in organic liquids are also possible.

Capillary gas chromatography, also known broadly as high-resolution gas chromatography (HRGC), has greatly facilitated the analysis of compounds such as styrene that can be measured by gas chromatography and has resulted in vast improvements in resolution and sensitivity. It has made the choice of a stationary phase less important than is the case with the use of packed columns. The instrumental capability to separate volatile analytes by HRGC is, for the most part, no longer the limiting factor in their analysis.

The specific analytical methods used to quantify styrene in biological and environmental media samples are summarized below. Table 6-1 lists the applicable analytical methods used for determining styrene in the biological fluids and tissues, and Table 6-2 lists the methods used for determining styrene in environmental samples.

6.1 BIOLOGICAL MATERIALS

Methods have been described for the determination of styrene in expired air (Kneip and Crable 1988a; Stewart et al. 1968), blood (Antoine et al. 1986; Bartolucci et al. 1986; Guillemin and Berode 1988; Withey and Collins 1977), urine (Dolara et al. 1984; Ghittori et al. 1987; Pezzagno et al. 1985), adipose tissue (Engstrom et al. 1978a), and other tissues (heart, lungs, liver, spleen, kidney, brain) (Withey and Collins 1977). These methods generally require styrene release from the sample matrix and collection on a

TABLE 6-1. Analytical Methods for Determining Styrene in Biological Materials

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Styrene analyte					
Adipose tissue	Evaporation into nitrogen collection as vapor	GC	No data	No data	Engstrom et al. 1978a
Breath[a]	Collection in Saran bag	GC/FID	0.05 ppm	No data	Stewart et al. 1968
Breath	Sorption onto silicagel, desorption into headspace	GC	0.1 ppm	No data	Kneip and Crable 1988a
Blood	Purge at 40-50°C with helium, collection on Tenax-GC/silica	GC/MS	No data	CV<5%	Antoine et al. 1986
Blood	Headspace analysis	GC/FID	No data	No data	Bartolucci et al. 1986
Blood	Collection in vacutainer with EDTA as anticoagulant, headspace analysis	GC	No data	No data	Guillemin and Berode 1988
Blood	Headspace analysis	GC	0.02 µg/mL	No data	Withey and Collins 1977
Heart, lungs, liver, spleen, kidney, brain	Hemogenate prepared for headspace analysis	GC	0.01 µg/g	No data	Withey and Collins 1977
Urine	Headspace from sample maintained at 37°C for 2 hr	GC/MS	No data	No data	Ghitori et al. 1987
Urine	Sorption on XAD-2, elution with n-hexane	HPLC/UV	<0.7 µg/L	72±10%	Dolara et al. 1984
Urine	Headspace analysis	GC/MS	No data	No data	Pezzagno et al. 1985
Styrene metabolite analyte					
Urine for MA	Extraction with ethyl acetate, derivatization to isopropyl ester	GC/FID	No data	No data	Korn et al. 1984
Urine for MA	Extraction with diethyl ether, silylation	GC	No data	No data	Engstrom et al. 1976
Urine for MA and PGA metabolites	Extraction and derivatization	GC/FID	0.05 ppm	94%MA 98% PGA	Bartolucci et al. 1986

TABLE 6-1 (Continued)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Urine for MA metabolite	Acidification, extraction, derivatization	HRGC/FID	10 mg/L	No data	Kneip and Crable 1988b
Urine for PGA metabolite	Reduction, acidification, extraction, derivatization	HRGC/FID	10 mg/L	No data	Kneip and Crable 1988c
Urine for MA and PGA metabolites	Extraction with ethyl acetate, derivatization to methyl esters with dizaomethane	GC	No data	No data	Sedivec et al. 1984
Urine for MA and PGA metabolites	Extraction with ethyl acetate, evaporation, derivatization	GC/FID	No data	97%-99% relative recovery	Baselt 1988a
Urine for MA, PGA, and hippuric acid metabolites	Direct injection	HPLC/UV	<1 µg/mL[b]	<3% deviation from true value at 5 µg/mL	Regnaud et al. 1987
Urine for MA and PGA (stereoselective)	Extraction and derivatization	HRGC/FID	No data	No data	Korn et al. 1987
Blood for styrene oxide	Extraction with n-hexanone, concentration by evaporation	GC/FID	1 ng/mL	72±8%	Kessler et al. 1990
Blood for styrene oxide	Extraction with benzene	GC/MS	10 ng/g	92±21%	Langvardt and Nolan 1991

[a]Unless otherwise designated, analyses are for styrene.
[b]Detection limits were 0.63 µg/mL for mandelic acid, 0.78 µg/mL for phenylglyoxylic acid, and 0.52 µg/mL for hippuric acid.

CV = coefficient of variation; EDTA = ethylene diaminetetracotic acid; FID = flame ionization detector; GC = gas chromatography; HPLC = high-performance liquid chromatography; HRGC = high-resolution gas chromatography; hr = hour(s); MA = mandelic acid; MS = mass spectrometry; PGA = phenylglyoxylic acid; UV = ultraviolet

TABLE 6-2. Analytical Methods for Determining Styrene in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Food	Homogenization, headspace sampling	GC/MS	(1 µg/kg	No data	Gilbert and Startin 1983
Air	Retention by activated carbon	GC[a]	No data	No data	ASTM 1989a
Air	Retention by activated carbon, elution with carbon disulfide	GC[b]	No data	No data	ASTM 1989b
Air	Retention by activated carbon, elution with carbon disulfide	HRGC/FID	0.01 mg/ sample	No data	NIOSH 1984
Water	Purge by helium, collection on activated charcoal/silica gel/ Tenax®	GC/PID	0.01 µg/L	96%-104%	EPA 1989f
Water	Purge by helium, collection on activated charcoal/silica gel/ Tenax®	GC/PID	0.008 µg/L	No data	EPA 1989g
Water	Purge by helium, collection on activated charcoal/silica gel/ Tenax®	HRGC/MS	0.20 µg/L	120% (at 1 µg/L)	EPA 1989h
Water	Purge by helium, collection on activated charcoal/silica gel/ Tenax®	HRGC/MS	0.04 µg/L	102%	EPA 1989i
Soil, low level	Purge by helium, collection on solid, thermal desorption	GC/MS	4 µg/kg	No data	EPA 1986c
Solid waste, nonwater miscible	Purge by helium, collection on solid, thermal desorption	GC/MS	500 µg/kg[c]	No data	EPA 1986c
Solid waste	Purge by helium, collection on solid, thermal desorption	GC/MS	500 µg/kg[c]	No data	EPA 1986b

[a]Absorption characteristics for sampling atmospheric vapor with activated carbon for subsequent analysis by GC.
[b]Generic method for the determination of organics.
[c]Estimated from detection limits in water.

FID = flame ionization detector; GC = gas chromatography; HRGC = high-resolution gas chromatography; MS = mass spectrometry; PID = photoionization detection; UV = ultraviolet

column of solid sorbent or collection as headspace gas. Cryogenic collection should also be possible. Of the available methods for detecting styrene, flame ionization detection (FID) is the most sensitive and mass spectrometry (MS) is the most specific.

The major metabolites of styrene in humans are MA and PGA. Detection of these metabolites in urine is the most commonly performed procedure as an indicator of exposure to styrene. Procedures have been described for their measurement in urine (Baselt 1988a; Dolara et al. 1984; Engstrom et al. 1976; Xneip and Crable 1988b; Kneip and Crable 1988c; Korn et al. 1984; Pezzagno et al. 1985; Sedivec et al. 1984; Sollenberg et al. 1988). Generally these styrene metabolites are converted.to volatile derivatives and measured gas chromatographically or determined directly by high performance liquid chromatography. Two other styrene metabolites that may result from exposure to styrene are 4-vinylphenol (Pfaffli et al. 1981) and styrene glycol-(phenyl ethylene glycol) (Guillemin and Berode 1988), but methods for the detection of these metabolites in biological materials have not been worked out in detail. Sensitive methods are also available for measuring styrene oxide in blood (Kessler et al. 1990; Langvardt and Nolan 1991), although these techniques are probably more useful in research on styrene toxicity than in detecting or quantifying styrene exposure.

Methods for detection of styrene and its metabolites in biological materials are summarized in Table 6-1.

6.2 ENVIRONMENTAL SAMPLES

Styrene determined in environmental samples is usually collected on solid sorbents (from air) or on solid sorbents after purging in a gas stream (water, soil, solid waste samples). Styrene from such samples is measured very sensitively by gas chromatography with flame ionization detection (GC/FID) and very specifically by gas chromatography with mass spectrometric detection (GC/MS). Methods for the determination of styrene in environmental samples have been standardized by the American Society for Testing and Materials (ASTM 1989b), U.S. Environmental Protection Agency (EPA 1986a, 1986b; EPA 1989b, 1989c, 1989d), and National Institute for Occupational Safety and Health (NIOSH 1984). As shown by the data in Table 6-1, relatively low detection limits (0.01 mg/sample, 0.10 µg /L in water, 4 µg /kg in soil, 500 µg /kg in solid waste) can be achieved for the determination of styrene in environmental samples and the accuracy appears to be acceptable for those limited cases in which accuracy data are available. No significant reports were found pertaining to styrene degradation products in environmental samples.

Methods for the determination of styrene in environmental samples are summarized in Table 6-2.

6.3 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of styrene is available. Where adequate information is not available, ATSDR, in conjunction with the NTP, is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of styrene.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that, if met, would reduce or eliminate the uncertainties of human health assessment. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

6.3.1 Data Needs

Methods for Determining Biomarkers of Exposure and Effect. Biological monitoring of styrene exposure has been reviewed (Guillemin and Berode 1988). Sensitive and selective methods are available for the qualitative and quantitative measurement of styrene and its two major metabolites, MA and PGA, in samples from exposed individuals after the analytes are separated from their biological sample matrix. The concentration of these metabolites in urine has been found to correlate with average exposure levels in air (Harkonen et al. 1978), and so may be used as a biomarker of exposure. However, measurements of MA and PGA are not specific for this purpose (Bartolucci et al. 1986) and these metabolites can result from the metabolism of other organic substances, particularly ethylbenzene (Baselt 1988b). As noted in Chapter 5 for studies of the general population, styrene has been identified in adipose tissue at concentrations of 8-350 ng/g (Stanley 1986), in blood at a mean concentration of 0.4 µg /L (Antoine et al. 1986) and in exhaled breath at mean concentrations of 0.7-1.6 µg /L. Levels of MA and PGA in biological samples from the general population probably are below the detection limits of methods that are currently used (Baselt 1988a). However, it is likely that normal background levels of these metabolites in unexposed individuals are too low to be of any significance. Although new and improved methods for the determination of styrene and its metabolites in biological samples need not have a high priority, additional work on standardization of these methods for use in biological samples accompanied by additional studies involving interlaboratory comparisons of recovery, accuracy, and precision data would be useful.

As discussed in Section 2.5.2, clinical means have been proposed to indicate exposure to styrene. In general, these are not sufficiently sensitive, specific, or well characterized. The most common symptom of

exposure, impairment of central nervous system function, is not at all unique to styrene. Neither cytogenic monitoring of peripheral lymphocytes nor unscheduled DNA synthesis have been sufficiently well characterized as biomarkers of exposure to styrene.

There is currently some information that can be used to correlate levels of biomarkers of exposure to styrene in'biological media with adverse health effects. Central nervous system depression has been correlated with a urinary MA concentration of 800 mg/L or higher and a decrement in psychomotor performance in association with a concentration of 1,200 mg/L or more (Harkonen et al. 1978). The styrene concentrations in air producing these effects and urinary MA levels were relatively high. Studies to determine if effects at lower levels of exposure could also be correlated to metabolite levels in urine would be valuable. However, the design of studies involving controlled inhalation exposures in humans is precluded by the potential carcinogenicity of styrene.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. In an occupational setting the medium that is of most concern for human exposure to styrene is air, although at Superfund sites contaminated groundwater may pose a greater danger. Methods are well developed for the determination of styrene in water and air with excellent selectivity and sensitivity (ASTM 1989a; EPA 1989f, 1989g, 1989i; NIOSH 1984). Methods for the determination of styrene in soil and waste samples have been available for a shorter length of time and require additional testing and validation (EPA 1986b, 1986c).

The detection limits for styrene in environmental media cited in Table 6-2 (0.01 mg/sample, typically 10 L) (NIOSH 1984), 0.04 µg /L in water (EPA 1989i), 4 µg /kg in soil (EPA 1986c) are low enough to enable the determination of styrene in any environmental medium likely to pose a hazard to health based upon information currently available in the literature. These detection limits are probably below most ambient background levels of styrene.

Sampling methodologies for compounds such as styrene continue to pose problems such as nonrepresentative samples, insufficient sample volumes, contamination, and labor-intensive, tedious extraction and purification procedures (Green and LePape 1987). It is desirable to have means to measure organic compounds such as styrene in situ in water and other environmental media without the need for sampling and extraction procedures to isolate the analyte prior to analysis.

In regard to methods for determining parent styrene and degradation products in environmental media the following conclusions may be drawn: Because styrene can be detected instrumentally and determined in air and normal water samples with totally adequate selectivity and sensitivity, no additional data are needed at this time. A moderate need exists to improve methodologies to determine styrene in soil, sludges, and solid wastes. Styrene degradation products are a different matter in that little information is available on their determination in environmental samples. In air these

compounds should consist predominantly of photochemical oxidation products, whereas in water and soil samples they are expected to be biodegradation products. Additional research is needed on the determination of these materials.

6.3.2 On-going Studies

The Environmental Health Laboratory Sciences Division of the Center for Environmental Health and Injury Control, Centers for Disease Control, is developing methods for the analysis of styrene and other volatile organic compounds in blood. These methods use purge-and-trap methodology and magnetic mass spectrometry which gives detection limits in the low parts per trillion range.

Research is underway at the Cooperative Institute for Research in Environmental Sciences (CIRES) at the University of Colorado, Boulder, to improve methods for the analysis of styrene and related compounds in environmental samples, particularly atmospheric samples.

Studies are also underway that would improve the means for determining styrene, its metabolites, and related compounds in biological samples and environmental media. Improvements continue to be made in chromatographic separation and detection. Problems associated with the collection of styrene on a sorbent trap, followed by thermal desorption, may be overcome with direct purging to a capillary column with whole column cryotrapping (Pankow and Rosen 1988). Current activities in the areas of supercritical fluid extraction (King 1989) and supercritical fluid chromatography (Smith 1988) include focus on compounds such as styrene and its metabolites in biological samples and environmental media. Fourier transform infrared flow cell detectors are sensitive and selective for the detection of compounds such as styrene that have been separated by supercritical fluid chromatography (Wieboldt et al. 1988). Immunoassay methods of analysis are very promising for the determination of various organic pollutants and toxicants, and it is reasonable to assume that styrene, and particularly its metabolites, are candidates for this type of analysis.

7. REGULATIONS AND ADVISORIES

Because of its potential to cause adverse health effects in exposed people, a number of regulations and guidelines have been established for styrene by various national and state agencies. These values are summarized in Table 7-1.

7. REGULATIONS AND ADVISORIES

TABLE 7-1. Regulations and Guidelines Applicable to Styrene

Agency	Description	Information	References
INTERNATIONAL			
IARC	Carcinogenic classification	Group 2B[a]	IARC 1987
NATIONAL			
Regulations:			
a. Air:			
OSHA	PEL TWA	50 ppm (215 mg/m^3)	OSHA 1989 (29 CFR 1910.1000) Table Z-1-A
	STEL	100 ppm (425 mg/m^3)	
b. Water:			
EPA ODW	MCLG	0.1 mg/L[b]	EPA 1991
	MCL	0.1 mg/L	
	Monitoring for unregulated contaminants	Yes	EPA 1987b
EPA OWRS	General permits under NPDES	Yes	40 CFR 122, Appendix D, Table V
	General Pretreatment Regulations for Existing and New Sources of Pollution	Yes	40 CFR 403
	Hazardous substance	Yes	40 CFR 116
	Reportable quantity	1,000 pounds	40 CFR 117.3
c. Other:			
EPA OERR	Reportable quantity	1,000 pounds	EPA 1989a (40 CFR 302.4)
EPA OSW	Groundwater monitoring list (Appendix IX)	Yes	EPA 1987c (40 CFR 264)
EPA OTS	Toxic chemical release reporting rule	Yes	EPA 1988a (40 CFR 372)
	Preliminary assessment information rule	Yes	EPA 1982 (40 CFR 712.30)
FDA	Food additive-synthetic flavoring substance	Yes	21 CFR 172.515
	Indirect food additive - adhesives, styrene block polymers	Yes	21 CFR 175.105, 177.181
	Component of polymers in paper in contact with dry food	Yes	21 CFR 176.180
	Residual styrene monomer limit in polystyrene intended for use in contact with food	1% by weight	21 CFR 177.1640
Guidelines:			
a. Air:			
ACGIH	TLV TWA	50 ppm (215 mg/m^3)	ACGIH 1988
	STEL	100 ppm (425 mg/m^3)	
NIOSH	IDLH	5,000 ppm	NIOSH 1985
	TWA (10 hr)	50 ppm	
	Ceiling (15 min)	100 ppm	
b. Water:			
EPA ODW	Health Advisories		EPA 1987a
	One-day (child)	22.5 mg/L	
	Ten-day (child)	2 mg/L	
	Longer-term (child)	2 mg/L	
	(adult)	7 mg/L	
	Lifetime	0.14 mg/L	

7. REGULATIONS AND ADVISORIES

TABLE 7-1 (Continued)

Agency	Description	Information	References
c. Other:			
EPA	Carcinogenic Classification (under review by EPA)	Group B2/C[c]	EPA 1989b
	Cancer slope factor	0.03 $(mg/kg/day)^{-1}$	EPA 1988b
	RfD (oral)	0.2 mg/kg/day	IRIS 1989
STATE			
Regulations and Guidelines:			
a. Air:	Acceptable ambient air concentrations		NATICH 1989
Connecticut		4.30 mg/m^3 (8 hr)	
Indiana		3.45 $\mu g/m^3$ (annual)	
Indiana (Indianapolis)		2.17 mg/m^3 (8 hr)	
Kansas		1.75 $\mu g/m^3$ (annual)	
Kansas (Kansas City)		3.45 $\mu g/m^3$ (annual)	
Massachusetts		115.81 $\mu g/m^3$ (24 hr)	
		1.75 $\mu g/m^3$ (allowable ambient level)	
Nevada		5.12 mg/m^3 (8 hr)	
New York		0.716 mg/m^3 (1 yr)	
North Carolina		42.5 mg/m^3 (15 min)	
		1.30 mg/m^3 (24 hr)	
North Carolina (Forsyth County)		1.34 mg/m^3 (24 hr)	
		42.5 mg/m^3 (15 min)	
North Dakota		2.15 mg/m^3 (8 hr)	
		4.25 mg/m^3 (1 hr)	
Rhode Island		30.0 $\mu g/m^3$ (annual)	
Vermont		0.512 mg/m^3 (annual)	
Virginia		3.60 mg/m^3 (24 hr)	
b. Water:	Drinking water quality standards		FSTRAC 1988
Arizona		140 $\mu g/L$	
Maine		270 $\mu g/L$	
Minnesota		140 $\mu g/L$	
Massachusetts		0.005 mg/L (guideline)	ORS 1989
Wisconsin		10 $\mu g/L$	

[a]Group 2B: possible human carcinogen.
[b]EPA proposed an MCLG and an MCL of 0.1 mg/L based on a Group C carcinogen classification and an MCLG of zero and an MCL of 0.005 mg/L based on a Group B2 carcinogen classification.
[c]Group B2: probable human carcinogen; Group C: Possibly carcinogenic to humans.

ACGIH = American Conference of Governmental Industrial Hygienists; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; IARC = International Agency for Research on Cancer; IDLH = Immediately Dangerous to Life or Health Level; MCL = Maximum Contaminant Level; MCLG = Maximum Contaminant Level Goal; NIOSH = National Institute for Occupational Safety and Health; NPDES = National Pollutant Discharge Elimination System; ODW = Office of Drinking Water; OERR = Office of Emergency and Remedial Response; OSHA = Occupational Safety and Health Administration; OSW = Office of Solid Wastes; OTS = Office of Toxic Substances; OWRS = Office of Water Regulations and Standards; PEL = Permissible Exposure Limit; RfD = Reference Dose; STEL = Short Term Exposure Limit; TLV = Threshold Limit Value; TWA = Time-Weighted Average

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9. GLOSSARY

Acute Exposure -- Exposure to a chemical for a duration of 14 days or less, as specified in the Toxicological Profiles.

Adsorption Coefficient (K_{oc}) -- The ratio of the amount of a chemical adsorbed per unit weight of organic carbon in the soil or sediment to the concentration of the chemical in solution at equilibrium.

Adsorption Ratio (K_d) -- The amount of a chemical adsorbed by a sediment or soil (i.e., the solid phase) divided by the amount of chemical in the solution phase, which is in equilibrium with the solid phase, at a fixed solid/solution ratio. It is generally expressed in micrograms of chemical sorbed per gram of soil or sediment.

Bioconcentration Factor (BCF) -- The quotient of the concentration of a chemical in aquatic organisms at a specific time or during a discrete time period of exposure divided by the concentration in the surrounding water at the same time or during the same period.

Cancer Effect Level (CEL) -- The lowest dose of chemical in a study, or group of studies, that produces significant increases in the incidence of cancer (or tumors) between the exposed population and its appropriate control.

Carcinogen -- A chemical capable of inducing cancer.

Ceiling Value -- A concentration of a substance that should not be exceeded, even instantaneously.

Chronic Exposure -- Exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

Developmental Toxicity -- The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.

Embryotoxicity and Fetotoxicity -- Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the insult occurred. The terms, as used here, include malformations and variations, altered growth, and in utero death.

EPA Health Advisory -- An estimate of acceptable drinking water levels for a chemical substance based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

Immediately Dangerous to Life or Health (IDLH) -- The maximum environmental concentration of a contaminant from which one could escape within 30 min without any escape-impairing symptoms or irreversible health effects.

9. GLOSSARY

Intermediate Exposure -- Exposure to a chemical for a duration of 15-364 days as specified in the Toxicological Profiles.

Immunologic Toxicity -- The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals.

In Vitro -- Isolated from the living organism and artificially maintained, as in a test tube.

In Vivo -- Occurring within the living organism.

Lethal Concentration$_{(Lo)}$ (LC $_{Lo}$) -- The lowest concentration of a chemical in air which has been reported to have caused death in humans or animals.

Lethal Concentration$_{(50)}$ (LC_{50}) -- A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

Lethal Dose $_{(Lo)}$ (LD $_{Lo}$) -- The lowest dose of a chemical introduced by a route other than inhalation that is expected to have caused death in humans or animals.

Lethal Dose $_{(50)}$ (LD_{50}) -- The dose of a chemical which has been calculated to cause death in 50% of a defined experimental animal population.

Lethal Time $_{(50)}$ (LT_{50}) -- A calculated period of time within which a specific concentration of a chemical is expected to cause death in 50% of a defined experimental animal population.

Lowest-Observed-Adverse-Effect Level (LOAEL) -- The lowest dose of chemical in a study or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Malformations -- Permanent structural changes that may adversely affect survival, development, or function.

Minimal Risk Level -- An estimate of daily human exposure to a chemical that is likely to be without an appreciable risk of deleterious effects (noncancerous) over a specified duration of exposure.

Mutagen -- A substance that causes mutations. A mutation is a change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

Neurotoxicity -- The occurrence of adverse effects on the nervous system following exposure to chemical.

No-Observed-Adverse-Effect Level (NOAEL) -- The dose of chemical at which there were no statistically or biologically significant increases in frequency

or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

Octanol-Water Partition Coefficient (K_{ow}) -- The equilibrium ratio of the concentrations of a chemical in n-octanol and water, in dilute solution. Permissible Exposure Limit (PEL) -- An allowable exposure level in workplace air averaged over an 8-hour shift.

q_1* -- The upper-bound estimate of the low-dose slope of the dose-response curve as determined by the multistage procedure. The q,* can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually µg/L for water, mg/kg/day for food, and µg/m^3 for air).

Reference Dose (RfD) -- An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the NOAEL (from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used *to* estimate RfDs and an additional modifying factor, which is based on a professional judgment of the entire database on the chemical. The RfDs are not applicable to nonthreshold effects such as cancer.

Reportable Quantity (RQ) -- The quantity of a hazardous substance that is considered reportable under CERCLA. Reportable quantities are: (1) 1 lb or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Sect. 311 of the Clean Water Act. Quantities are measured over a 24-hour period.

Reproductive Toxicity -- The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

Short-Term Exposure Limit (STEL) -- The maximum concentration to which workers can be exposed for up to 15 min continually. No more than four excursions are allowed per day, and there must be at least 60 min between exposure periods. The daily TLV-TWA may not be exceeded.

Target Organ Toxicity -- This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

9. GLOSSARY

Teratogen -- A chemical that causes structural defects that affect the development of an organism.

Threshold Limit Value (TLV) -- A concentration of a substance to which most workers can be exposed without adverse effect. The TLV may be expressed as a TWA, as a STEL, or as a CL.

Time-weighted Average (TWA) -- An allowable exposure concentration averaged over a normal 8-hour workday or 40-hour workweek.

Toxic Dose (TD_{50}) -- A calculated dose of a chemical, introduced by a route other than inhalation, which is expected to cause a specific toxic effect in 50% of a defined experimental animal population.

Uncertainty Factor (UF) -- A factor used in operationally deriving the RfD from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of human, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using LOAEL data rather than NOAEL data. Usually each of these factors is set equal to 10.

APPENDIX A

USER'S GUIDE

Chapter 1

Public Health Statement .

This chapter of the profile is a health effects summary written in nontechnical language. Its intended audience is the general public especially people living in the vicinity of a hazardous waste site or substance release. If the Public 'Health Statement were removed from the rest of the document, it would still communicate to the lay public essential information about the substance. The major headings in the Public Health Statement are useful to find specific topics of concern. The topics are written in a question and answer format. The answer to each question includes a sentence that will direct the reader to chapters in the profile that will provide more information on the given topic.

Chapter 2

Tables and Figures for Levels of Significant Exposure (LSE)

Tables (2-1, 2-2, and 2-3) and figures (2-1 and 2-2) are used to summarize health effects by duration of exposure and endpoint and to illustrate graphically levels of exposure associated with those effects. All entries in these tables and figures represent studies that provide reliable, quantitative estimates of No-Observed-Adverse-Effect Levels (NOAELs), Lowest-Observed- Adverse-Effect Levels (LOAELs) for Less Serious and Serious health effects, or Cancer Effect Levels (CELs). In addition, these tables and figures illustrate differences in response by species, Minimal Risk Levels (MRLs) to humans for noncancer end points, and EPA's estimated range associated with an upper-bound individual lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. The LSE tables and figures can be used for a quick review of the health effects and to locate data for a specific exposure scenario. The LSE tables and figures should always be used in conjunction with the text.

The legends presented below demonstrate the application of these *tables* and figures. A representative example of LSE Table 2-1 and Figure 2-1 are shown. The numbers in the left column of the legends correspond to the numbers in the example table and figure.

LEGEND

See LSE Table 2-1

(1) Route of Exposure One of the first considerations when reviewing the toxicity of a substance using these tables and figures should be the relevant and appropriate route of exposure. When sufficient data exist,

three LSE tables and two LSE figures are presented in the document. The three LSE tables present data on the three principal routes of exposure, i.e., inhalation, oral, and dermal (LSE Table 2-1, 2-2, and 2-3, respectively). LSE figures are limited to the inhalation (LSE Figure 2-1) and oral (LSE Figure 2-2) routes.

(2) Exposure Duration Three exposure periods: acute (14 days or less); intermediate (15 to 364 days); and chronic (365 days or more) are presented within each route of exposure. In this example, an inhalation study of intermediate duration exposure is reported.

(3). Health Effect the major categories of health effects included in LSE tables and figures are death, systemic, immunological, neurological, developmental, reproductive, and cancer. NOAEL's and LOAELs can be reported in the tables and figures for all effects but cancer. Systemic effects are further defined in the "System" column of the LSE table.

(4). Key to Figure Each key number in the LSE table links study information to one or more data points using the same key number in the corresponding LSE figure. In this example, the study represented by key number 18 has been used to define a NOAEL and a Less Serious LOAEL (also see the two "18r" data points in Figure 2-1).

(5). Species The test species, whether animal or human, are identified in this column.

(6). Exposure Frequency / Duration The duration of the study and the weekly and daily exposure regimen are provided in this column. This permits comparison of NOAELs and LOAELs from different studies. In this case (key number 18), rats were exposed to [substance x] via inhalation for 13 weeks, 5 days per week, for 6 hours per day.

(7). System This column further defines the systemic effects. These systems include: respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, and dermal/ocular. "Other" refers to any systemic effect (e.g., a decrease in body weight) not covered in these systems. In the example of key number 18, one systemic effect (respiratory) was investigated in this study.

(8). NOAEL A No-Observed-Adverse-Effect Level (NOAEL) is the highest exposure level at which no harmful effects were seen in the organ system studied. Key number 18 reports a NOAEL of 3 ppm for the respiratory system which was used to derive an intermediate exposure, inhalation MRL of 0.005 ppm (see footnote "c").

(9) LOAEL A Lowest-Observed-Adverse-Effect Level (LOAEL) is the lowest exposure level used in the study that caused a harmful health effect. LOAELs have been classified into "Less Serious" and "Serious" effects. These distinctions help readers identify the levels of exposure at which adverse health effects first appear and the gradation of effects with increasing dose. A brief description of the specific end point used to

quantify the adverse effect accompanies the LOAEL. The "Less Serious" respiratory effect reported in key number 18 (hyperplasia) occurred at a LOEL of 10 ppm.

(10) Reference The complete reference citation is given in Chapter 8 of the profile.

(11) CEL A Cancer Effect Level (CEL) is the lowest exposure level associated with the onset of carcinogenesis. In experimental or epidemiological studies. CELs are always considered serious effects. The LSE tables and figures do not contain NOAELs for cancer, but the text may report doses which did not cause a measurable increase in cancer.

(12) Footnotes Explanations of abbreviations or reference notes for data in the LSE tables are found in the footnotes. Footnote "c" indicates the NOAEL of 3 ppm in key number 18 was used to derive an MRL of 0.005 ppm.

LEGEND

See LSE Figure 2-1

LSE figures graphically illustrate the data presented in the corresponding LSE tables. Figures help the reader quickly compare health effects according to exposure levels for particular exposure duration.

(13) Exposure Duration the same exposure periods appear as in the LSE table. In this example, health effects observed within the intermediate and chronic exposure periods are illustrated.

(14) Health Effect these are the categories of health effects for which reliable quantitative data exist. The same health effects appear in the LSE table.

(15) Levels of Exposure Exposure levels for each health effect in the LSE tables are graphically displayed in the LSE figures. Exposure levels are reported on the log scale "y" axis. Inhalation exposure is reported in mg/m^3 or ppm and oral exposure is reported in mg/kg/day.

(16) NOAEL In this example, 18r NOAEL is the critical end point for which an intermediate inhalation exposure MRL is based. As you can see from the LSE figure key, the open-circle symbol indicates a NOAEL for the test species (rat). The key number 18 corresponds to the entry in the LSE table. The dashed descending arrow indicates the extrapolation from the exposure level of 3 ppm (see entry 18 in the Table) to the MRL of 0.005 ppm (see footnote "b" in the LSE table).

(17) CEL Key number 38r is one of three studies for which Cancer Effect Levels (CELs) were derived. The diamond symbol refers to a CEL for the test species (rat). The number 38 corresponds to the entry in the LSE table.

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(18). Estimated Upper-Bound Human Cancer Risk Levels This is the range associated with the upper-bound for lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. These risk levels are derived from EPA's Human Health Assessment Group's upper-bound estimates of the slope of the cancer dose response curve at low dose levels (q_1*).

(19). Key to LSE Figure The Key explains the abbreviations and symbols used in the figure.

SAMPLE

1 → TABLE 2-1. Levels of Significant Exposure to [Chemical x] - Inhalation

Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect) Less serious (ppm)	LOAEL (effect) Serious (ppm)	Reference
2 → INTERMEDIATE EXPOSURE							
3 → Systemic	5	6	7	8	9		10
4 → 18	Rat	13 wk 5d/wk 6hr/d	Resp	3[b]	10 (hyperplasia)		Nitschke et al. 1981
CHRONIC EXPOSURE							
Cancer						11	
38	Rat	18 mo 5d/wk 7hr/d				20 (CEL, multiple organs)	Wong et al. 1982
39	Rat	89-104 wk 5d/wk 6hr/d				10 (CEL, lung tumors, nasal tumors)	NTP 1982
40	Mouse	79-103 wk 5d/wk 6hr/d				10 (CEL, lung tumors, hemangiosarcomas)	NTP 1982

[a] The number corresponds to entries in Figure 2-1.

12 → [b] Used to derive an intermediate inhalation Minimal Risk Level (MRL) of 5×10^{-3} ppm; dose adjusted for intermittent exposure and divided by an uncertainty factor of 100 (10 for extrapolation from animal to humans, 10 for human variability).

CEL = cancer effect level; d = day(s); hr = hour(s); LOAEL = lowest-observed-adverse-effect level; mo = month(s); NOAEL = no-observed-adverse-effect level; Resp = respiratory; wk = week(s)

SAMPLE

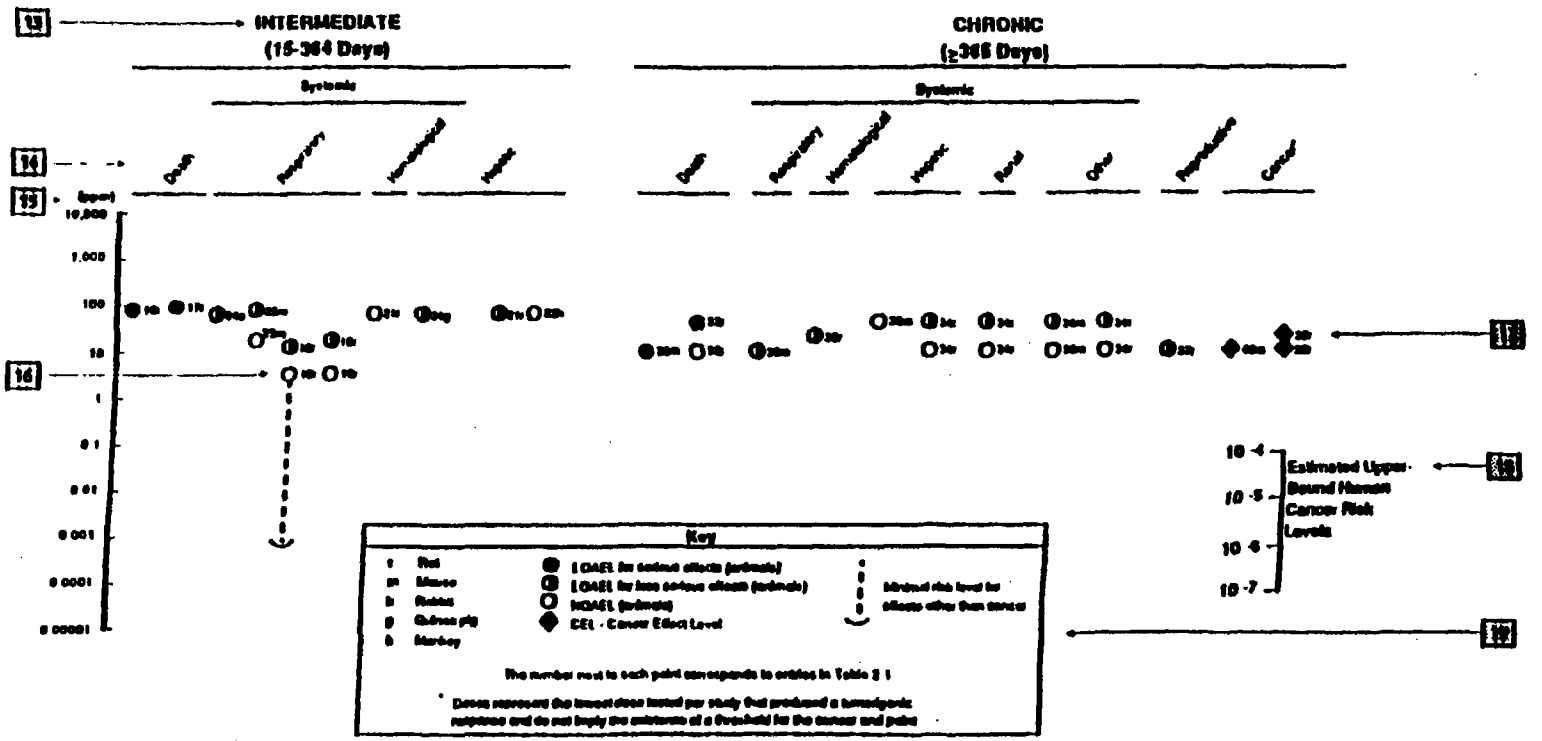

FIGURE 2-1. Levels of Significant Exposure to [Chemical X]-Inhalation

APPENDIX A

Chapter 2 (Section2.4)

Relevance to Public Health

The Relevance to Public Health section provides a health effects summary based on evaluations of existing toxicological, epidemiological, and toxicokinetic information. This summary is designed to present interpretive, weight-of-evidence discussions for human health end points by addressing the following questions.

1. What effects are known to occur in humans?

2. What effects observed in animals are likely to be of concern to humans?

3. What exposure conditions are likely to be of concern to humans, especially around hazardous waste sites?

The section discusses health effects by end point. Human data are presented first, then animal data. Both are organized by route of exposure (inhalation, oral, and dermal) and by duration (acute, intermediate, and chronic). In vitro data and data from parenteral routes (intramuscular, intravenous, subcutaneous, etc.) are also considered in this section. If data are located in the scientific literature, a table of genotoxicity information is included.

The carcinogenic potential of the profiled substance is qualitatively evaluated, when appropriate, using existing toxicokinetic, genotoxic, and carcinogenic data. ATSDR does not currently assess cancer potency or perform cancer risk assessments. MRLs for noncancer end points if derived, and the end points from which they were derived are indicated and discussed in the appropriate section(s).

Limitations to existing scientific literature that prevent a satisfactory evaluation of the relevance to public health are identified in the Identification of Data Needs section.

Interpretation of Minimal Risk Levels

Where sufficient toxicologic information was available, MRLs were derived. MRLs are specific for route (inhalation or oral) and duration (acute, intermediate, or chronic) of exposure. Ideally, MRLs can be derived from all six exposure scenarios (e.g., Inhalation - acute, -intermediate, -chronic; Oral - acute, - intermediate, - chronic). These MRLs are not meant to support regulatory action, but to aquaint health professionals with exposure levels at which adverse health effects are not expected to occur in humans. They should help physicians and public health officials determine the safety of a community living near a substance emission, given the concentration of a contaminant in air or the estimated daily dose received via food or water. MRLs are based largely on toxicological studies in animals and on reports of human occupational exposure.

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MRL users should be familiar with the toxicological information on which the number is based. Section 2.4, "Relevance to Public Health," contains basic information known about the substance. Other sections such as 2.6, "Interactions with Other Chemicals" and 2.7, "Populations that are Unusually Susceptible" provide important supplemental information.

MRL users should also understand the MRL derivation methodology. MRLs are derived using a modified version of the risk assessment methodology used by the Environmental Protection Agency (EPA) (Barnes and Dourson, 1988; EPA 1989a) to derive reference doses (RfDs) for lifetime exposure.

To derive an MRL, ATSDR generally selects the end point which, in its best judgement, represents the most sensitive humanhealth effect for a given exposure route and duration. ATSDR cannot make this judgement or derive an MRL unless information (quantitative or qualitative) is available for all potential effects (e.g., systemic, neurological, and developmental). In order to compare NOAELs and LOAELs for specific end points, all inhalation exposure levels are adjusted for 24hr exposures and all intermittent exposures for inhalation and oral routes of intermediate and chronic duration are adjusted for continous exposure (i.e., 7 days/week). If the information and reliable quantitative data on the chosen end point are available, ATSDR derives an MRL using the most sensitive species (when information from multiple species is available) with the highest NOAEL that does not exceed any adverse effect levels. The NOAEL is the most suitable end point for deriving an MRL. When a NOAEL is not available, a Less Serious LOAEL can be used to derive an MRL, and an uncertainty factor (UF) of 10 is employed. MRLs are not derived from Serious LOAELs. Additional uncertainty factors of 10 each are used for human variability to protect sensitive subpopulations (people who are most susceptible to the health effects caused by the substance) and for interspecies variability (extrapolation from animals to humans). In deriving an MRL, these individual uncertainty factors are multiplied together. The product is then divided into the adjusted inhalation concentration or oral dosage selected from the study. Uncertainty factors used in developing a substance-specific MRL are provided in the footnotes of the LSE Tables.

APPENDIX B

ACRONYMS, ABBREVIATIONS, AND SYMBOLS USED IN TEXT

ACGIH	American Conference of Governmental Industrial Hygienists
ADME	Absorption, Distribution, Metabolism, and Excretion
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
BSC	Board of Scientific Counselors
CDC	Centers for Disease Control
CEL	Cancer Effect Level
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
CLP	Contract Laboratory Program
cm	centimeter
CNS	central nervous system
DHEW	Department of Health, Education, and Welfare
DHHS	Department of Health and Human Services
DOL	Department of Labor
ECG	electrocardiogram
EEG	electroencephalogram
EPA	Environmental Protection Agency
EKG	see ECG
FAO	Food and Agricultural Organization of the United Nations
FEMA	Federal Emergency Management Agency
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
f_1	first generation
fpm	feet per minute
ft	foot
FR	Federal Register
g	gram
GC	gas chromatography
HPLC	high performance liquid chromatography
hr	hour
IDLH	Immediately Dangerous to Life and Health
IARC	International Agency for Research on Cancer
ILO	International Labor Organization
in	inch
Kd	adsorption ratio
kg	kilogram
Koc	octanol-soil partition coefficient
Kow	octanol-water partition coefficient
L	liter
LC	liquid chromatography
LC_{Lo}	lethal concentration low
LC_{50}	lethal concentration 50 percent kill
LD_{Lo}	lethal dose low
LD_{50}	lethal dose 50 percent kill
LOAEL	lowest-observed-adverse-effect level
LSE	Levels of Significant Exposure
m	meter
MA	Mandelic acid

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mg	milligram
min	minute
mL	milliliter
mm	millimeters
mmol	millimole
mppcf	millions of particles per cubic foot
MRL	Minimal Risk Level
MS	mass spectroscopy
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute for Occupational Safety and Health
NIOSHTIC	NIOSH's Computerized Information Retrieval System
nm	nanometer
ng	nanogram
NHANES	National Health and Nutrition Examination Survey
nmol	nanomole
NOAEL	no-observed-adverse-effect level
NOES	National Occupational Exposure Survey
NOHS	National Occupational Hazard Survey
NPL	National Priorities List
NRC	National Research Council
NTIS	National Technical Information Service
NTP	National Toxicology Program
OSHA	Occupational Safety and Health Administration
PEL	permissible exposure limit
pg	picogram
PGA	Phenylglyoxlic acid
pmol	picomole
PHS	Public Health Service
PMR	proportional mortality ratio
ppb	parts per billion
ppm	parts per million
ppt	parts per trillion
REL	recommended exposure limit
RfD	Reference Dose
RTECS	Registry of Toxic Effects of Chemical Substances
sec	second
SCE	sister chromatid exchange
SIC	Standard Industrial Classification
SMR	standard mortality ratio
STEL	short-term exposure limit
STORET	STORAGE and RETRIEVAL
TLV	threshold limit value
TSCA	Toxic Substances Control Act
TRI	Toxic Release Inventory
TWA	time-weighted average
U.S.	United States
UF	uncertainty factor
WHO	World Health Organization
>	greater than

APPENDIX B

$\geq$	greater than or equal to
$=$	equal to
$<$	less than
$\leq$	less than or equal to
%	percent
α	alpha
β	beta
δ	delta
γ	gamma
μm	micron
μg	microgram

APPENDIX C

PEER REVIEW

A peer review panel was assembled for styrene. The panel consisted of the following members: Dr. Arthur Gregory, private consultant, Washington, DC; Dr. James Withey, Research Scientist, Environmental Health Center, Ottawa, Ontario, Canada; and Dr. Carroll Snyder, Research Professor/Director, Laboratory of Inhalation Carcinogenesis and Toxicology, New York University, New York, NY. These experts collectively have knowledge of styrene's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. A second panel of reviewers was assembled to review the sections on mitigation of effects. This panel consisted of: Dr. Brent Burton, Medical Director, Oregon Poison Center, Oregon Health Sciences University, Portland, Oregon; Dr. Alan Hall, Private Consultant, Evergreen, Colorado; and Dr. Alan Woolf, Director of Clinical Pharmacology and Toxicology, Massachusetts Poison Control System, The Children's Hospital, Boston, Massachusetts. All reviewers were selected in conformity with the conditions for peer review specified in Section 104(i)(13) of the Comprehensive Environmental Response, Compensation, and Liability Act, as amended.

Scientists from the Agency for Toxic Substances and Disease Registry (ATSDR) have reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply its approval of the profile's final content. The responsibility for the content of this profile lies with the ATSDR.

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TOXICITY SUMMARY
FOR
TOLUENE

January 1994

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Prepared for

OAK RIDGE RESERVATION ENVIRONMENTAL
RESTORATION PROGRAM

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EXECUTIVE SUMMARY

Toluene is a colorless liquid widely used as raw material in the production of organic compounds and as a solvent (EPA, 1990). It is readily absorbed from the gastrointestinal and respiratory tracts and, to a lesser degree, through the skin. Toluene is distributed throughout the body, with accumulation in tissues with high lipid content. It is metabolized in the liver, primarily to hippuric acid and benzoyl glucuronide, compounds that are rapidly excreted in the urine (EPA, 1990; ATSDR, 1989).

In humans and animals, the primary effect associated with inhalation exposure to toluene is central nervous system (CNS) depression. Short-term exposure of humans to 100–1500 ppm has elicited CNS effects such as fatigue, confusion, incoordination, and impairments in reaction time, perception, and motor control and function (NTP, 1990). Exposure to concentrations ranging from 10,000–30,000 ppm has resulted in narcosis and deaths (WHO, 1985). Prolonged abuse of toluene or solvent mixtures containing toluene has led to permanent CNS effects. Exposure to high concentrations of toluene (1500 ppm) has produced hearing loss in rats (Pryor et al., 1984). Hepatomegaly and impaired liver and kidney function have been reported in some humans chronically exposed to toluene (Askergren, 1984; Szilard et al., 1978; Greenburg et al., 1942). Toluene vapors may cause eye irritation (Andersen et al., 1983), and prolonged or repeated dermal contact may produce drying of skin and dermatitis (ATSDR, 1989; NIOSH, 1973).

In experimental animals, subchronic inhalation exposure to $\geq$ 2500 ppm toluene resulted in increased liver and kidney weights (rats and mice), increased heart weights (rats), increased lung weights, and centrilobular hypertrophy of the liver (mice) (NTP, 1990). Chronic inhalation exposure to 600 or 1200 ppm for 2 years produced degeneration of olfactory and respiratory epithelia of rats and minimal hyperplasia of bronchial epithelia in mice (NTP, 1990).
Subchronic oral administration of toluene at doses ranging from 312 to 5000 mg/kg/day produced clinical signs of neurotoxicity at $\geq$ 2500 mg/kg in rats and mice. Other effects observed at higher doses in rats included increased relative liver, kidney, and heart weights (females only) and necrosis of the brain and hemorrhage of the urinary bladder (NTP, 1990).

Equivocal evidence shows that exposure to toluene in utero causes an increased risk of CNS abnormalities and developmental delay in humans (Goodwin, 1988; Hersh et al., 1985; Holmberg, 1979). Animal studies, in which toluene was administered by inhalation, showed that exposure results in fetotoxicity and delayed skeletal development but does not cause internal or external malformations in rats (Courtney et al., 1986; Litton Bionetics, 1978). An oral study noted an increased incidence of embryonic deaths, cleft palate, and maternal toxicity in mice administered 1 mL/kg toluene during gestation (Nawrot and Staples, 1979).

An oral reference dose (RfD) of 2 mg/kg/day for subchronic exposure (EPA, 1993) and 0.2 mg/kg/day for chronic exposure (EPA, 1992) to toluene was calculated based on a no-observed-adverse-effect level (NOAEL) of 223 mg/kg/day and a lowest-observed-adverse-effect level (LOAEL) of 446 mg/kg/day from a 13-week subchronic gavage study in rats (NTP, 1990). Increased liver and kidney weights in males were identified as the critical effects. A subchronic (EPA, 1993) and chronic inhalation reference concentration (RfC) of 0.4 mg/m^3 (EPA, 1992) was calculated based on results of a battery of neurological tests with occupationally exposed female subjects (Foo et al., 1990).

An increased incidence of hemolymphoreticular neoplasms was reported in rats exposed to 500

mg/kg of toluene by gavage for 2 years (Maltoni et al., 1985); however, results from two long-term inhalation studies (NTP, 1990; Gibson and Hardisty, 1983) indicate that toluene is not carcinogenic at concentrations up to 1200 ppm. Based on U.S. Environmental Protection Agency (EPA) guidelines, toluene was assigned to weight-of-evidence group D, not classifiable as to human carcinogenicity (EPA, 1992).

1. INTRODUCTION

Toluene ($C_6H_5CH_3$; CAS No. 108-88-3), also known as methylbenzene and phenylmethane, is a colorless liquid with a sweet pungent odor (HSDB, 1992). It has a molecular weight of 92.15, a density of 0.8669 g/mL at 20°C, and an octanol/water partition coefficient of 2.79 (Lide, 1991; Mabey et al., 1982). Toluene is isolated by distillation of reformed or pyrolized petroleum and coal tar; however, most of the toluene produced remains as a benzene-toluene-xylene (BTX) mixture for use in gasoline. The primary use of isolated toluene is in the production of benzene and for backblending into gasoline to increase octane ratings (EPA, 1990). Toluene is also used as raw material in the production of benzyl chloride, benzoic acid, phenol, cresols, vinyl toluene, TNT, and toluene diisocyanate (U.S. Air Force, 1989); as a solvent for paints and coatings; and in adhesives, inks, and pharmaceuticals (EPA, 1990).

Inhalation is the primary route of toluene exposure for the general population and for occupationally exposed individuals. Evaporation of gasoline and automobile exhaust is the largest source of toluene in the environment, and industries that use toluene as a solvent are the second largest source (EPA, 1984). Toluene is also a common indoor contaminant due to releases from common household products and from cigarette smoke (ATSDR, 1989). Nonatmospheric releases of toluene are relatively small (e.g., to water and soil) and are estimated to comprise less than 1% of total toluene releases (ATSDR, 1989). In the atmosphere, toluene is degraded by reaction with hydroxyl radicals, with a typical half-life of about 13 hours. It is highly volatile, and volatilization is likely to be the predominant removal process from soil and water. Toluene is also subject to microbial degradation. Because of volatilization and biodegradation, toluene levels in the environment are not expected to increase over time (EPA, 1990; ATSDR, 1989).

2. METABOLISM AND DISPOSITION

2.1 ABSORPTION

Toluene is readily absorbed from the respiratory and gastrointestinal tracts and, to a lesser extent, through the skin. Animal studies suggest that absorption from the gastrointestinal tract is complete. Absorption data for humans and animals indicate that pulmonary absorption is 85–90% during brief exposures but nearer to 50% during extended exposures (< 1 hour). In humans, toluene has been detected in the arterial blood within 10 seconds after initiation of inhalation exposures; exercise greatly increases the absorption of toluene (EPA, 1990). Cutaneous absorption is approximately 1% of that absorbed by the lungs when there is exposure to the vapor; however, dermal absorption of the liquid may be higher. Because toluene evaporates readily, it is unlikely that significant absorption will occur by this route.

2.2 DISTRIBUTION

Distribution of toluene following absorption occurs throughout the body, with accumulation in adipose tissue, other tissues with high fat content, and highly vascular tissues. High levels of toluene were found in the brain and liver of an individual who had died following an episode of glue sniffing (Paterson and Sarvesvaran, 1983). Autoradiography studies using mice indicate that

immediately after inhalation exposure, a high level of radioactivity is present in the body fat, bone marrow, spinal nerves, spinal cord, and white matter of the brain. Radioactivity was also observed in the blood, kidney, and liver but at lower levels (Bergman, 1979). In one individual who died 30 minutes after ingestion of toluene, the liver had the highest concentration of toluene, followed by the pancreas, brain, heart, blood, body fat, and cerebrospinal fluid (Ameno et al., 1989). Since retention time of toluene is usually considered to be less than 24 hours, bioaccumulation of toluene is unlikely (EPA, 1990).

2.3 METABOLISM

The initial step in toluene metabolism is side-chain hydroxylation to benzyl alcohol by P-450 enzymes in the liver, followed by oxidation to benzaldehyde by alcohol dehydrogenase and subsequently to benzoic acid by aldehyde dehydrogenase. Benzoic acid is then conjugated with glycine to form hippuric acid, the major urinary metabolite. Benzoic acid can also react with glucuronic acid to form benzoyl glucuronide (ATSDR, 1989). Ring hydroxylation to *o*- and *p*-cresol is considered a minor metabolic pathway (EPA, 1990).

2.4 EXCRETION

Toluene excretion in humans and animals is dose-dependent and clearance from the body is rapid. Toluene is primarily excreted in the urine as the metabolite, hippuric acid, which accounts for 60–70% of absorbed toluene. Excretion of hippuric acid is usually complete within 24 hours after exposure. The glucuronide conjugate of benzoic acid excreted in the urine represents 10–20% of absorbed toluene. Elimination of unchanged toluene by the lungs and possibly by the skin may also account for 10–20% of the absorbed dose (EPA, 1990).

3. NONCARCINOGENIC HEALTH EFFECTS

3.1 ORAL EXPOSURES

3.1.1 Acute Toxicity

3.1.1.1 Human

Ingestion of approximately 60 mL toluene was fatal to a male mental patient, with death occurring within 30 minutes of ingestion (Ameno et al., 1989). Autopsy results showed constriction and necrosis of myocardial fibers, a markedly swollen liver, congestion and hemorrhage of the lungs, and acute tubular necrosis. Severe depression of CNS function was thought to be the probable cause of death.

3.1.1.2 Animal

The acute oral toxicity of toluene in rats appears to be age-dependent. For adult rats, the reported LD_{50} values range from 5.5 to 7.3 g/kg. For younger adult, 14-day-old, or newborn rats, the LD_{50} values are 5.3–5.9, 2.6, or <1 g/kg, respectively (EPA, 1990).

3.1.2 Subchronic Toxicity

3.1.2.1 Human

Information on the subchronic oral toxicity of toluene in humans was not available.

3.1.2.2 Animal

F344 and Sprague-Dawley rats administered daily doses of 620 mg/kg by gavage for 4 weeks developed hearing loss that was attributed to damage of the outer hair cells of the inner ear (Sullivan, 1986).

Depressed immune responses were reported in mice exposed to toluene in drinking water. Male mice administered doses of 105 mg/kg/day of toluene for 28 days had decreased thymus weights, mixed lymphocyte culture responses, and antibody plaque-forming cell responses (Hsieh et al., 1989). Mitogen-stimulated lymphocyte proliferation and interleukin-2 immunity were decreased at doses of 22 and 105 mg/kg/day. Other effects included increased levels of neurotransmitters in the brain at doses of 5, 22, or 105 mg/kg/day and increased liver weights at 105 mg/kg/day.

In an National Toxicology Program (NTP) study (1990), F344/N rats and B6C3F$_1$ mice of both sexes were administered toluene in corn oil by gavage at doses of 0, 312, 625, 1250, 2500, or 5000 mg/kg, 5 days/week for 13 weeks. All rats receiving 5000 mg/kg died within the first week, all mice receiving 5000 mg/kg died, and 40% of mice receiving 2500 mg/kg also died. Rats exposed to doses $\geq$ 2500 mg/kg of toluene exhibited prostration, hypoactivity, ataxia, piloerection, lacrimation, excess salivation, and body tremors. In male rats, absolute and relative liver and kidney weights were significantly ($p < 0.05$) increased at doses $\geq$ 625 mg/kg. In females, absolute and relative liver, kidney, and heart weights were all significantly increased at doses $\geq$ 1250 mg/kg ($p < 0.01$ for all comparisons except $p < 0.05$ for absolute kidney and heart weights at 1250 mg/kg). Histopathologic lesions were seen in the liver, kidneys, brain, and urinary bladder of rats. Hepatocellular hypertrophy occurred at $\geq$ 2500 mg/kg. Nephrosis was observed in rats that died, and damage to the tubular epithelium of the kidney occurred in terminally sacrificed rats. In the brain, mineralized foci and necrosis of neuronal cells were observed in male and female rats at 5000 mg/kg and males at 2500 mg/kg. Hemorrhage of the bladder (mucosa and muscularis) was seen in male and female rats at 5000 mg/kg and males at 2500 mg/kg. Signs of toxicity seen in mice receiving $\geq$ 2500 mg/kg included subconvulsive jerking, prostration, impaired grasping reflex, bradypnea, hypothermia, ataxia, and hypoactivity. By week 13, the mean body weight of males given 2500 mg/kg was significantly ($p < 0.05$) lower than that of controls. No adverse effects were reported in rats exposed to the lowest dose, 312 mg/kg/day, or in mice exposed to doses < 2500 mg/kg/day.

In an early subchronic gavage study, Wolf et al. (1956) observed no adverse effects in female Wistar rats treated with 0, 118, 354, or 590 mg/kg of toluene in olive oil, 5 days/week for 27–28 weeks (Wolf et al., 1956).

3.1.3 Chronic Toxicity

Information on the chronic oral toxicity of toluene in humans or animals was not available.

3.1.4 Developmental and Reproductive Toxicity

3.1.4.1 Human

Information on the developmental and reproductive toxicity of toluene in humans following oral exposure was not available.

3.1.4.2 Animal

Oral administration of a single dose of 2350 mg/kg/day of toluene on gestational days 7–14 had no effect on the number of viable litters of mice and single doses of 1800 or 2350 mg/kg/day did not cause developmental effects (Seidenberg et al., 1986; Smith, 1983).

Kostas and Hotchin (1981) exposed female NYLAR mice to 16, 80, or 400 ppm toluene in drinking water beginning at the mating period and continuing throughout gestation and lactation. Upon weaning, the offspring were exposed to the same drinking water solutions until the time of behavioral testing—45–55 days of age. Rotorod performance was affected in all toluene-exposed groups, but there was an inverse dose-relationship. Decreased open-field activity was seen at 400 ppm. Offspring mortality rate, development of eye or ear openings, and surface-righting response of offspring was not affected.

Nawrot and Staples (1979) administered 0.3, 0.5, or 1.0 mL/kg (260, 433, or 867 mg/kg) of toluene in cottonseed oil by gavage 3 times/day on days 6–15 of gestation or 1.0 mL/kg (867 mg/kg) on days 12–15 of gestation to pregnant CD-1 mice. Increased embryonic lethality was reported in all groups treated with toluene on days 6–15 of gestation. Fetal weight was reduced in the mid- and high-dosed groups, and the incidence of cleft palate was increased in high-dosed fetuses. Maternal toxicity (decreased weight gain) was the only effect noted in mice treated on days 12–15 of gestation.

3.1.5 Reference Dose

3.1.5.1 Subchronic

ORAL RfD: 2 mg/kg/day (U.S. EPA, 1993)
NOAEL: 223 mg/kg/day
LOAEL: 446 mg/kg/day
UNCERTAINTY FACTOR: 100

PRINCIPAL STUDY: NTP, 1990

COMMENTS: The same study, described in Subsect. 3.1.2.2, was used for the derivation of the subchronic and chronic RfD. The dose was adjusted for discontinuous exposure (5 days/week). An uncertainty factor of 100 was applied to account for interspecies extrapolation (10) and intraspecies variability (10).

3.1.5.2 Chronic

ORAL RfD: 0.2 mg/kg/day (U.S. EPA, 1992)
NOAEL: 223 mg/kg/day
LOAEL: 446 mg/kg/day
UNCERTAINTY FACTOR: 1000
CONFIDENCE:
Study: High
Data Base: Medium

RfD: Medium

VERIFICATION DATE: 6/20/90

PRINCIPAL STUDY: NTP, 1990

COMMENTS: The RfD is based on a gavage study with rats exposed to toluene for 13 weeks, with increased liver and kidney weights as critical effect. The dose was adjusted for discontinuous exposure (5 days/week). An uncertainty factor of 1000 was applied to account for interspecies extrapolation (10), intraspecies variability (10), and for the use of a subchronic study for chronic RfD derivation (10). Confidence in the data base and RfD is rated medium because the available oral studies are all subchronic and because of a lack of reproductive toxicity studies (EPA, 1992).

3.2 INHALATION EXPOSURES

3.2.1 Acute Toxicity

3.2.1.1 Human

Acute toxicity data of toluene in humans come from experimental exposures, case reports of intentional abuse (glue sniffing), and accidental occupational exposures. The major acute effects of toluene in humans are CNS dysfunction and neurological impairment. Studies reviewed by NTP (1990) showed that individuals developed fatigue, drowsiness, impaired cognitive function, incoordination, and irritation of the eyes and throat after a single exposure to toluene at concentrations ranging from 50 to 1500 ppm for 3–8 hours. These effects increased in severity with increases in concentration and progressed to nausea, staggering gait, confusion, extreme nervousness, muscular fatigue, and insomnia lasting for several days (NTP, 1990). Exposure to concentrations ranging from 10,000 to 30,000 ppm have resulted in narcosis and death (WHO, 1985).

In a controlled exposure study, Andersen et al. (1983) exposed human subjects to 0, 10, 40, or 100 ppm toluene for 6 hours on each of 4 consecutive days. Eye and nose irritation occurred at 100 ppm, without affecting nasal mucous flow or lung function. The subjects frequently reported headaches, dizziness, and a feeling of intoxication. These effects were not reported in the 10- or 40-ppm exposure groups. No effects were seen in performance tests.

3.2.1.2 Animal

LC_{50} values for 6- to 7-hour exposures are 12,200 ppm for rats and 5300–7000 ppm for mice (EPA, 1990). Central nervous system effects are the primary toxic effects following acute inhalation exposure to toluene. The CNS response is biphasic, with an initial excitable phase followed by depression.

Rats exposed to 10,000 to 15,000 ppm toluene for 60 minutes exhibited an initial increase in locomotor activity; however, at continued exposure, locomotor activity decreased and eventually ceased (Hinman, 1987). Rats exposed to 125, 250, or 500 ppm toluene for 4 hours showed a decline in trained neuromuscular responses 20 hours after exposure (Kishi et al., 1988). Exposure of weanling or young rats to 7550 mg/m^3 (~2000 ppm), 8 hours/day for 3 days or to 5660 mg/m^3

(~1500 ppm) for 14 hours resulted in hearing loss (Pryor et al., 1984). Acute exposure of monkeys caused impaired cognitive and motor abilities when exposed to 1000 or 2000 ppm, concentrations that were below those causing overt clinical signs of neurotoxicity such as ataxia and tremors (Taylor and Evans, 1985).

3.2.2 Subchronic Toxicity

3.2.2.1 Human

Echeverria et al. (1989) exposed volunteers to 0, 74, or 151 ppm toluene for 7 hours over 3 days. This exposure sequence was repeated for a total of 42 exposures over a 3-month period. A battery of performance tests showed that visual perception was affected and manual dexterity differed from control values at both exposure levels. However, psychomotor test results were unaffected by toluene exposure. Subjective symptoms such as eye irritation, headache, and somnolence increased with exposure.

Individuals who had abused toluene for at least 1 year reported disturbed behavior; slow thought and speech; illusionary misinterpretations; tactile, auditory, and visual hallucinations; and delusional ideas (Evans and Raistrik, 1987).

3.2.2.2 Animal

Pryor et al. (1984) found irreversible high frequency hearing loss in rats exposed to toluene at concentrations of 1200 ppm, 12 hours/day for 5 weeks. Rats exposed at weaning age exhibited a more pronounced hearing loss than young adult rats.

Ungvary et al. (1980) exposed male and female CFY rats to 1000 mg/m^3 (265 ppm) toluene 6 hours/day, 5 days/week for 6 months. No adverse effects were seen in males; however, females exhibited increased cytochrome P-450 levels, decreased body weights, and increased liver-to-body weight ratios. Exposure to 3500 mg/m^3 (928 ppm) (males only), 8 hours/day, 5 days/week for 6 months produced effects similar to those elicited in females at the lower dose.

In an NTP (1990) study, F344/N rats and B6C3F$_1$ mice were exposed to 0, 100, 652, 1250, 2500, or 3000 ppm toluene 6.5 hours/day, 5 days/week for 15 weeks (rats) or 14 weeks (mice). All female rats survived exposure to 3000 ppm, but 8/10 male rats died within 2 weeks at this exposure level. Decreased body weights and increased relative liver, kidney, and heart weights were seen in rats exposed to the two higher concentrations compared with those of controls. All female mice and 5/10 male mice exposed to 3000 ppm and 7/10 female mice exposed to 2500 ppm died during the first 2 weeks. The body weights of all exposed groups were lower than those of controls. Relative liver weights were increased in mice exposed to $\geq$ 625 ppm. Increased relative lung weights were seen at $\geq$ 1250 ppm and increased relative kidney weights at $\geq$ 1250 ppm (females only). Centrilobular atrophy of the liver occurred in all male mice exposed to 2500 ppm and in 70% of male mice exposed to 3000 ppm.

No effects on the kidneys, lungs, spleen, or heart were observed in rats, guinea pigs, dogs, or monkeys continuously exposed to 107 ppm toluene for 90 days (Jenkins et al., 1970). In addition, no treatment-related effects were observed on the brain and spinal cord of dogs and monkeys, and no significant changes were observed in hematological parameters in any of the species tested.

3.2.3 Chronic Toxicity

3.2.3.1 Human

Occupational exposure studies that have investigated the potential neurotoxicity of toluene have not shown severe neurological effects. Rotogravure printers exposed to an estimated 117 ppm toluene for up to 22 years exhibited no clinically significant adverse effects on the nervous system (Juntunen et al., 1985). Occupational studies by Yin et al. (1987) and Lee et al. (1988) reported subjective symptoms such as headaches, sore throats, and dizziness following exposure to approximately 100 ppm toluene. Foo et al. (1990) conducted a cross-sectional study involving 30 female workers employed at an electronic assembly plant where toluene was emitted from glue. The toluene workers were employed for an average of 5.7 years and exposed to time-weighted-average (TWA) air concentrations of 88 ppm (332 mg/m^3) toluene; a control group was exposed to 13 ppm (49 mg/m^3) (TWA). A battery of eight neurobehavioral tests showed that the exposed group had a poorer performance in 6 of 8 tests administered when compared with the control group.

Cerebellar dysfunction, mental retardation, abnormal encephalograms, brain atrophy, and visual impairment were observed in long-term abusers of pure toluene (6–14 years) (NTP, 1990). Clinical studies of toluene sniffers suggest that ototoxicity as well as vestibular deficits may occur after prolonged inhalation exposure (Winneke, 1992).

Some studies have reported effects on the kidney and liver following inhalation exposure to toluene. Askergren (1984) reported increased protein excretion and increased excretion of erythrocytes and leukocytes/tubular epithelial cells in construction workers exposed to toluene. Renal tubular effects, indicated by metabolic acidosis (hypokalemia, hypophosphatemia, and hyperchloremia), have been associated with abusers of toluene-containing solvents (NTP, 1990). Krusell et al. (1985), however, indicated that there is no causal relationship between toluene exposure alone and renal injury. Hepatomegaly was observed in airplane painters exposed to 100–1150 ppm toluene in air for up to 5 years (Greenburg et al., 1942) and in 20–50% of workers exposed to toluene at 53–80 ppm for 2–14 years (Szilard et al., 1978).

Although early studies (before the mid-1950s) have associated chronic exposure to toluene with myelotoxic effects, most recent studies generally indicate that toluene does not cause toxic effects in blood and bone marrow. The previously observed hematologic effects are now attributed to concurrent exposure to benzene, a common contaminant of toluene at that time (NTP, 1990; ATSDR, 1989).

3.2.3.2 Animal

F344/N rats and $B6C3F_1$ mice were exposed by inhalation to 0, 600, or 1200 ppm toluene 6.5 hours/day, 5 days/week for 15 months or 2 years (NTP, 1990). Mean body weights and survival of rats and mice were generally similar to those seen in controls throughout the 2-year study. All rats exhibited nephropathy, with an increased severity in toluene-exposed animals. At 15 months, goblet cell hyperplasia and degeneration of olfactory and respiratory epithelium were increased in exposed rats. At 2 years, erosion of the olfactory epithelium and degeneration of respiratory epithelium were significantly ($p < 0.05$) increased in males and females at both doses. Mice exposed to 1200 ppm exhibited minimal hyperplasia of the bronchial epithelium. No other biologically important increases in non-neoplastic lesions were seen in exposed mice. The lesions observed in this study were considered mild and are not unusual with solvent exposures.

In an earlier 2-year inhalation bioassay, male and female F344 rats were exposed to 0, 30, 100,

or 300 ppm toluene, 6 hours/day, 5 days/week (Gibson and Hardisty, 1983). Except for a dose-related decrease in hematocrit values in females exposed to 100 and 300 ppm and increased corpuscular hemoglobin concentrations in high-dosed females, all clinical chemistry, hematology, and urinalysis values were normal at the termination of the study. No other adverse effects were observed.

3.2.4 Developmental and Reproductive Toxicity

3.2.4.1 Human

Evidence for human developmental effects from case reports and occupational exposure studies is equivocal because these studies are confounded by exposure to multiple organic solvents during pregnancy. A retrospective study of 14 women exposed to mixed solvents, including toluene, suggested an increased risk of CNS abnormalities and defects of neural tube closure in children exposed in utero (Holmberg, 1979). In another study, microcephaly, CNS dysfunction, attentional deficits, minor craniofacial and limb abnormalities, developmental delay, and variable growth were observed in three children exposed in utero to toluene as a result of maternal solvent abuse (Hersh et al., 1985). A third study reported growth retardation and dysmorphism in five infants whose mothers were chronic paint sniffers (Goodwin, 1988).

3.2.4.2 Animal

Retarded bone ossification and growth inhibition were observed in fetuses of Charles River rats exposed to 400 ppm toluene, 6 hours/day on days 6–15 of gestation (Litton Bionetics, 1978), but no teratogenic effects were observed in the study. No compound-related effects on sperm or adverse effects on estrous cycle were seen in Fischer 344 rats or $B6C3F_1$ mice exposed to toluene at concentrations ranging from 100 to 3000 ppm, 6.5 hours/day, 5 days/week for 15 weeks (rats) or 14 weeks (mice) (NTP, 1990).

Pregnant CD-1 mice, exposed daily to 200 or 400 ppm toluene for 7 hours during gestational days 7–16, showed a significant increase in dilated renal pelves at 200 ppm but not at 400 ppm (Courtney et al., 1986). At 400 ppm, a significant shift in the fetal rib profile was observed. Both exposure concentrations caused maternal toxicity. Hudak and Ungvary (1978) observed decreased body weights but no malformations in fetuses of CFLP mice continuously exposed by inhalation to 133 ppm toluene on days 6–13 of gestation. Retarded skeletal development resulting in poorly ossified sternebrae, split vertebral centra, and shortened free ribs was reported in CFY rats continuously exposed to 230 or 399 ppm toluene on days 1–8 of development (Hudak and Ungvary, 1978). Fetuses of rats exposed to 399 ppm on days 9–14 of gestation exhibited extra ribs and fused sternebrae. No increases in visceral or external malformations were identified in mice or rats.

Deaths, but no teratogenic effects, were observed in fetuses of New Zealand rabbits continuously exposed to 266 ppm toluene on days 6–20 of gestation (Ungvary and Tatrai, 1985).

3.2.5 Reference Concentration

3.2.5.1 Subchronic

INHALATION RfC: 0.4 mg/m^3 (U.S. EPA, 1993)
LOAEL: 332 mg/m^3
UNCERTAINTY FACTOR: 300

PRINCIPAL STUDY: Foo et al., 1990

COMMENTS: The chronic inhalation RfC was adopted as the subchronic inhalation RfC. The study is described in Subsect. 3.2.3.1.

3.2.5.2 Chronic

INHALATION RfC: 0.4 mg/m^3 (U.S. EPA, 1992)
LOAEL: 332 mg/m^3
UNCERTAINTY FACTOR: 300

PRINCIPAL STUDY: Foo et al., 1990

CONFIDENCE:
Study: Medium
Data Base: Medium
RfC: Medium

COMMENTS: The chronic RfC was based on results of a battery of neurological tests in occupationally exposed females. Adverse neurological effects at atmospheric concentrations of 332 mg/m^3 were considered the lowest-observed-adverse-effect level (LOAEL). An uncertainty factor (UF) of 300 was used to account for intraspecies variability (10), for the use of a LOAEL (10), and for data base deficiencies (3). The data base and RfC were given a medium rating because long-term data in humans are not available for neurotoxicity endpoints and the reproductive/developmental studies in animals were not comprehensive.

3.3 OTHER ROUTES OF EXPOSURE

3.3.1 Acute Toxicity

3.3.1.1 Humans

Eye irritation has been reported in humans following exposure to toluene vapors (Andersen et al., 1983). The liquid splashed in the eyes has caused a transient disturbance of the eyes, with healing complete within 48 hours (Grant, 1986).

3.3.2.2 Animals

The LD_{50} value reported for New Zealand rabbits following a single dermal application is 14.1 mL/kg (12.2 g/kg); for Wistar rats, the LD_{50} following an intraperitoneal injection is 1.64 g/kg (EPA, 1990).

Undiluted toluene applied to intact and abraded skin of rabbits for 24 hours produced moderate skin irritation (Guillot et al., 1982). Direct application of toluene to the conjunctiva has resulted in slight to moderately severe irritation of rabbit eyes (ATSDR, 1989).

3.3.2 Subchronic Toxicity

3.3.2.1 Human

Prolonged or repeated skin contact may cause drying and dermatitis due to the degreasing action of toluene and its removal of protective skin oils (ATSDR, 1989; NIOSH, 1973).

3.3.2.1 Animal

Information on the subchronic toxicity of toluene by other routes of exposure in animals was not available.

3.3.3 Chronic Toxicity

Information on the chronic toxicity of toluene by other routes of exposure in humans or animals was not available.

3.3.4 Developmental and Reproductive Toxicity

Information on the developmental or reproductive toxicity of toluene by other routes of exposure in humans or animals was not available.

3.4 TARGET ORGANS/CRITICAL EFFECTS

3.4.1 Oral Exposures

3.4.1.1 Primary Target Organs

1. Central nervous system: Subchronic exposure to toluene caused necrosis and mineralization of brain cells and hearing loss in rats and altered brain levels of neurotransmitters in mice. Pre- and post-natal exposure affected rotorod performance and open-field activity in mice.

2. Kidneys: Subchronic exposure to toluene produced nephrosis, damage to tubular epithelium, and increased kidney weights in rats.

3. Liver: Subchronic exposure to toluene produced increased liver weights in rats and mice and hepatocellular hypertrophy in rats.

4. Reproduction: Embryonic deaths, reduced fetal weights, and cleft palates were observed in mice exposed to toluene during gestation.

3.4.1.2 Other Target Organs

1. Immune system: Depressed immune responses were observed in rats following subchronic exposure to toluene.

2. Urinary bladder: Hemorrhage of the bladder mucosa and muscularis were observed in rats following subchronic exposure to toluene.

3.4.2 Inhalation Exposures

3.4.2.1 Primary Target Organs

1. Central nervous system: Chronic occupational exposure to toluene has resulted in headaches, dizziness, and impaired neurobehavioral performance. Brain dysfunction, abnormal encephalograms, brain atrophy, mental retardation, and visual and hearing impairment have been reported in long-term abusers of toluene. Subchronic exposure of rats produced a high frequency hearing loss.

2. Kidneys: Chronic exposure of workers to toluene has resulted in abnormalities of kidney function. Renal tubular effects have been associated with abuse of toluene-containing solvents. Chronic exposure to toluene has caused nephropathy in rats.

3. Liver: Hepatomegaly has been reported in workers chronically exposed to toluene. Increased liver weights were reported in rats following subchronic exposure to toluene.

4. Respiratory system: Sore throat was one of the symptoms reported in workers chronically exposed to toluene. Chronic exposure of rats has produced lesions in olfactory and respiratory epithelia.

3.4.2.2 Other Target Organs

Reproduction: Equivocal evidence shows that exposure to toluene in utero causes an increased risk of CNS abnormalities and developmental delay in humans. Exposure during gestation has resulted in delayed skeletal maturation in rats and mice.

3.4.3 Other Routes of Exposure

Skin: Repeated or prolonged contact may cause drying and dermatitis.

4. CARCINOGENICITY

4.1 ORAL EXPOSURES

4.1.1 Human

Information on the carcinogenicity of toluene in humans following oral exposure was not available.

4.1.2 Animal

In a 2-year gavage study, Maltoni et al. (1985) administered 500 mg/kg of toluene, 4 to 5 days/week to 40 male and 40 female Sprague-Dawley rats. At the end of the study, 8% of the treated males and 17.5% of the treated females developed hemolymphoreticular neoplasms compared with 7% of the treated males and 3% of the female controls, respectively.

4.2 INHALATION EXPOSURES

4.2.1 Human

Svensson et al. (1990) studied a cohort of 1020 rotogravure workers exposed to toluene and employed for a minimum of 3 months in eight plants from 1925 to 1985. The overall incidence of tumors during the time period 1958–1985 was not increased. Among specific tumors, only those of the respiratory tract were significantly increased (16 observed vs 9 expected). However, statistical significance was not attained when only workers with an exposure period of at least 5 years and a latency period of at least 10 years were considered. Results of a retrospective cohort mortality study of 1008 male oil refinery workers exposed to toluene and other chemicals indicated that worker mortality due to all causes of death and to cancer were lower than that for the general population (Wen et al., 1985).

4.2.2 Animal

Two long-term bioassays found no evidence of carcinogenicity in rats and mice following inhalation of toluene. Compared with controls, the incidence of treatment-related neoplastic lesions was not increased in male and female F344 rats exposed to 30, 100, or 300 ppm, 6 hours/day, 5 days/week for 24 months (Gibson and Hardisty, 1983). Similarly, there was no evidence of carcinogenic activity in male and female F344/N rats or male and female $B6C3F_1$ mice exposed to 600 or 1200 ppm toluene, 6.5 hours/day, 5 days/week for 24 months (NTP, 1990).

4.3 OTHER ROUTES OF EXPOSURE

4.3.1 Human

Information on the carcinogenicity of toluene in humans by other routes of exposure was not available.

4.3.2 Animal

Several studies examined the carcinogenicity of toluene following repeated dermal application in mice. Toluene applied to the shaved skin of male A/He, C3HeB, and SRW mice, three times weekly for life produced no carcinogenic response (Poel, 1963). No skin papillomas or carcinomas were observed in albino mice that received twice weekly dermal applications of toluene for 50 weeks (Coombs et al., 1973). One skin papilloma and one skin carcinoma was reported in a group of mice treated twice weekly for 72 weeks with 1 drop of a 0.2% solution of toluene (Lijinsky and Garcia, 1972). In initiation/promotion studies, toluene was reported to have little or no promoting activity after initiation with 7,12-dimethylbenz(α)anthracene (DMBA) (EPA, 1990). Toluene inhibited skin carcinogenesis in mice in the two-stage model using benzo[*a*]pyrene or DMBA as tumor initiators and phorbol-12-myristate-13-acetate as a tumor promoter (Weiss et al., 1986).

4.4 EPA WEIGHT-OF-EVIDENCE

Classification—Group D; not classifiable as to human carcinogenicity (EPA, 1992)
Basis: No human data and inadequate animal data. Toluene did not produce positive results in the majority of genotoxicity assays.

4.5 CARCINOGENICITY SLOPE FACTORS

No carcinogenicity slope factors were calculated.

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ATTACHMENT D

Estimates of Carcinogenic and Noncarcinogenic Risk – RME Scenario

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Attachment D

Summary of Chemicals of Potential Concern and Exposure Point Concentrations by Receptor and Media
Reasonable Maximum Exposure

			Commercial/Industrial				Recreational			
	Residential		General Industrial Worker		Maintenance Worker	Construction Worker	Recreational User	Swimmer/Wader		Fisherman
Chemical	Surface and Subsurface	Indoor Air	Surface Soil	Indoor Air [a]	Surface Soil	Surface and Subsurface	Surface Soil	Sediment	Surface Water	Fish Tissue
Inorganics										
Antimony	-	-	-	-	-	-	-	3.73	-	-
Arsenic	5.07	-	3.65	-	4.81	4.90	5.27	-	-	-
Cadmium	-	-	-	-	-	-	1.26	-	-	-
Iron	-	-	-	-	-	-	-	20,077	-	-
Lead	90.48	-	-	-	99.31	88.74	103	-	-	-
Manganese	-	-	-	-	-	-	-	190	-	-
Thallium	0.82	-	-	-	-	-	1.02	-	-	-
Vanadium	-	-	-	-	-	-	-	26.72	-	-
SVOCs										
1-Methylnaphthalene	150	-	-	-	-	1,314	-	11.91	-	0.62
2-Methylnaphthalene	144	-	-	-	-	1,412	-	24.37	-	-
Acenaphthene	36.42	-	-	-	-	441	-	-	-	-
Benzo(a)anthracene	24.59	-	-	-	2.67	197	3.44	9.31	-	0.170
Benzo(a)pyrene	19.51	-	0.18	-	5.23	172.82	6.37	9.14	-	0.019
Benzo(e)pyrene	-	-	-	-	-	-	-	-	-	0.010
Benzo(b)fluoranthene	21.28	-	-	-	4.90	102	6.41	5.56	-	0.015
Benzo(k)fluoranthene	10.12	-	-	-	-	119	1.80	5.58	-	-
Chrysene	23.38	-	-	-	-	181	-	-	-	-
Dibenzo(a,h)anthracene	3.12	-	-	-	-	26.19	-	-	-	0.0076
Dibenzofuran	9.93	-	-	-	-	89.23	-	-	-	0.0026
Fluoranthene	63.62	-	-	-	-	329	-	-	-	-
Fluorene	45.88	-	-	-	-	282	-	-	-	-
Indeno(1,2,3-cd)pyrene	5.34	-	-	-	3.30	93.43	4.29	4.79	-	-
Naphthalene	188	-	-	-	-	1,173	-	26.68	-	-
Phenanthrene	144	-	-	-	-	-	-	-	-	-
Pyrene	85.60	-	-	-	-	485	-	-	-	-
VOCs										
1,2,4-Trichlorobenzene	29.62	-	-	-	-	181	-	-	-	-
1,2,4-Trimethylbenzene	6.06	-	-	38.76	-	3.56	-	-	-	-
1,3,5-Trimethylbenzene	15.74	-	-	9.32	-	17.06	-	-	-	-
1,4-Dichlorobenzene	-	-	-	961.57	-	-	-	-	-	-
Benzene	14.29	-	-	38.32	-	14.30	-	-	-	-
Ethylbenzene	-	-	-	-	-	44.35	-	-	-	-
n-Butyl benzene	-	-	-	-	-	39.87	-	-	-	-
sec-Butyl benzene	-	-	-	-	-	43.35	-	-	-	-
Carbon tetrachloride	-	-	-	10.70	-	-	-	-	-	-
Methylene Chloride	-	-	-	4.86	-	-	-	-	-	-
Toluene	-	-	-	-	-	29.55	-	-	-	-
Trichloroethylene	-	-	-	3.16	-	-	-	-	-	-
Xylenes (total)	52.19	-	-	-	-	187	-	-	-	-

Notes:
All units are in milligram/kilogram (mg/kg)
a - Maximum concentrations were used due to lack sufficient data for statistical analysis.

Attachment D

Table 1a
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Incidental Ingestion of Soil Pathway (0-10 feet) – Carcinogenic Effects

$$Ing\text{-}Risk = \frac{(Csoil \times SFo \times CF \times EF \times SIRadj \times FI)}{ATc}$$

Equation / Units	Ing - Risk unitless	= (	Csoil mg/kg	×	SFo kg-day/mg	×	CF kg/mg	×	EF days/year	×	SIRadj mg-yr/kg-day	×	FI unitless	) ÷ (	ATc days	)
Arsenic	1.19E-05	= (	5.07E+00	×	1.50E+00	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Lead	NA	= (	9.05E+01	×	a	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Thallium	NA	= (	8.17E-01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25550	)
1-Methylnaphthalene	NA	= (	1.50E+02	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
2-Methylnaphthalene	NA	= (	1.44E+02	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Acenaphthene	NA	= (	3.64E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Benzo(a)anthracene	2.81E-05	= (	2.46E+01	×	7.30E-01	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Benzo(a)pyrene	2.23E-04	= (	1.95E+01	×	7.30E+00	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Benzo(b)fluoranthene	2.43E-05	= (	2.13E+01	×	7.30E-01	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Benzo(k)fluoranthene	1.16E-06	= (	1.01E+01	×	7.30E-02	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Chrysene	2.67E-07	= (	2.34E+01	×	7.30E-03	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Dibenzo(a,h)anthracene	3.56E-05	= (	3.12E+00	×	7.30E+00	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Dibenzofuran	NA	= (	9.93E+00	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Fluoranthene	NA	= (	6.36E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Fluorene	NA	= (	4.59E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Indeno(1,2,3-cd)pyrene	6.11E-06	= (	5.34E+00	×	7.30E-01	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Naphthalene	NA	= (	1.86E+02	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Phenanthrene	NA	= (	1.44E+02	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Pyrene	NA	= (	8.56E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
1,2,4-Trichlorobenzene	NA	= (	2.96E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	6.06E+00	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	1.57E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Benzene	1.23E-06	= (	1.43E+01	×	5.50E-02	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Xylenes (total)	NA	= (	5.22E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – Soil Concentration
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
SIRadj – Age-adjusted Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 1b
Risk Calculations: Reasonable Maximum Exposure
Residential Child: Incidental Ingestion of Soil Pathway (0-10 feet) – Noncarcinogenic Effects

$$Ing\text{-}HQ = \frac{(Csoil \times CF \times EF \times EDc \times SIRc \times FI)}{(BWc \times ATn \times RfDo)}$$

Equation / Units	Ing - HQ unitless	=	Csoil mg/kg	×	CF kg/mg	×	EF days/year	×	EDc years	×	SIRc mg/day	×	FI unitless	) ÷ (	BWc kg	×	ATn days	×	RfDo [b] mg/kg-day	)
Arsenic	2.16E-01	= (	5.07E+00	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	3.0E-04	)
Lead	NA	= (	9.05E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	a	)
Thallium	1.31E-02	= (	8.17E-01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	8.0E-04	)
1-Methylnaphthalene	2.74E-02	= (	1.50E+02	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	7.0E-02	)
2-Methylnaphthalene	4.60E-01	= (	1.44E+02	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	4.0E-03	)
Acenaphthene	7.76E-04	= (	3.64E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	6.0E-01	)
Benzo(a)anthracene	NA	= (	2.46E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	= (	1.95E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	= (	2.13E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.01E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	NV	)
Chrysene	NA	= (	2.34E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	3.12E+00	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	NV	)
Dibenzofuran	6.35E-02	= (	9.93E+00	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	2.0E-03	)
Fluoranthene	2.03E-03	= (	6.36E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	4.0E-01	)
Fluorene	1.47E-03	= (	4.59E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	4.0E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (	5.34E+00	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	NV	)
Naphthalene	1.19E-01	= (	1.86E+02	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	2.0E-02	)
Phenanthrene	NA	= (	1.44E+02	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	NV	)
Pyrene	3.65E-03	= (	8.56E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	3.0E-01	)
1,2,4-Trichlorobenzene	3.79E-02	= (	2.96E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	1.0E-02	)
1,2,4-Trimethylbenzene	1.55E-03	= (	6.06E+00	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	5.0E-02	)
1,3,5-Trimethylbenzene	4.02E-04	= (	1.57E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	5.0E-01	)
Benzene	4.57E-02	= (	1.43E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	4.0E-03	)
Xylenes (total)	1.87E-03	= (	5.22E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	3.6E-01	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
EDc – Exposure Duration, child
SIRc – Soil Ingestion Rate, child
FI – Fraction Ingested from Contaminated Source
BWc – Body Weight, child
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment D

Table 2a
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Dermal Contact with Soil Pathway (0-10 feet) – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{EV} \times \text{SCRadj} \times \text{ABSd})}{\text{ATc}}$$

Equation / Units	Derm - Risk unitless	=	Csoil mg/kg	×	SFabs kg-day/mg	×	CF kg/mg	×	EF days/year	×	EV events/day	×	SCRadj mg-yr/kg-event	×	ABSd unitless	÷	ATc days
Arsenic	1.18E-06	=	5.07E+00	×	1.58E+00	×	1E-06	×	350	×	1	×	360	×	3.00E-02	÷	25,550
Lead	NA	=	9.05E+01	×	a	×	1E-06	×	350	×	1	×	360	×	NA	÷	25,550
Thallium	NA	=	8.17E-01	×	NV	×	1E-06	×	350	×	1	×	360	×	NA	÷	25,550
1-Methylnaphthalene	NA	=	1.50E+02	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	÷	25,550
2-Methylnaphthalene	NA	=	1.44E+02	×	NV	×	1E-06	×	350	×	1	×	360	×	1.00E-01	÷	25,550
Acenaphthene	NA	=	3.64E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	÷	25,550
Benzo(a)anthracene	1.15E-05	=	2.46E+01	×	7.30E-01	×	1E-06	×	350	×	1	×	360	×	1.30E-01	÷	25,550
Benzo(a)pyrene	9.14E-05	=	1.95E+01	×	7.30E+00	×	1E-06	×	350	×	1	×	360	×	1.30E-01	÷	25,550
Benzo(b)fluoranthene	9.97E-06	=	2.13E+01	×	7.30E-01	×	1E-06	×	350	×	1	×	360	×	1.30E-01	÷	25,550
Benzo(k)fluoranthene	4.74E-07	=	1.01E+01	×	7.30E-02	×	1E-06	×	350	×	1	×	360	×	1.30E-01	÷	25,550
Chrysene	1.10E-07	=	2.34E+01	×	7.30E-03	×	1E-06	×	350	×	1	×	360	×	1.30E-01	÷	25,550
Dibenzo(a,h)anthracene	1.46E-05	=	3.12E+00	×	7.30E+00	×	1E-06	×	350	×	1	×	360	×	1.30E-01	÷	25,550
Dibenzofuran	NA	=	9.93E+00	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	÷	25,550
Fluoranthene	NA	=	6.36E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	÷	25,550
Fluorene	NA	=	4.59E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	÷	25,550
Indeno(1,2,3-cd)pyrene	2.50E-06	=	5.34E+00	×	7.30E-01	×	1E-06	×	350	×	1	×	360	×	1.30E-01	÷	25,550
Naphthalene	NA	=	1.86E+02	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	÷	25,550
Phenanthrene	NA	=	1.44E+02	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	÷	25,550
Pyrene	NA	=	8.56E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	÷	25,550
1,2,4-Trichlorobenzene	NA	=	2.96E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	NV	÷	25,550
1,2,4-Trimethylbenzene	NA	=	6.06E+00	×	NV	×	1E-06	×	350	×	1	×	360	×	NA	÷	25,550
1,3,5-Trimethylbenzene	NA	=	1.57E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	NA	÷	25,550
Benzene	NA	=	1.43E+01	×	5.50E-02	×	1E-06	×	350	×	1	×	360	×	NA	÷	25,550
Xylenes (total)	NA	=	5.22E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	NA	÷	25,550

Notes:

Derm - Risk – *Dermal Risk*
Csoil – Soil Concentration
SFabs – Absorbed slope factor (SFo ÷ ABSgi)
CF – Unit Conversion Factor
EF – Exposure Frequency
EV – Event Frequency
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

SCRadj – *Age-adjusted Soil Contact Rate*
ABSd – Dermal Soil Absorption Factor
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment D

Table 2b
Risk Calculations: Reasonable Maximum Exposure
Residential Child: Dermal Contact with Soil Pathway (0-10 feet) – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{EDc} \times \text{EV} \times \text{SAc} \times \text{AFc} \times \text{ABSd})}{(\text{BWc} \times \text{ATn} \times \text{RfDabs})}$$

Equation / Units	Derm - HQ unitless	= (Csoil mg/kg	× CF kg/mg	× EF days/year	× EDc years	× EV events/day	× SAc cm²	× AFc mg/cm²-event	× ABSd unitless	) ÷ (BWc kg	× ATn days	× RfDabs [b] mg/kg-day	)
Arsenic	1.91E-02	= (5.07E+00	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 3.00E-02	) ÷ (15	× 2,190	× 2.85E-04	)
Lead	NA	= (9.05E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× NA	) ÷ (15	× 2,190	× a	)
Thallium	NA	= (8.17E-01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× NA	) ÷ (15	× 2,190	× 8.00E-04	)
1-Methylnaphthalene	9.98E-03	= (1.50E+02	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× 7.00E-02	)
2-Methylnaphthalene	1.29E-01	= (1.44E+02	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.00E-01	) ÷ (15	× 2,190	× 4.00E-03	)
Acenaphthene	2.82E-04	= (3.64E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× 6.00E-01	)
Benzo(a)anthracene	NA	= (2.46E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× NV	)
Benzo(a)pyrene	NA	= (1.95E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× NV	)
Benzo(b)fluoranthene	NA	= (2.13E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× NV	)
Benzo(k)fluoranthene	NA	= (1.01E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× NV	)
Chrysene	NA	= (2.34E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× NV	)
Dibenzo(a,h)anthracene	NA	= (3.12E+00	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× NV	)
Dibenzofuran	2.31E-02	= (9.93E+00	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× 2.00E-03	)
Fluoranthene	7.40E-04	= (6.36E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× 4.00E-01	)
Fluorene	5.34E-04	= (4.59E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× 4.00E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (5.34E+00	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× NV	)
Naphthalene	4.33E-02	= (1.86E+02	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× 2.00E-02	)
Phenanthrene	NA	= (1.44E+02	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× NV	)
Pyrene	1.33E-03	= (8.56E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× 3.00E-01	)
1,2,4-Trichlorobenzene	NA	= (2.96E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× NV	) ÷ (15	× 2,190	× NV	)
1,2,4-Trimethylbenzene	NA	= (6.06E+00	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× NA	) ÷ (15	× 2,190	× 5.00E-02	)
1,3,5-Trimethylbenzene	NA	= (1.57E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× NA	) ÷ (15	× 2,190	× 5.00E-01	)
Benzene	NA	= (1.43E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× NA	) ÷ (15	× 2,190	× 4.00E-03	)
Xylenes (total)	NA	= (5.22E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× NA	) ÷ (15	× 2,190	× 3.57E-01	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
EDc – Exposure Duration, child
EV – Event Frequency
SAc – Skin Surface Area, child
AFc – Soil-to-skin Adherence Factor, child
ABSd – Dermal Soil Absorption Factor
BWc – Body Weight, child
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo × ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment D

Table 3a
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Inhalation of Soil-derived Chemicals Pathway (0-10 feet)– Carcinogenic Effects

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{EF} \times \text{SInhRadj} \times [(1/\text{VF}) + (1/\text{PEF})])}{\text{ATc}}$$

Equation	Inh - Risk	= (	Csoil	×	SFi	×	EF	×	SInhRadj	× [	1	/	VF_{adult}	+	1	/	PEF	]) + (	ATc	)
Units	unitless		mg/kg		kg-day/mg		days/year		m3-yr/kg-day				m^3/kg				m^3/kg		days	
Arsenic	1.72E-09	= (	5.07E+00	×	1.51E+01	×	350	×	10.86	× [	1	/	NA	+	1	/	6.58E+09	]) + (	25,550	)
Lead	NA	= (	9.05E+01	×	a	×	350	×	10.86	× [	1	/	NA	+	1	/	6.58E+09	]) + (	25,550	)
Thallium	NA	= (	8.17E-01	×	NV	×	350	×	10.86	× [	1	/	NA	+	1	/	6.58E+09	]) + (	25,550	)
1-Methylnaphthalene	NA	= (	1.50E+02	×	NV	×	350	×	10.86	× [	1	/	3.28E+04	+	1	/	6.58E+09	]) + (	25,550	)
2-Methylnaphthalene	NA	= (	1.44E+02	×	NV	×	350	×	10.86	× [	1	/	3.11E+04	+	1	/	6.58E+09	]) + (	25,550	)
Acenaphthene	NA	= (	3.64E+01	×	NV	×	350	×	10.86	× [	1	/	6.00E+04	+	1	/	6.58E+09	]) + (	25,550	)
Benzo(a)anthracene	NA	= (	2.46E+01	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Benzo(a)pyrene	1.36E-09	= (	1.95E+01	×	3.08E+00	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Benzo(b)fluoranthene	NA	= (	2.13E+01	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Benzo(k)fluoranthene	NA	= (	1.01E+01	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Chrysene	NA	= (	2.34E+01	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Dibenzo(a,h)anthracene	NA	= (	3.12E+00	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Dibenzofuran	NA	= (	9.93E+00	×	NV	×	350	×	10.86	× [	1	/	4.98E+04	+	1	/	6.58E+09	]) + (	25,550	)
Fluoranthene	NA	= (	6.36E+01	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Fluorene	NA	= (	4.59E+01	×	NV	×	350	×	10.86	× [	1	/	9.16E+04	+	1	/	6.58E+09	]) + (	25,550	)
Indeno(1,2,3-cd)pyrene	NA	= (	5.34E+00	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Naphthalene	NA	= (	1.86E+02	×	NV	×	350	×	10.86	× [	1	/	2.87E+04	+	1	/	6.58E+09	]) + (	25,550	)
Phenanthrene	NA	= (	1.44E+02	×	NV	×	350	×	10.86	× [	1	/	1.46E+05	+	1	/	6.58E+09	]) + (	25,550	)
Pyrene	NA	= (	8.56E+01	×	NV	×	350	×	10.86	× [	1	/	3.05E+05	+	1	/	6.58E+09	]) + (	25,550	)
1,2,4-Trichlorobenzene	NA	= (	2.96E+01	×	NV	×	350	×	10.86	× [	1	/	1.44E+05	+	1	/	6.58E+09	]) + (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	6.06E+00	×	NV	×	350	×	10.86	× [	1	/	5.47E+03	+	1	/	6.58E+09	]) + (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	1.57E+01	×	NV	×	350	×	10.86	× [	1	/	4.52E+03	+	1	/	6.58E+09	]) + (	25,550	)
Benzene	1.82E-05	= (	1.43E+01	×	2.73E-02	×	350	×	10.86	× [	1	/	3.20E+03	+	1	/	6.58E+09	]) + (	25,550	)
Xylenes (total)	NA	= (	5.22E+01	×	NV	×	350	×	10.86	× [	1	/	4.43E+03	+	1	/	6.58E+09	]) + (	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Soil Concentration
SFi – Inhalation Slope Factor
EF – Exposure frequency
SInhRadj – Age-adjusted Soil Inhalation Rate
VF – Volatilization Factor
PEF – Particulate Emission Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 3b
Risk Calculations: Reasonable Maximum Exposure
Residential Child: Inhalation of Soil-derived Pathway (0-10 feet) – Noncarcinogenic Effects

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{InhRc} \times \text{EF} \times \text{EDc} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BWc} \times \text{ATn} \times \text{RfDi})}$$

Equation / Units	Inh - HQ unitless	=	Csoil mg/kg	×	InhRc m³/day	×	EF days/year	×	EDc year	×	[	1	/	VF_{child} m³/kg	+	1	/	PEF m³/kg	]	+	BWc kg	×	ATn days	×	RfDi (b) mg/kg-day	)
Arsenic	NA	= (	5.07E+00	×	10	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
Lead	NA	= (	9.05E+01	×	10	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	a	)
Thallium	NA	= (	8.17E-01	×	10	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
1-Methylnaphthalene	NA	= (	1.50E+02	×	10	×	350	×	6	×	[	1	/	1.47E+04	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
2-Methylnaphthalene	NA	= (	1.44E+02	×	10	×	350	×	6	×	[	1	/	1.39E+04	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
Acenaphthene	NA	= (	3.64E+01	×	10	×	350	×	6	×	[	1	/	2.68E+04	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
Benzo(a)anthracene	NA	= (	2.46E+01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	= (	1.95E+01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	= (	2.13E+01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.01E+01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
Chrysene	NA	= (	2.34E+01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	3.12E+00	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
Dibenzofuran	NA	= (	9.93E+00	×	10	×	350	×	6	×	[	1	/	2.23E+04	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
Fluoranthene	NA	= (	6.36E+01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
Fluorene	NA	= (	4.59E+01	×	10	×	350	×	6	×	[	1	/	4.10E+04	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	= (	5.34E+00	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
Naphthalene	1.08E+01	= (	1.86E+02	×	10	×	350	×	6	×	[	1	/	1.29E+04	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	8.57E-04	)
Phenanthrene	NA	= (	1.44E+02	×	10	×	350	×	6	×	[	1	/	6.54E+04	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
Pyrene	NA	= (	8.56E+01	×	10	×	350	×	6	×	[	1	/	1.36E+05	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	NV	)
1,2,4-Trichlorobenzene	2.58E-01	= (	2.96E+01	×	10	×	350	×	6	×	[	1	/	6.42E+04	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	1.14E-03	)
1,2,4-Trimethylbenzene	9.27E-01	= (	6.06E+00	×	10	×	350	×	6	×	[	1	/	2.44E+03	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	1.71E-03	)
1,3,5-Trimethylbenzene	2.92E-01	= (	1.57E+01	×	10	×	350	×	6	×	[	1	/	2.02E+03	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	1.70E-02	)
Benzene	7.46E-01	= (	1.43E+01	×	10	×	350	×	6	×	[	1	/	1.43E+03	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	8.57E-03	)
Xylenes (total)	5.88E-01	= (	5.22E+01	×	10	×	350	×	6	×	[	1	/	1.98E+03	+	1	/	6.58E+09	]	+ (	15	×	2,190	×	2.86E-02	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Csoil – Soil Concentration
InhRc – Inhalation Rate, child
EF – Exposure frequency
EDc – Exposure duration, child
VF – Volatilization Factor
PEF – Particulate Emission Factor
BWc – Body Weight, child
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment D

Table 3c
Residential Scenario: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} \times \frac{(3.14 \times D_A \times T)^{1/2}}{(2 \times \rho_b \times D_A)} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} $(g/m^2\text{-}s)/(kg/m^3)$	π	D_A (cm^2/s)	T_{adult} (s)	T_{child} (s)	2	ρb (g/cm^3)	10^{-4} (m^2/cm^2)	VF_{adult} (m^3/kg)
1-Methylnaphthalene	73.32	3.14	1.95E-05	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.28E+04
2-Methylnaphthalene	73.32	3.14	2.17E-05	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.11E+04
Acenaphthene	73.32	3.14	5.82E-06	9.46E+08	1.89E+08	2	1.38	1.00E-04	6.00E+04
Benzo(a)anthracene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Benzo(a)pyrene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Benzo(b)fluoranthene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Benzo(k)fluoranthene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Chrysene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Dibenzo(a,h)anthracene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Dibenzofuran	73.32	3.14	8.46E-06	9.46E+08	1.89E+08	2	1.38	1.00E-04	4.98E+04
Fluoranthene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Fluorene	73.32	3.14	2.50E-06	9.46E+08	1.89E+08	2	1.38	1.00E-04	9.16E+04
Indeno(1,2,3-cd)pyrene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Naphthalene	73.32	3.14	2.54E-05	9.46E+08	1.89E+08	2	1.38	1.00E-04	2.87E+04
Phenanthrene	73.32	3.14	9.79E-07	9.46E+08	1.89E+08	2	1.38	1.00E-04	1.46E+05
Pyrene	73.32	3.14	2.25E-07	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.05E+05
1,2,4-Trichlorobenzene	73.32	3.14	1.02E-06	9.46E+08	1.89E+08	2	1.38	1.00E-04	1.44E+05
1,2,4-Trimethylbenzene	73.32	3.14	7.01E-04	9.46E+08	1.89E+08	2	1.38	1.00E-04	5.47E+03
1,3,5-Trimethylbenzene	73.32	3.14	1.02E-03	9.46E+08	1.89E+08	2	1.38	1.00E-04	4.52E+03
Benzene	73.32	3.14	2.05E-03	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.20E+03
Xylenes (total)	73.32	3.14	1.07E-03	9.46E+08	1.89E+08	2	1.38	1.00E-04	4.43E+03

Notes:

Default values are as presented in *Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites* (USEPA 2002).

VF_{adult} – Volatilization Factor (m^3/kg) for adults (calculated)

VF_{child} – *Volatilization Factor (m^3/kg) for children (calculated)*

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source $(g/m^2\text{-}s)/(kg/m^3)$(Value used is for Minneapolis, MN.)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T_{adult} – Exposure interval (s) for adults

T_{Child} – Exposure interval (s) for children

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated; PAHs are not considered volatile chemicals

Attachment D

Table 3d
Residential Scenario: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical Units	VOC?	θa (Lair /Lsoil)	Di (cm²/s)	H' unitless	θw (Lwater /Lsoil)	Dw (cm²/s)	η (Lpore /Lsoil)	ρb (g/cm³)	ρs (g/cm³)	Kd (cm³/g)	D_A (cm²/s)
1-Methylnaphthalene	Yes	3.29E-01	6.31E-02	1.64E-02	0.15	7.13E-06	4.79E-01	1.38	2.65	3.75E+01	1.95E-05
2-Methylnaphthalene	Yes	3.29E-01	4.80E-02	2.12E-02	0.15	7.84E-06	4.79E-01	1.38	2.65	1.79E+01	2.17E-05
Acenaphthene	Yes	3.29E-01	4.21E-02	7.44E-03	0.15	7.69E-06	4.79E-01	1.38	2.65	3.67E+01	5.82E-06
Benzo(a)anthracene	No	3.29E-01	5.10E-02	4.91E-04	0.15	9.00E-06	4.79E-01	1.38	2.65	1.39E+03	NC
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Benzo(b)fluoranthene	No	3.29E-01	2.26E-02	2.69E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.82E+03	NC
Benzo(k)fluoranthene	No	3.29E-01	2.26E-02	2.39E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Chrysene	No	3.29E-01	2.48E-02	2.14E-04	0.15	6.21E-06	4.79E-01	1.38	2.65	1.42E+03	NC
Dibenzo(a,h)anthracene	No	3.29E-01	2.02E-02	5.03E-06	0.15	5.18E-06	4.79E-01	1.38	2.65	1.57E+04	NC
Dibenzofuran	Yes	3.29E-01	5.51E-02	8.71E-03	0.15	7.04E-06	4.79E-01	1.38	2.65	6.78E+01	8.46E-06
Fluoranthene	No	3.29E-01	3.02E-02	3.62E-04	0.15	6.35E-06	4.79E-01	1.38	2.65	4.25E+02	NC
Fluorene	Yes	3.29E-01	3.63E-02	3.93E-03	0.15	7.88E-06	4.79E-01	1.38	2.65	6.78E+01	2.50E-06
Indeno(1,2,3-cd)pyrene	No	3.29E-01	1.90E-02	1.42E-05	0.15	5.66E-06	4.79E-01	1.38	2.65	1.61E+04	NC
Naphthalene	Yes	3.29E-01	5.90E-02	1.80E-02	0.15	7.50E-06	4.79E-01	1.38	2.65	1.10E+01	2.54E-05
Phenanthrene	Yes	3.29E-01	3.33E-02	1.73E-03	0.15	7.47E-06	4.79E-01	1.38	2.65	1.25E+02	9.79E-07
Pyrene	Yes	3.29E-01	2.72E-02	4.87E-04	0.15	7.24E-06	4.79E-01	1.38	2.65	4.16E+02	2.25E-07
1,2,4-Trichlorobenzene	Yes	3.29E-01	3.00E-02	1.42E-03	0.15	8.23E-06	4.79E-01	1.38	2.65	1.07E+01	1.02E-06
1,2,4-Trimethylbenzene	Yes	3.29E-01	6.44E-02	2.52E-01	0.15	7.92E-06	4.79E-01	1.38	2.65	4.31E+00	7.01E-04
1,3,5-Trimethylbenzene	Yes	3.29E-01	6.02E-02	3.59E-01	0.15	8.67E-06	4.79E-01	1.38	2.65	4.22E+00	1.02E-03
Benzene	Yes	3.29E-01	8.80E-02	2.27E-01	0.15	9.80E-06	4.79E-01	1.38	2.65	9.93E-01	2.05E-03
Xylenes (total)	Yes	3.29E-01	7.14E-02	2.71E-01	0.15	9.34E-06	4.79E-01	1.38	2.65	2.66E+00	1.07E-03

Notes:

D_A – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's Law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User'S Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density
Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm³ /g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)
VOC? – Volatile organic compounds; If no, an apparent diffusivity was not calculated.
NV – no value available
NC – not calculated

Attachment D
TABLE 3e
(RAGS D IEUBK LEAD WORKSHEET)
Site Name: NSP Ashland Lakefront
Receptor: Residential Child (Age 0 - 84 Months) Exposure to Surface and Subsurface Soil

1. Lead Screening Questions

Medium	Lead Concentration Used in Model Run		Basis for Lead Concentration Used For Model Run	Lead Screening Concentration		Basis for Lead Screening Level
	Value	Units		Value	Units	
Soil	90.5	mg/kg	Average Detected Value	400	mg/kg	Recommended Soil Screening Level
Water	4	ug/L	Model Default Value	15	ug/L	Recommended Drinking Water Action Level

2. Lead Model Questions

Question	Response for Residential Lead Model
What lead model (version and date) was used?	IEUBKwin v1.0 build 263; December 2005
Where are the input values located in the risk assessment report?	Located in Attachment A, Table 13.
What range of media concentrations were used for the model?	Average concentration was used for soil. Data are located in Attachment B1, Table 1. Model default values were used for all other media.
What statistics were used to represent the exposure concentration terms and where are the data on concentrations in the risk assessment that support use of these statistics?	Average concentration was used for soil. Data are located in Table 4-8A and 4-8B of the RI Report.
Was soil sample taken from top 2 cm? If not, why?	No. As outlined in the approved RI/FS Workplan (URS, 2005), residential receptors are assumed to be exposed to exposed soil at depths between 0 and 10 feet.
Was soil sample sieved? What size screen was used? If not sieved, provide rationale.	No. Samples were prepared in accordance with the Field Sampling Plan approved by the USEPA.
What was the point of exposure/location?	Samples were collected from the upper bluff area near the former ravine.
Where are the output values located in the risk assessment report?	Located in Attachment B8.
Was the model run using default values only?	No. Site-specific soil concentration values used. All other model values are default.
Was the default soil bioavailability used?	Yes. Default is 30%
Was the default soil ingestion rate used?	Yes Default values for 7 age groups are 85, 135, 135, 100, 090, and 85 mg/day.
If non-default values were used, where is the rationale for the values located in the risk assessment report?	Not applicable to this evaluation.

3. Final Result

Medium	Result	Comment/PRG
Surface Soil and Groundwater	Input value of 88.74 mg/kg in surface soil and 4 ug/L in groundwater results in 0.128% of residential children above a blood lead level of 10 ug/dL. Geometric mean blood lead = 2.423 ug/dL. This does not exceed the blood lead goal as described in the 1994 OSWER Directive of no more than 5% of children exceeding 10 ug/dL blood lead.	

Attachment D
TABLE 3e
(RAGS D IEUBK LEAD WORKSHEET)
Site Name: NSP Ashland Lakefront
Receptor: Residential Child (Age 0 - 84 Months) Exposure to Surface and Subsurface Soil

LEAD MODEL FOR WINDOWS Version 1.0

==========

Model Version: 1.0 Build 263
User Name:
Date:
Site Name:
Operable Unit:
Run Mode: Research

==========

The time step used in this model run: 1 - Every 4 Hours (6 times a day).

****** Air ******

Indoor Air Pb Concentration: 30.000 percent of outdoor.
Other Air Parameters:

Age	Time Outdoors (hours)	Ventilation Rate (m^3/day)	Lung Absorption (%)	Outdoor Air Pb Conc (ug Pb/m^3)
.5-1	1.000	2.000	32.000	0.100
1-2	2.000	3.000	32.000	0.100
2-3	3.000	5.000	32.000	0.100
3-4	4.000	5.000	32.000	0.100
4-5	4.000	5.000	32.000	0.100
5-6	4.000	7.000	32.000	0.100
6-7	4.000	7.000	32.000	0.100

****** Diet ******

Age	Diet Intake(ug/day)
.5-1	5.530
1-2	5.780
2-3	6.490
3-4	6.240
4-5	6.010
5-6	6.340
6-7	7.000

****** Drinking Water ******

Water Consumption:

Age	Water (L/day)
.5-1	0.200
1-2	0.500
2-3	0.520
3-4	0.530
4-5	0.550
5-6	0.580
6-7	0.590

Drinking Water Concentration: 4.000 ug Pb/L

Attachment D
TABLE 3e
(RAGS D IEUBK LEAD WORKSHEET)
Site Name: NSP Ashland Lakefront
Receptor: Residential Child (Age 0 - 84 Months) Exposure to Surface and Subsurface Soil

****** Soil & Dust ******

Multiple Source Analysis Used
Average multiple source concentration: 73.350 ug/g
Mass fraction of outdoor soil to indoor dust conversion factor: 0.700
Outdoor airborne lead to indoor household dust lead concentration: 100.000
Use alternate indoor dust Pb sources? No

Age	Soil (ug Pb/g)	House Dust (ug Pb/g)
.5-1	90.500	73.350
1-2	90.500	73.350
2-3	90.500	73.350
3-4	90.500	73.350
4-5	90.500	73.350
5-6	90.500	73.350
6-7	90.500	73.350

****** Alternate Intake ******

Age	Alternate (ug Pb/day)
.5-1	0.000
1-2	0.000
2-3	0.000
3-4	0.000
4-5	0.000
5-6	0.000
6-7	0.000

****** Maternal Contribution: Infant Model ******
Maternal Blood Concentration: 2.500 ug Pb/dL
****
CALCULATED BLOOD LEAD AND LEAD UPTAKES:
****

Year	Air (ug/day)	Diet (ug/day)	Alternate (ug/day)	Water (ug/day)
.5-1	0.021	2.614	0.000	0.378
1-2	0.034	2.724	0.000	0.943
2-3	0.062	3.076	0.000	0.986
3-4	0.067	2.982	0.000	1.013
4-5	0.067	2.903	0.000	1.063
5-6	0.093	3.074	0.000	1.125
6-7	0.093	3.400	0.000	1.146

Year	Soil+Dust (ug/day)	Total (ug/day)	Blood (ug/dL)
.5-1	1.954	4.967	2.7
1-2	3.095	6.795	2.9
2-3	3.113	7.237	2.7
3-4	3.138	7.200	2.5
4-5	2.350	6.382	2.2
5-6	2.123	6.416	2.0
6-7	2.008	6.647	1.9

Attachment D
Table 3f
Calculations of Blood Lead Concentrations (PbBs)
U.S. EPA Technical Review Workgroup for Lead, Adult Lead Committee
Version date 05/19/03

Exposure Variable	PbB Equation[1] 1*	2**	Description of Exposure Variable	Units	Values for Non-Residential Exposure Scenario: Using Equation 1 GSDi = Hom	Using Equation 1 GSDi = Het	Using Equation 2 GSDi = Hom	Using Equation 2 GSDi = Het
PbS	X	X	*Soil lead concentration*	ug/g or ppm	94.08	94.08	94.08	94.08
$R_{fetal/maternal}$	X	X	Fetal/maternal PbB ratio	--	0.9	0.9	0.9	0.9
BKSF	X	X	Biokinetic Slope Factor	ug/dL per ug/day	0.4	0.4	0.4	0.4
GSD_i	X	X	Geometric standard deviation PbB	--	2.1	2.3	2.1	2.3
PbB_0	X	X	*Baseline PbB*	ug/dL	1.5	1.7	1.5	1.7
IR_S	X		Soil ingestion rate (including soil-derived indoor dust)	g/day	0.050	0.050	--	--
IR_{S+D}		X	Total ingestion rate of outdoor soil and indoor dust	g/day	--	--	0.050	0.050
W_S		X	Weighting factor; fraction of IR_{S+D} ingested as outdoor soil	--	--	--	1.0	1.0
K_{SD}		X	Mass fraction of soil in dust	--	--	--	0.7	0.7
$AF_{S,D}$	X	X	Absorption fraction (same for soil and dust)	--	0.12	0.12	0.12	0.12
$EF_{S,D}$	X	X	Exposure frequency (same for soil and dust)	days/yr	219	219	219	219
$AT_{S,D}$	X	X	Averaging time (same for soil and dust)	days/yr	365	365	365	365
PbB_{adult}	**PbB of adult worker, geometric mean**			**ug/dL**	**1.6**	**1.8**	**1.6**	**1.8**
$PbB_{fetal,0.95}$	**95th percentile PbB among fetuses of adult workers**			**ug/dL**	**5.0**	**6.5**	**5.0**	**6.5**
PbB_t	**Target PbB level of concern (e.g., 10 ug/dL)**			**ug/dL**	**10.0**	**10.0**	**10.0**	**10.0**
$P(PbB_{fetal} > PbB_t)$	**Probability that fetal PbB > PbB_t, assuming lognormal distribution**			**%**	**0.5%**	**1.5%**	**0.5%**	**1.5%**

[1] Equation 1 does not apportion exposure between soil and dust ingestion (excludes W_S, K_{SD}).
When $IR_S = IR_{S+D}$ and $W_S = 1.0$, the equations yield the same $PbB_{fetal,0.95}$.

***Equation 1, based on Eq. 1, 2 in USEPA (1996).**

PbB_{adult} =	$(PbS*BKSF*IR_{S+D}*AF_{S,D}*EF_S/AT_{S,D}) + PbB_0$
$PbB_{fetal,0.95}$ =	$PbB_{adult} * (GSD_i^{1.645} * R)$

****Equation 2, alternate approach based on Eq. 1, 2, and A-19 in USEPA (1996).**

PbB_{adult} =	$PbS*BKSF*([(IR_{S+D})*AF_S*EF_S*W_S]+[K_{SD}*(IR_{S+D})*(1-W_S)*AF_D*EF_D])/365+PbB_0$
$PbB_{fetal,0.95}$ =	$PbB_{adult} * (GSD_i^{1.645} * R)$

Source: U.S. EPA (1996). Recommendations of the Technical Review Workgroup for Lead for an Interim Approach to Assessing Risks Associated with Adult Exposures to Lead in Soil

Attachment D
TABLE 3g
(RAGS D IEUBK LEAD WORKSHEET)
Site Name: NSP Ashland Lakefront
Receptor: Residential Child (Age 0 - 84 Months) Exposure to Surface Soil

1. Lead Screening Questions

Medium	Lead Concentration Used in Model Run		Basis for Lead Concentration Used For Model Run	Lead Screening Concentration		Basis for Lead Screening Level
	Value	Units		Value	Units	
Soil	83.4	mg/kg	Average Detected Value	400	mg/kg	Recommended Soil Screening Level
Water	4	ug/L	Model Default Value	15	ug/L	Recommended Drinking Water Action Level

2. Lead Model Questions

Question	Response for Residential Lead Model
What lead model (version and date) was used?	IEUBKwin v1.0 build 263; December 2005
Where are the input values located in the risk assessment report?	Located in Attachment A, Table 13.
What range of media concentrations were used for the model?	Average concentration was used for soil. Data are located in Attachment B1, Table 1. Model default values were used for all other media.
What statistics were used to represent the exposure concentration terms and where are the data on concentrations in the risk assessment that support use of these statistics?	Average concentration was used for soil. Data are located in Table 4-8A and 4-8B of the RI Report.
Was soil sample taken from top 2 cm? If not, why?	No. As outlined in the approved RI/FS Workplan (URS, 2005), residential receptors are assumed to be exposed to exposed soil at depths between 0 and 10 feet.
Was soil sample sieved? What size screen was used? If not sieved, provide rationale.	No. Samples were prepared in accordance with the Field Sampling Plan approved by the USEPA.
What was the point of exposure/location?	Samples were collected from the upper bluff area near the former ravine.
Where are the output values located in the risk assessment report?	Located in Attachment B8.
Was the model run using default values only?	No. Site-specific soil concentration values used. All other model values are default.
Was the default soil bioavailability used?	Yes. Default is 30%
Was the default soil ingestion rate used?	Yes Default values for 7 age groups are 85, 135, 135, 100, 090, and 85 mg/day.
If non-default values were used, where is the rationale for the values located in the risk assessment report?	Not applicable to this evaluation.

3. Final Result

Medium	Result	Comment/PRG
Surface Soil and Groundwater	Input value of 83.4 mg/kg in surface soil and 4 ug/L in groundwater results in 0.105% of residential children above a blood lead level of 10 ug/dL. Geometric mean blood lead = 2.357 ug/dL. This does not exceed the blood lead goal as described in the 1994 OSWER Directive of no more than 5% of children exceeding 10 ug/dL blood lead.	

Attachment D
TABLE 3g
(RAGS D IEUBK LEAD WORKSHEET)
Site Name: NSP Ashland Lakefront
Receptor: Residential Child (Age 0 - 84 Months) Exposure to Surface Soil

LEAD MODEL FOR WINDOWS Version 1.0

==========

Model Version: 1.0 Build 263
User Name:
Date:
Site Name:
Operable Unit:
Run Mode: Research

==========

The time step used in this model run: 1 - Every 4 Hours (6 times a day).

****** Air ******

Indoor Air Pb Concentration: 30.000 percent of outdoor.
Other Air Parameters:

Age	Time Outdoors (hours)	Ventilation Rate (m^3/day)	Lung Absorption (%)	Outdoor Air Pb Conc (ug Pb/m^3)
.5-1	1.000	2.000	32.000	0.100
1-2	2.000	3.000	32.000	0.100
2-3	3.000	5.000	32.000	0.100
3-4	4.000	5.000	32.000	0.100
4-5	4.000	5.000	32.000	0.100
5-6	4.000	7.000	32.000	0.100
6-7	4.000	7.000	32.000	0.100

****** Diet ******

Age	Diet Intake(ug/day)
.5-1	5.530
1-2	5.780
2-3	6.490
3-4	6.240
4-5	6.010
5-6	6.340
6-7	7.000

****** Drinking Water ******

Water Consumption:

Age	Water (L/day)
.5-1	0.200
1-2	0.500
2-3	0.520
3-4	0.530
4-5	0.550
5-6	0.580
6-7	0.590

Drinking Water Concentration: 4.000 ug Pb/L

Attachment D
TABLE 3g
(RAGS D IEUBK LEAD WORKSHEET)
Site Name: NSP Ashland Lakefront
Receptor: Residential Child (Age 0 - 84 Months) Exposure to Surface Soil

Attachment D
TABLE 3g
(RAGS D IEUBK LEAD WORKSHEET)
Site Name: NSP Ashland Lakefront
Receptor: Residential Child (Age 0 - 84 Months) Exposure to Surface Soil

****** Soil & Dust ******

Multiple Source Analysis Used
Average multiple source concentration: 68.380 ug/g

Mass fraction of outdoor soil to indoor dust conversion factor: 0.700
Outdoor airborne lead to indoor household dust lead concentration: 100.000
Use alternate indoor dust Pb sources? No

Age	Soil (ug Pb/g)	House Dust (ug Pb/g)
.5-1	83.400	68.380
1-2	83.400	68.380
2-3	83.400	68.380
3-4	83.400	68.380
4-5	83.400	68.380
5-6	83.400	68.380
6-7	83.400	68.380

****** Alternate Intake ******

Age	Alternate (ug Pb/day)
.5-1	0.000
1-2	0.000
2-3	0.000
3-4	0.000
4-5	0.000
5-6	0.000
6-7	0.000

****** Maternal Contribution: Infant Model ******

Maternal Blood Concentration: 2.500 ug Pb/dL

****
CALCULATED BLOOD LEAD AND LEAD UPTAKES:
****

Year	Air (ug/day)	Diet (ug/day)	Alternate (ug/day)	Water (ug/day)
.5-1	0.021	2.618	0.000	0.379
1-2	0.034	2.729	0.000	0.944
2-3	0.062	3.081	0.000	0.988
3-4	0.067	2.986	0.000	1.015
4-5	0.067	2.906	0.000	1.064
5-6	0.093	3.077	0.000	1.126
6-7	0.093	3.402	0.000	1.147

Year	Soil+Dust (ug/day)	Total (ug/day)	Blood (ug/dL)
.5-1	1.814	4.832	2.6
1-2	2.874	6.581	2.8
2-3	2.890	7.021	2.6
3-4	2.913	6.980	2.5
4-5	2.180	6.216	2.2

Attachment D
TABLE 3g
(RAGS D IEUBK LEAD WORKSHEET)
Site Name: NSP Ashland Lakefront
Receptor: Residential Child (Age 0 - 84 Months) Exposure to Surface Soil

5-6	1.969	6.265	2.0
6-7	1.862	6.504	1.8

Attachment D

Table 4a
Risk Calculations: Reasonable Maximum Exposure
Recreational Adult: Incidental Ingestion of Soil Pathway – Carcinogenic Effects

$$\text{Ing-Risk} = \frac{(\text{Csoil} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	= (	Csoil	×	SFo	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		mg/day		unitless		kg		days	
Aluminum	NA	= (	9.53E+03	×	NV	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	25,550	)
Arsenic	1.79E-07	= (	5.48E+00	×	1.50E+00	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	25,550	)
Cadmium	NA	= (	1.35E+00	×	NV	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	25,550	)
Iron	NA	= (	2.55E+04	×	NV	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	25,550	)
Lead	NA	= (	1.08E+02	×	a	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	25,550	)
Manganese	NA	= (	3.47E+02	×	NV	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	25,550	)
Thallium	NA	= (	1.04E+00	×	NV	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	25,550	)
Vanadium	NA	= (	3.66E+01	×	NV	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	25,550	)
Zinc	NA	= (	4.61E+02	×	NV	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	25,550	)
Benzo(a)anthracene	5.74E-08	= (	3.60E+00	×	7.30E-01	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	1.13E-06	= (	7.10E+00	×	7.30E+00	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	1.09E-07	= (	6.85E+00	×	7.30E-01	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	3.07E-09	= (	1.93E+00	×	7.30E-02	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	7.52E-08	= (	4.72E+00	×	7.30E-01	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – Soil Concentration
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 4b
Risk Calculations: Reasonable Maximum Exposure
Recreational Adult: Incidental Ingestion of Soil Pathway – Noncarcinogenic Effects

$$Ing\text{-}HQ = \frac{(Csoil \times CF \times EF \times ED \times SIR \times FI)}{(BW \times ATn \times RfDo)}$$

Equation	Ing - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATn	×	RfDo [b]	)
Units	unitless		mg/kg		kg/mg		days/year		years		mg/day		unitless		kg		days		mg/kg-day	
Aluminum	4.85E-04	= (	9.53E+03	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	10,950	×	1.0E+00	)
Arsenic	9.30E-04	= (	5.48E+00	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	10,950	×	3.0E-04	)
Cadmium	6.89E-05	= (	1.35E+00	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	10,950	×	1.0E-03	)
Iron	4.32E-03	= (	2.55E+04	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	10,950	×	3.0E-01	)
Lead	NA	= (	1.08E+02	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	10,950	×	a	)
Manganese	1.26E-04	= (	3.47E+02	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	10,950	×	1.4E-01	)
Thallium	6.60E-05	= (	1.04E+00	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	10,950	×	8.0E-04	)
Vanadium	2.66E-04	= (	3.66E+01	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	10,950	×	7.0E-03	)
Zinc	7.82E-05	= (	4.61E+02	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	10,950	×	3.0E-01	)
Benzo(a)anthracene	NA	= (	3.60E+00	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	10,950	×	NV	)
Benzo(a)pyrene	NA	= (	7.10E+00	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	10,950	×	NV	)
Benzo(b)fluoranthene	NA	= (	6.85E+00	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	10,950	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.93E+00	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	10,950	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	= (	4.72E+00	×	1E-06	×	52	×	30	×	50	×	0.5	) ÷ (	70	×	10,950	×	NV	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment D

Table 5a
Risk Calculations: Reasonable Maximum Exposure
Recreational Adult: Dermal Contact with Soil Pathway – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATc})}$$

Equation	Derm - Risk	= (	Csoil	×	SFabs	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		events/day		cm^2		mg/cm^2-event		unitless		kg		days	
Aluminum	NA	= (	9.53E+03	×	NV	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	NA	) ÷ (	70	×	25,550	)
Arsenic	6.94E-08	= (	5.48E+00	×	1.58E+00	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	3.00E-02	) ÷ (	70	×	25,550	)
Cadmium	NA	= (	1.35E+00	×	NV	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	1.00E-03	) ÷ (	70	×	25,550	)
Iron	NA	= (	2.55E+04	×	NV	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	NA	) ÷ (	70	×	25,550	)
Lead	NA	= (	1.08E+02	×	NV	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	NA	) ÷ (	70	×	25,550	)
Manganese	NA	= (	3.47E+02	×	NV	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	NA	) ÷ (	70	×	25,550	)
Thallium	NA	= (	1.04E+00	×	NV	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	NA	) ÷ (	70	×	25,550	)
Vanadium	NA	= (	3.66E+01	×	NV	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	NA	) ÷ (	70	×	25,550	)
Zinc	NA	= (	4.61E+02	×	NV	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	NA	) ÷ (	70	×	25,550	)
Benzo(a)anthracene	9.13E-08	= (	3.60E+00	×	7.30E-01	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	1.80E-06	= (	7.10E+00	×	7.30E+00	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	1.74E-07	= (	6.85E+00	×	7.30E-01	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	4.88E-09	= (	1.93E+00	×	7.30E-02	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.20E-07	= (	4.72E+00	×	7.30E-01	×	1E-06	×	52	×	30	×	1	×	4373	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csoil – Soil Concentration
SFabs – Absorbed slope factor (SFo + ABSgi)
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
SSAF – Soil-to-skin Adherence Factor
ABSd – Dermal Soil Absorption Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 5b
Risk Calculations: Reasonable Maximum Exposure
Recreational Adult: Dermal Contact with Soil Pathway – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATn} \times \text{RfDabs})}$$

Equation / Units	Derm - HQ unitless	= (	Csoil mg/kg	×	CF kg/mg	×	EF days/year	×	ED years	×	EV events/day	×	SA cm²	×	SSAF mg/cm²-event	×	ABSd unitless	) ÷ (	BW kg	×	ATn days	×	RfDabs (b) mg/kg-day	)
Aluminum	NA	= (	9.53E+03	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	NA	) ÷ (	70	×	10,950	×	NV	)
Arsenic	3.60E-04	= (	5.48E+00	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	3.00E-02	) ÷ (	70	×	10,950	×	2.85E-04	)
Cadmium	3.37E-05	= (	1.35E+00	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	1.00E-03	) ÷ (	70	×	10,950	×	2.50E-05	)
Iron	NA	= (	2.55E+04	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	NA	) ÷ (	70	×	10,950	×	NV	)
Lead	NA	= (	1.08E+02	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	NA	) ÷ (	70	×	10,950	×	NV	)
Manganese	NA	= (	3.47E+02	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	NA	) ÷ (	70	×	10,950	×	5.60E-03	)
Thallium	NA	= (	1.04E+00	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	NA	) ÷ (	70	×	10,950	×	8.00E-04	)
Vanadium	NA	= (	3.66E+01	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	NA	) ÷ (	70	×	10,950	×	1.82E-04	)
Zinc	NA	= (	4.61E+02	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	NA	) ÷ (	70	×	10,950	×	3.00E-01	)
Benzo(a)anthracene	NA	= (	3.60E+00	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	1.30E-01	) ÷ (	70	×	10,950	×	NV	)
Benzo(a)pyrene	NA	= (	7.10E+00	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	1.30E-01	) ÷ (	70	×	10,950	×	NV	)
Benzo(b)fluoranthene	NA	= (	6.85E+00	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	1.30E-01	) ÷ (	70	×	10,950	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.93E+00	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	1.30E-01	) ÷ (	70	×	10,950	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	= (	4.72E+00	×	1E-06	×	52	×	30	×	1	×	4,373	×	0.1	×	1.30E-01	) ÷ (	70	×	10,950	×	NV	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Soil Concentration
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
ABSd – Dermal Soil Absorption Factor
BW – Body Weight
ATn – Averaging time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo ×ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.
SSAF – Soil-to-skin Adherence Factor

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment D

Table 6a
Risk Calculations: Reasonable Maximum Exposure
Recreational Adult: Inhalation of Soil -Derived Chemicals Pathway– Carcinogenic Effects

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFI} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times [(1/\text{VF}) + (1/\text{PEF})])}{(\text{BW} \times \text{ATc})}$$

Equation	Inh - Risk	=	(	Csoil	×	SFi	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	)	÷	(	BW	×	ATc	)
Units	unitless			mg/kg		kg-day/mg		m³/hour		hours/day		days/year		year					m³/kg				m³/kg					kg		days	
Aluminum	NA	=	(	9.53E+03	×	NV	×	1.00	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	70	×	25,550	)
Arsenic	1.09E-10	=	(	5.48E+00	×	1.51E+01	×	1.00	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	70	×	25,550	)
Cadmium	1.13E-11	=	(	1.35E+00	×	6.30E+00	×	1.00	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	70	×	25,550	)
Iron	NA	=	(	2.55E+04	×	NV	×	1.00	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	70	×	25,550	)
Lead	NA	=	(	1.08E+02	×	a	×	1.00	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	70	×	25,550	)
Manganese	NA	=	(	3.47E+02	×	NV	×	1.00	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	70	×	25,550	)
Thallium	NA	=	(	1.04E+00	×	NV	×	1.00	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	70	×	25,550	)
Vanadium	NA	=	(	3.66E+01	×	NV	×	1.00	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	70	×	25,550	)
Zinc	NA	=	(	4.61E+02	×	NV	×	1.00	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	70	×	25,550	)
Benzo(a)anthracene	NA	=	(	3.60E+00	×	NV	×	1.00	×	2	×	52	×	30	×	[	1	/	NC	+	1	/	1.32E+09	]	)	÷	(	70	×	25,550	)
Benzo(a)pyrene	2.90E-11	=	(	7.10E+00	×	3.08E+00	×	1.00	×	2	×	52	×	30	×	[	1	/	NC	+	1	/	1.32E+09	]	)	÷	(	70	×	25,550	)
Benzo(b)fluoranthene	NA	=	(	6.85E+00	×	NV	×	1.00	×	2	×	52	×	30	×	[	1	/	NC	+	1	/	1.32E+09	]	)	÷	(	70	×	25,550	)
Benzo(k)fluoranthene	NA	=	(	1.93E+00	×	NV	×	1.00	×	2	×	52	×	30	×	[	1	/	NC	+	1	/	1.32E+09	]	)	÷	(	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	NA	=	(	4.72E+00	×	NV	×	1.00	×	2	×	52	×	30	×	[	1	/	NC	+	1	/	1.32E+09	]	)	÷	(	70	×	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Soil Concentration
SFI – Inhalation Slope Factor
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VF – Volatilization Factor
PEF – Particulate Emission Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 6b

Risk Calculations: Reasonable Maximum Exposure

Recreational Adult: Inhalation of Soil-Derived Chemicals Pathway – Noncarcinogenic Effects

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BW} \times \text{ATn} \times \text{RfDi})}$$

Equation	Inh - HQ	=	(	Csoil	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	÷	(	BW	×	ATn	×	RfDi [(b)]	)
Units	unitless			mg/kg		m³/hour		hours/day		days/year		year					m³/kg				m³/kg				kg		days		mg/kg-day	
Aluminum	2.06E-05	=	(	9.53E+03	×	1	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	÷	(	70	×	10,950	×	1.43E-03	)
Arsenic	NA	=	(	5.48E+00	×	1	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	÷	(	70	×	10,950	×	NV	)
Cadmium	1.61E-08	=	(	1.35E+00	×	1	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	÷	(	70	×	10,950	×	2.60E-04	)
Iron	NA	=	(	2.55E+04	×	1	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	÷	(	70	×	10,950	×	NV	)
Lead	NA	=	(	1.08E+02	×	1	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	÷	(	70	×	10,950	×	a	)
Manganese	7.52E-05	=	(	3.47E+02	×	1	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	÷	(	70	×	10,950	×	1.43E-05	)
Thallium	NA	=	(	1.04E+00	×	1	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	÷	(	70	×	10,950	×	NV	)
Vanadium	NA	=	(	3.66E+01	×	1	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	÷	(	70	×	10,950	×	NV	)
Zinc	NA	=	(	4.61E+02	×	1	×	2	×	52	×	30	×	[	1	/	NA	+	1	/	1.32E+09	]	÷	(	70	×	10,950	×	NV	)
Benzo(a)anthracene	NA	=	(	3.60E+00	×	1	×	2	×	52	×	30	×	[	1	/	NC	+	1	/	1.32E+09	]	÷	(	70	×	10,950	×	NV	)
Benzo(a)pyrene	NA	=	(	7.10E+00	×	1	×	2	×	52	×	30	×	[	1	/	NC	+	1	/	1.32E+09	]	÷	(	70	×	10,950	×	NV	)
Benzo(b)fluoranthene	NA	=	(	6.85E+00	×	1	×	2	×	52	×	30	×	[	1	/	NC	+	1	/	1.32E+09	]	÷	(	70	×	10,950	×	NV	)
Benzo(k)fluoranthene	NA	=	(	1.93E+00	×	1	×	2	×	52	×	30	×	[	1	/	NC	+	1	/	1.32E+09	]	÷	(	70	×	10,950	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	=	(	4.72E+00	×	1	×	2	×	52	×	30	×	[	1	/	NC	+	1	/	1.32E+09	]	÷	(	70	×	10,950	×	NV	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Csoil – Soil Concentration
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VF – Volatilization Factor
PEF – Particulate Emission Factor
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment D

Table 6c
Recreational Scenario: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} \times \frac{(3.14 \times D_A \times T)^{1/2}}{(2 \times \rho_b \times D_A)} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} $(g/m^2\text{-}s)/(kg/m^3)$	π	D_A (cm^2/s)	T (s)	2	ρb (g/cm^3)	10^{-4} (m^2/cm^2)	VF (m^3/kg)
Benzo(a)anthracene	73.32	3.14	NC	9.46E+08	2	1.38	1.00E-04	NC
Benzo(a)pyrene	73.32	3.14	NC	9.46E+08	2	1.38	1.00E-04	NC
Benzo(b)fluoranthene	73.32	3.14	NC	9.46E+08	2	1.38	1.00E-04	NC
Benzo(k)fluoranthene	73.32	3.14	NC	9.46E+08	2	1.38	1.00E-04	NC
Indeno(1,2,3-cd)pyrene	73.32	3.14	NC	9.46E+08	2	1.38	1.00E-04	NC

Notes: Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

VF – Volatilization Factor (m^3/kg) (calculated)

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source $(g/m^2\text{-}s)/(kg/m^3)$(Value used is for Minneapolis, MN.)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T – Exposure interval (s)

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated; PAHs are not considered volatile chemicals

Attachment D

Table 6d
Recreational Scenario: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical	VOC?	θa	Di	H'	θw	Dw	η	ρb	ρs	Kd	D_A
Units		(Lair /Lsoil)	(cm^2/s)	unitless	(Lwater /Lsoil)	(cm^2/s)	(Lpore /Lsoil)	(g/cm^3)	(g/cm^3)	(cm^3/g)	(cm^2/s)
Benzo(a)anthracene	No	3.29E-01	5.10E-02	4.91E-04	0.15	9.00E-06	4.79E-01	1.38	2.65	1.39E+03	NC
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Benzo(b)fluoranthene	No	3.29E-01	2.26E-02	2.69E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.82E+03	NC
Benzo(k)fluoranthene	No	3.29E-01	4.90E-02	1.35E-05	0.15	5.65E-05	4.79E-01	1.38	2.65	1.61E+04	NC
Indeno(1,2,3-cd)pyrene	No	3.29E-01	1.90E-02	1.42E-05	0.15	5.66E-06	4.79E-01	1.38	2.65	1.61E+04	NC

Notes:

D_A – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User'S Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density
Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm^3/g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)
VOC? – Volatile organic compounds; If no, an apparent diffusivity was not calculated.
NV – no value available
NC – not calculated

Attachment D

Table 7a
Risk Calculations: Reasonable Maximum Exposure
Recreational Adolescent: Incidental Ingestion of Soil Pathway – Carcinogenic Effects

$$\text{Ing-Risk} = \frac{(\text{Csoil} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	= (	Csoil	×	SFo	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		mg/day		unitless		kg		days	
Aluminum	NA	= (	9.53E+03	×	NV	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	25,550	)
Arsenic	1.07E-07	= (	5.48E+00	×	1.50E+00	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	25,550	)
Cadmium	NA	= (	1.35E+00	×	NV	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	25,550	)
Iron	NA	= (	2.55E+04	×	NV	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	25,550	)
Lead	NA	= (	1.08E+02	×	a	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	25,550	)
Manganese	NA	= (	3.47E+02	×	NV	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	25,550	)
Thallium	NA	= (	1.04E+00	×	NV	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	25,550	)
Vanadium	NA	= (	3.66E+01	×	NV	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	25,550	)
Zinc	NA	= (	4.61E+02	×	NV	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	25,550	)
Benzo(a)anthracene	3.42E-08	= (	3.60E+00	×	7.30E-01	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	25,550	)
Benzo(a)pyrene	6.73E-07	= (	7.10E+00	×	7.30E+00	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	25,550	)
Benzo(b)fluoranthene	6.50E-08	= (	6.85E+00	×	7.30E-01	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	25,550	)
Benzo(k)fluoranthene	1.83E-09	= (	1.93E+00	×	7.30E-02	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	4.48E-08	= (	4.72E+00	×	7.30E-01	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – Soil Concentration
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 7b
Risk Calculations: Reasonable Maximum Exposure
Recreational Adolescent: Incidental Ingestion of Soil Pathway – Noncarcinogenic Effects

$$Ing\text{-}HQ = \frac{(Csoil \times CF \times EF \times ED \times SIR \times FI)}{(BW \times ATn \times RfDo)}$$

Equation	Ing - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATn	×	RfDo [b]	)
Units	unitless		mg/kg		kg/mg		days/year		years		mg/day		unitless		kg		days		mg/kg-day	
Aluminum	7.23E-04	= (	9.53E+03	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	4,380	×	1.0E+00	)
Arsenic	1.39E-03	= (	5.48E+00	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	4,380	×	3.0E-04	)
Cadmium	1.03E-04	= (	1.35E+00	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	4,380	×	1.0E-03	)
Iron	6.43E-03	= (	2.55E+04	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	4,380	×	3.0E-01	)
Lead	NA	= (	1.08E+02	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	4,380	×	a	)
Manganese	1.88E-04	= (	3.47E+02	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	4,380	×	1.4E-01	)
Thallium	9.83E-05	= (	1.04E+00	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	4,380	×	8.0E-04	)
Vanadium	3.96E-04	= (	3.66E+01	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	4,380	×	7.0E-03	)
Zinc	1.17E-04	= (	4.61E+02	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	4,380	×	3.0E-01	)
Benzo(a)anthracene	NA	= (	3.60E+00	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	4,380	×	NV	)
Benzo(a)pyrene	NA	= (	7.10E+00	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	4,380	×	NV	)
Benzo(b)fluoranthene	NA	= (	6.85E+00	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	4,380	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.93E+00	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	4,380	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	= (	4.72E+00	×	1E-06	×	52	×	12	×	50	×	0.5	) ÷ (	47	×	4,380	×	NV	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment D

Table 8a
Risk Calculations: Reasonable Maximum Exposure
Recreational Adolescent: Dermal Contact with Soil Pathway – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATc})}$$

Equation / Units	Derm - Risk unitless	=	Csoil mg/kg	×	SFabs kg-day/mg	×	CF kg/mg	×	EF days/year	×	ED years	×	EV events/day	×	SA cm^2	×	SSAF mg/cm^2-event	×	ABSd unitless	)	÷	(	BW kg	×	ATc days	)
Aluminum	NA	= (	9.53E+03	×	NV	×	1E-06	×	12	×	12	×	1	×	4,373	×	0.1	×	NA	)	÷	(	47	×	25,550	)
Arsenic	9.54E-09	= (	5.48E+00	×	1.58E+00	×	1E-06	×	12	×	12	×	1	×	4,373	×	0.1	×	3.00E-02	)	÷	(	47	×	25,550	)
Cadmium	NA	= (	1.35E+00	×	NV	×	1E-06	×	12	×	12	×	1	×	4,373	×	0.1	×	1.00E-03	)	÷	(	47	×	25,550	)
Iron	NA	= (	2.55E+04	×	NV	×	1E-06	×	12	×	12	×	1	×	4,373	×	0.1	×	NA	)	÷	(	47	×	25,550	)
Lead	NA	= (	1.08E+02	×	NV	×	1E-06	×	12	×	12	×	1	×	4,373	×	0.1	×	NA	)	÷	(	47	×	25,550	)
Manganese	NA	= (	3.47E+02	×	NV	×	1E-06	×	12	×	12	×	1	×	4,373	×	0.1	×	NA	)	÷	(	47	×	25,550	)
Thallium	NA	= (	1.04E+00	×	NV	×	1E-06	×	12	×	12	×	1	×	4,373	×	0.1	×	NA	)	÷	(	47	×	25,550	)
Vanadium	NA	= (	3.66E+01	×	NV	×	1E-06	×	12	×	12	×	1	×	4,373	×	0.1	×	NA	)	÷	(	47	×	25,550	)
Zinc	NA	= (	4.61E+02	×	NV	×	1E-06	×	12	×	12	×	1	×	4,373	×	0.1	×	NA	)	÷	(	47	×	25,550	)
Benzo(a)anthracene	1.26E-08	= (	3.60E+00	×	7.30E-01	×	1E-06	×	12	×	12	×	1	×	4,373	×	0.1	×	1.30E-01	)	÷	(	47	×	25,550	)
Benzo(a)pyrene	2.47E-07	= (	7.10E+00	×	7.30E+00	×	1E-06	×	12	×	12	×	1	×	4,373	×	0.1	×	1.30E-01	)	÷	(	47	×	25,550	)
Benzo(b)fluoranthene	2.39E-08	= (	6.85E+00	×	7.30E-01	×	1E-06	×	12	×	12	×	1	×	4,373	×	0.1	×	1.30E-01	)	÷	(	47	×	25,550	)
Benzo(k)fluoranthene	6.71E-10	= (	1.93E+00	×	7.30E-02	×	1E-06	×	12	×	12	×	1	×	4,373	×	0.1	×	1.30E-01	)	÷	(	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.65E-08	= (	4.72E+00	×	7.30E-01	×	1E-06	×	12	×	12	×	1	×	4373	×	0.1	×	1.30E-01	)	÷	(	47	×	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csoil – Soil Concentration
SFabs – Absorbed slope factor (SFo + ABSgi)
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

SA – Skin Surface Area
SSAF – Soil-to-skin Adherence Factor
ABSd – Dermal Soil Absorption Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment D

Table 8b
Risk Calculations: Reasonable Maximum Exposure
Recreational Adolescent: Dermal Contact with Soil Pathway – Noncarcinogenic Effects

$$Derm\text{-}HQ = \frac{(Csoil \times CF \times EF \times ED \times EV \times SA \times SSAF \times ABSd)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm - HQ	=	(	Csoil	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	)	÷	(	BW	×	ATn	×	RfDabs (b)	)
Units	unitless			mg/kg		kg/mg		days/year		years		events/day		cm^2		mg/cm^2-event		unitless				kg		days		mg/kg-day	
Aluminum	NA	=	(	9.53E+03	×	1E-06	×	52	×	12	×	1	×	4,373	×	0.1	×	NA	)	÷	(	47	×	4,380	×	NV	)
Arsenic	5.36E-04	=	(	5.48E+00	×	1E-06	×	52	×	12	×	1	×	4,373	×	0.1	×	3.00E-02	)	÷	(	47	×	4,380	×	2.85E-04	)
Cadmium	5.03E-05	=	(	1.35E+00	×	1E-06	×	52	×	12	×	1	×	4,373	×	0.1	×	1.00E-03	)	÷	(	47	×	4,380	×	2.50E-05	)
Iron	NA	=	(	2.55E+04	×	1E-06	×	52	×	12	×	1	×	4,373	×	0.1	×	NA	)	÷	(	47	×	4,380	×	NV	)
Lead	NA	=	(	1.08E+02	×	1E-06	×	52	×	12	×	1	×	4,373	×	0.1	×	NA	)	÷	(	47	×	4,380	×	NV	)
Manganese	NA	=	(	3.47E+02	×	1E-06	×	52	×	12	×	1	×	4,373	×	0.1	×	NA	)	÷	(	47	×	4,380	×	5.60E-03	)
Thallium	NA	=	(	1.04E+00	×	1E-06	×	52	×	12	×	1	×	4,373	×	0.1	×	NA	)	÷	(	47	×	4,380	×	8.00E-04	)
Vanadium	NA	=	(	3.66E+01	×	1E-06	×	52	×	12	×	1	×	4,373	×	0.1	×	NA	)	÷	(	47	×	4,380	×	1.82E-04	)
Zinc	NA	=	(	4.61E+02	×	1E-06	×	52	×	12	×	1	×	4,373	×	0.1	×	NA	)	÷	(	47	×	4,380	×	3.00E-01	)
Benzo(a)anthracene	NA	=	(	3.60E+00	×	1E-06	×	52	×	12	×	1	×	4,373	×	0.1	×	1.30E-01	)	÷	(	47	×	4,380	×	NV	)
Benzo(a)pyrene	NA	=	(	7.10E+00	×	1E-06	×	52	×	12	×	1	×	4,373	×	0.1	×	1.30E-01	)	÷	(	47	×	4,380	×	NV	)
Benzo(b)fluoranthene	NA	=	(	6.85E+00	×	1E-06	×	52	×	12	×	1	×	4,373	×	0.1	×	1.30E-01	)	÷	(	47	×	4,380	×	NV	)
Benzo(k)fluoranthene	NA	=	(	1.93E+00	×	1E-06	×	52	×	12	×	1	×	4,373	×	0.1	×	1.30E-01	)	÷	(	47	×	4,380	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	=	(	4.72E+00	×	1E-06	×	52	×	12	×	1	×	4,373	×	0.1	×	1.30E-01	)	÷	(	47	×	4,380	×	NV	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Soil Concentration
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
ABSd – Dermal Soil Absorption Factor
BW – Body Weight
ATn – Averaging time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo ×ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.
SSAF – Soil-to-skin Adherence Factor

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment D

Table 9a
Risk Calculations: Reasonable Maximum Exposure
Recreational Adolescent: Inhalation of Soil -Derived Chemicals Pathway– Carcinogenic Effects

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFI} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times [(1/\text{VF}) + (1/\text{PEF})])}{(\text{BW} \times \text{ATc})}$$

Equation	Inh - Risk	=	(	Csoil	×	SFi	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	)	÷	(	BW	×	ATc	)
Units	unitless			mg/kg		kg-day/mg		m³/hour		hours/day		days/year		year					m³/kg				m³/kg					kg		days	
Aluminum	NA	=	(	9.53E+03	×	NV	×	1.00	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	)	+	(	47	×	25,550	)
Arsenic	6.52E-11	=	(	5.48E+00	×	1.51E+01	×	1.00	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	)	+	(	47	×	25,550	)
Cadmium	6.74E-12	=	(	1.35E+00	×	6.30E+00	×	1.00	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	)	+	(	47	×	25,550	)
Iron	NA	=	(	2.55E+04	×	NV	×	1.00	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	)	+	(	47	×	25,550	)
Lead	NA	=	(	1.08E+02	×	a	×	1.00	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	)	+	(	47	×	25,550	)
Manganese	NA	=	(	3.47E+02	×	NV	×	1.00	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	)	+	(	47	×	25,550	)
Thallium	NA	=	(	1.04E+00	×	NV	×	1.00	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	)	+	(	47	×	25,550	)
Vanadium	NA	=	(	3.66E+01	×	NV	×	1.00	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	)	+	(	47	×	25,550	)
Zinc	NA	=	(	4.61E+02	×	NV	×	1.00	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	)	+	(	47	×	25,550	)
Benzo(a)anthracene	NA	=	(	3.60E+00	×	NV	×	1.00	×	2	×	52	×	12	×	[	1	/	NC	+	1	/	1.32E+09	]	)	+	(	47	×	25,550	)
Benzo(a)pyrene	1.73E-11	=	(	7.10E+00	×	3.08E+00	×	1.00	×	2	×	52	×	12	×	[	1	/	NC	+	1	/	1.32E+09	]	)	+	(	47	×	25,550	)
Benzo(b)fluoranthene	NA	=	(	6.85E+00	×	NV	×	1.00	×	2	×	52	×	12	×	[	1	/	NC	+	1	/	1.32E+09	]	)	+	(	47	×	25,550	)
Benzo(k)fluoranthene	NA	=	(	1.93E+00	×	NV	×	1.00	×	2	×	52	×	12	×	[	1	/	NC	+	1	/	1.32E+09	]	)	+	(	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	NA	=	(	4.72E+00	×	NV	×	1.00	×	2	×	52	×	12	×	[	1	/	NC	+	1	/	1.32E+09	]	)	+	(	47	×	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Soil Concentration
SFi – Inhalation Slope Factor
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VF – Volatilization Factor
PEF – Particulate Emission Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 9b
Risk Calculations: Reasonable Maximum Exposure
Recreational Adolescent: Inhalation of Soil-Derived Chemicals Pathway – Noncarcinogenic Effects

$$\text{Inh - HQ} = \frac{(Csoil \times IR \times ET \times EF \times ED \times ([1/VF] + [1/PEF]))}{(BW \times ATn \times RfDi)}$$

Equation	Inh - HQ	=	(	Csoil	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	+	(	BW	×	ATn	×	RfDi [b]	)
Units	unitless			mg/kg		m³/hour		hours/day		days/year		year					m³/kg				m³/kg				kg		days		mg/kg-day	
Links Only	NA	=	(	–	×	1	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	47	×	4,380	×	1.43E-03	)
Aluminum	3.07E-05	=	(	9.53E+03	×	1	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	47	×	4,380	×	1.43E-03	)
Arsenic	NA	=	(	5.48E+00	×	1	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	47	×	4,380	×	NV	)
Cadmium	2.40E-08	=	(	1.35E+00	×	1	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	47	×	4,380	×	2.60E-04	)
Iron	NA	=	(	2.55E+04	×	1	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	47	×	4,380	×	NV	)
Lead	NA	=	(	1.08E+02	×	1	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	47	×	4,380	×	a	)
Manganese	1.12E-04	=	(	3.47E+02	×	1	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	47	×	4,380	×	1.43E-05	)
Thallium	NA	=	(	1.04E+00	×	1	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	47	×	4,380	×	NV	)
Vanadium	NA	=	(	3.66E+01	×	1	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	47	×	4,380	×	NV	)
Zinc	NA	=	(	4.61E+02	×	1	×	2	×	52	×	12	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	47	×	4,380	×	NV	)
Benzo(a)anthracene	NA	=	(	3.60E+00	×	1	×	2	×	52	×	12	×	[	1	/	NC	+	1	/	1.32E+09	]	+	(	47	×	4,380	×	NV	)
Benzo(a)pyrene	NA	=	(	7.10E+00	×	1	×	2	×	52	×	12	×	[	1	/	NC	+	1	/	1.32E+09	]	+	(	47	×	4,380	×	NV	)
Benzo(b)fluoranthene	NA	=	(	6.85E+00	×	1	×	2	×	52	×	12	×	[	1	/	NC	+	1	/	1.32E+09	]	+	(	47	×	4,380	×	NV	)
Benzo(k)fluoranthene	NA	=	(	1.93E+00	×	1	×	2	×	52	×	12	×	[	1	/	NC	+	1	/	1.32E+09	]	+	(	47	×	4,380	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	=	(	4.72E+00	×	1	×	2	×	52	×	12	×	[	1	/	NC	+	1	/	1.32E+09	]	+	(	47	×	4,380	×	NV	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Csoil – *Soil Concentration*
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VF – Volatilization Factor
PEF – Particulate Emission Factor
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment D

Table 9c
Recreational Scenario: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} \times \frac{(3.14 \times D_A \times T)^{1/2}}{(2 \times \rho_b \times D_A)} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} $(g/m^2\text{-}s)/(kg/m^3)$	π	D_A (cm^2/s)	T (s)	2	ρb (g/cm^3)	10^{-4} (m^2/cm^2)	VF (m^2/kg)
Benzo(a)anthracene	73.32	3.14	NC	3.78E+08	2	1.38	1.00E-04	NC
Benzo(a)pyrene	73.32	3.14	NC	3.78E+08	2	1.38	1.00E-04	NC
Benzo(b)fluoranthene	73.32	3.14	NC	3.78E+08	2	1.38	1.00E-04	NC
Benzo(k)fluoranthene	73.32	3.14	NC	3.78E+08	2	1.38	1.00E-04	NC
Indeno(1,2,3-cd)pyrene	73.32	3.14	NC	3.78E+08	2	1.38	1.00E-04	NC

Notes: Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

VF – NA

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source $(g/m^2\text{-}s)/(kg/m^3)$(Value used is for Minneapolis, MN.)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T – Exposure interval (s)

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated; PAHs are not considered volatile chemicals

Attachment D

Table 9d
Recreational Scenario: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical Units	VOC?	θa (Lair /Lsoil)	Di (cm^2/s)	H' unitless	θw (Lwater /Lsoil)	Dw (cm^2/s)	η (Lpore /Lsoil)	ρb (g/cm^3)	ρs (g/cm^3)	Kd (cm^3/g)	D_A (cm^2/s)
Benzo(a)anthracene	No	3.29E-01	5.10E-02	4.91E-04	0.15	9.00E-06	4.79E-01	1.38	2.65	1.39E+03	NC
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Benzo(b)fluoranthene	No	3.29E-01	2.26E-02	2.69E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.82E+03	NC
Benzo(k)fluoranthene	No	3.29E-01	4.90E-02	1.35E-05	0.15	5.65E-05	4.79E-01	1.38	2.65	1.61E+04	NC
Indeno(1,2,3-cd)pyrene	No	3.29E-01	1.90E-02	1.42E-05	0.15	5.66E-06	4.79E-01	1.38	2.65	1.61E+04	NC

Notes:

NA – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User's Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density
Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm^3 /g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)
VOC? – Volatile organic compounds; If no, an apparent diffusivity was not calculated.
NV – no value available
NC – not calculated

Attachment D

Table 10a
Risk Calculations: Reasonable Maximum Exposure
Recreational Child: Incidental Ingestion of Soil Pathway – Carcinogenic Effects

$$\text{Ing-Risk} = \frac{(\text{Csoil} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	=	(	Csoil	×	SFo	×	CF	×	EF	×	ED	×	SIR	×	FI	)	÷	(	BW	×	ATc	)
Units	unitless			mg/kg		kg-day/mg		kg/mg		days/year		years		mg/day		unitless				kg		days	
Aluminum	NA	=	(	9.53E+03	×	NV	×	1E-06	×	52	×	6	×	400	×	0.5	)	÷	(	15	×	25,550	)
Arsenic	1.34E-06	=	(	5.48E+00	×	1.50E+00	×	1E-06	×	52	×	6	×	400	×	0.5	)	÷	(	15	×	25,550	)
Cadmium	NA	=	(	1.35E+00	×	NV	×	1E-06	×	52	×	6	×	400	×	0.5	)	÷	(	15	×	25,550	)
Iron	NA	=	(	2.55E+04	×	NV	×	1E-06	×	52	×	6	×	400	×	0.5	)	÷	(	15	×	25,550	)
Lead	NA	=	(	1.08E+02	×	a	×	1E-06	×	52	×	6	×	400	×	0.5	)	÷	(	15	×	25,550	)
Manganese	NA	=	(	3.47E+02	×	NV	×	1E-06	×	52	×	6	×	400	×	0.5	)	÷	(	15	×	25,550	)
Thallium	NA	=	(	1.04E+00	×	NV	×	1E-06	×	52	×	6	×	400	×	0.5	)	÷	(	15	×	25,550	)
Vanadium	NA	=	(	3.66E+01	×	NV	×	1E-06	×	52	×	6	×	400	×	0.5	)	÷	(	15	×	25,550	)
Zinc	NA	=	(	4.61E+02	×	NV	×	1E-06	×	52	×	6	×	400	×	0.5	)	÷	(	15	×	25,550	)
Benzo(a)anthracene	4.28E-07	=	(	3.60E+00	×	7.30E-01	×	1E-06	×	52	×	6	×	400	×	0.5	)	÷	(	15	×	25,550	)
Benzo(a)pyrene	8.44E-06	=	(	7.10E+00	×	7.30E+00	×	1E-06	×	52	×	6	×	400	×	0.5	)	÷	(	15	×	25,550	)
Benzo(b)fluoranthene	8.15E-07	=	(	6.85E+00	×	7.30E-01	×	1E-06	×	52	×	6	×	400	×	0.5	)	÷	(	15	×	25,550	)
Benzo(k)fluoranthene	2.29E-08	=	(	1.93E+00	×	7.30E-02	×	1E-06	×	52	×	6	×	400	×	0.5	)	÷	(	15	×	25,550	)
Indeno(1,2,3-cd)pyrene	5.61E-07	=	(	4.72E+00	×	7.30E-01	×	1E-06	×	52	×	6	×	400	×	0.5	)	÷	(	15	×	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – Soil Concentration
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 10b
Risk Calculations: Reasonable Maximum Exposure
Recreational Child: Incidental Ingestion of Soil Pathway – Noncarcinogenic Effects

$$\text{Ing - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation	Ing - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATn	×	RfDo [b]	)
Units	unitless		mg/kg		kg/mg		days/year		years		mg/day		unitless		kg		days		mg/kg-day	
Aluminum	1.81E-02	= (	9.53E+03	×	1E-06	×	52	×	6	×	400	×	0.5	) ÷ (	15	×	2,190	×	1.0E+00	)
Arsenic	3.47E-02	= (	5.48E+00	×	1E-06	×	52	×	6	×	400	×	0.5	) ÷ (	15	×	2,190	×	3.0E-04	)
Cadmium	2.57E-03	= (	1.35E+00	×	1E-06	×	52	×	6	×	400	×	0.5	) ÷ (	15	×	2,190	×	1.0E-03	)
Iron	1.61E-01	= (	2.55E+04	×	1E-06	×	52	×	6	×	400	×	0.5	) ÷ (	15	×	2,190	×	3.0E-01	)
Lead	NA	= (	1.08E+02	×	1E-06	×	52	×	6	×	400	×	0.5	) ÷ (	15	×	2,190	×	a	)
Manganese	4.71E-03	= (	3.47E+02	×	1E-06	×	52	×	6	×	400	×	0.5	) ÷ (	15	×	2,190	×	1.4E-01	)
Thallium	2.46E-03	= (	1.04E+00	×	1E-06	×	52	×	6	×	400	×	0.5	) ÷ (	15	×	2,190	×	8.0E-04	)
Vanadium	9.92E-03	= (	3.66E+01	×	1E-06	×	52	×	6	×	400	×	0.5	) ÷ (	15	×	2,190	×	7.0E-03	)
Zinc	2.92E-03	= (	4.61E+02	×	1E-06	×	52	×	6	×	400	×	0.5	) ÷ (	15	×	2,190	×	3.0E-01	)
Benzo(a)anthracene	NA	= (	3.60E+00	×	1E-06	×	52	×	6	×	400	×	0.5	) ÷ (	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	= (	7.10E+00	×	1E-06	×	52	×	6	×	400	×	0.5	) ÷ (	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	= (	6.85E+00	×	1E-06	×	52	×	6	×	400	×	0.5	) ÷ (	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.93E+00	×	1E-06	×	52	×	6	×	400	×	0.5	) ÷ (	15	×	2,190	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	= (	4.72E+00	×	1E-06	×	52	×	6	×	400	×	0.5	) ÷ (	15	×	2,190	×	NV	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment D

Table 11a
Risk Calculations: Reasonable Maximum Exposure
Recreational Child: Dermal Contact with Soil Pathway – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATc})}$$

Equation	Derm - Risk	= (	Csoil	×	SFabs	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless		kg		days	
Aluminum	NA	= (	9.53E+03	×	NV	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	25,550	)
Arsenic	1.18E-07	= (	5.48E+00	×	1.58E+00	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	3.00E-02	) ÷ (	15	×	25,550	)
Cadmium	NA	= (	1.35E+00	×	NV	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	1.00E-03	) ÷ (	15	×	25,550	)
Iron	NA	= (	2.55E+04	×	NV	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	25,550	)
Lead	NA	= (	1.08E+02	×	NV	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	25,550	)
Manganese	NA	= (	3.47E+02	×	NV	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	25,550	)
Thallium	NA	= (	1.04E+00	×	NV	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	25,550	)
Vanadium	NA	= (	3.66E+01	×	NV	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	25,550	)
Zinc	NA	= (	4.61E+02	×	NV	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	25,550	)
Benzo(a)anthracene	1.56E-07	= (	3.60E+00	×	7.30E-01	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	25,550	)
Benzo(a)pyrene	3.07E-06	= (	7.10E+00	×	7.30E+00	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	25,550	)
Benzo(b)fluoranthene	2.96E-07	= (	6.85E+00	×	7.30E-01	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	25,550	)
Benzo(k)fluoranthene	8.34E-09	= (	1.93E+00	×	7.30E-02	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	25,550	)
Indeno(1,2,3-cd)pyrene	2.04E-07	= (	4.72E+00	×	7.30E-01	×	1E-06	×	52	×	6	×	1	×	2800	×	0.2	×	1.30E-01	) ÷ (	15	×	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csoil – Soil Concentration
SFabs – Absorbed slope factor (SFo + ABSgi)
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
SSAF – Soil-to-skin Adherence Factor
ABSd – Dermal Soil Absorption Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 11b
Risk Calculations: Reasonable Maximum Exposure
Recreational Child: Dermal Contact with Soil Pathway – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATn} \times \text{RfDabs})}$$

Equation	Derm - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) ÷ (	BW	×	ATn	×	RfDabs (b)	)
Units	unitless		mg/kg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless		kg		days		mg/kg-day	
Aluminum	NA	= (	9.53E+03	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	NV	)
Arsenic	3.07E-03	= (	5.48E+00	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	3.00E-02	) ÷ (	15	×	2,190	×	2.85E-04	)
Cadmium	2.88E-04	= (	1.35E+00	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	1.00E-03	) ÷ (	15	×	2,190	×	2.50E-05	)
Iron	NA	= (	2.55E+04	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	NV	)
Lead	NA	= (	1.08E+02	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	NV	)
Manganese	NA	= (	3.47E+02	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	5.60E-03	)
Thallium	NA	= (	1.04E+00	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	8.00E-04	)
Vanadium	NA	= (	3.66E+01	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	1.82E-04	)
Zinc	NA	= (	4.61E+02	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	3.00E-01	)
Benzo(a)anthracene	NA	= (	3.60E+00	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	= (	7.10E+00	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	= (	6.85E+00	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.93E+00	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	= (	4.72E+00	×	1E-06	×	52	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Soil Concentration
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
ABSd – Dermal Soil Absorption Factor
BW – Body Weight
ATn – Averaging time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo ×ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.
SSAF – Soil-to-skin Adherence Factor

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment D

Table 12a
Risk Calculations: Reasonable Maximum Exposure
Recreational Child: Inhalation of Soil -Derived Chemicals Pathway– Carcinogenic Effects

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times [(1/\text{VF}) + (1/\text{PEF})])}{(\text{BW} \times \text{ATc})}$$

Equation	Inh - Risk	=	(	Csoil	×	SFi	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	)	÷	(	BW	×	ATc	)
Units	unitless			mg/kg		kg-day/mg		m^3/hour		hours/day		days/year		year					m^3/kg				m^3/kg					kg		days	
Links Only	NA	=	(	1	×	NV	×	1.20	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	15	×	25,550	)
Aluminum	NA	=	(	9.53E+03	×	NV	×	1.20	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	15	×	25,550	)
Arsenic	1.23E-10	=	(	5.48E+00	×	1.51E+01	×	1.20	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	15	×	25,550	)
Cadmium	1.27E-11	=	(	1.35E+00	×	6.30E+00	×	1.20	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	15	×	25,550	)
Iron	NA	=	(	2.55E+04	×	NV	×	1.20	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	15	×	25,550	)
Lead	NA	=	(	1.08E+02	×	a	×	1.20	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	15	×	25,550	)
Manganese	NA	=	(	3.47E+02	×	NV	×	1.20	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	15	×	25,550	)
Thallium	NA	=	(	1.04E+00	×	NV	×	1.20	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	15	×	25,550	)
Vanadium	NA	=	(	3.66E+01	×	NV	×	1.20	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	15	×	25,550	)
Zinc	NA	=	(	4.61E+02	×	NV	×	1.20	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	)	÷	(	15	×	25,550	)
Benzo(a)anthracene	NA	=	(	3.60E+00	×	NV	×	1.20	×	2	×	52	×	6	×	[	1	/	NC	+	1	/	1.32E+09	]	)	÷	(	15	×	25,550	)
Benzo(a)pyrene	3.25E-11	=	(	7.10E+00	×	3.08E+00	×	1.20	×	2	×	52	×	6	×	[	1	/	NC	+	1	/	1.32E+09	]	)	÷	(	15	×	25,550	)
Benzo(b)fluoranthene	NA	=	(	6.85E+00	×	NV	×	1.20	×	2	×	52	×	6	×	[	1	/	NC	+	1	/	1.32E+09	]	)	÷	(	15	×	25,550	)
Benzo(k)fluoranthene	NA	=	(	1.93E+00	×	NV	×	1.20	×	2	×	52	×	6	×	[	1	/	NC	+	1	/	1.32E+09	]	)	÷	(	15	×	25,550	)
Indeno(1,2,3-cd)pyrene	NA	=	(	4.72E+00	×	NV	×	1.20	×	2	×	52	×	6	×	[	1	/	NC	+	1	/	1.32E+09	]	)	÷	(	15	×	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Soil Concentration
SFi – Inhalation Slope Factor
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

VF – Volatilization Factor
PEF – Particulate Emission Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated

Attachment D

Table 12b
Risk Calculations: Reasonable Maximum Exposure
Recreational Child: Inhalation of Soil-Derived Chemicals Pathway – Noncarcinogenic Effects

$$Inh\text{-}HQ = \frac{(Csoil \times IR \times ET \times EF \times ED \times ([1/VF] + [1/PEF]))}{(BW \times ATn \times RfDi)}$$

Equation	Inh - HQ	=	(	Csoil	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	+	(	BW	×	ATn	×	RfDi [b]	)
Units	unitless			mg/kg		m³/hour		hours/day		days/year		year					m³/kg				m³/kg				kg		days		mg/kg-day	
Links Only	NA	=	(	–	×	1.2	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	15	×	2,190	×	1.43E-03	)
Aluminum	1.16E-04	=	(	9.53E+03	×	1.2	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	15	×	2,190	×	1.43E-03	)
Arsenic	NA	=	(	5.48E+00	×	1.2	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	15	×	2,190	×	NV	)
Cadmium	9.03E-08	=	(	1.35E+00	×	1.2	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	15	×	2,190	×	2.60E-04	)
Iron	NA	=	(	2.55E+04	×	1.2	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	15	×	2,190	×	NV	)
Lead	NA	=	(	1.08E+02	×	1.2	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	15	×	2,190	×	a	)
Manganese	4.21E-04	=	(	3.47E+02	×	1.2	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	15	×	2,190	×	1.43E-05	)
Thallium	NA	=	(	1.04E+00	×	1.2	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	15	×	2,190	×	NV	)
Vanadium	NA	=	(	3.66E+01	×	1.2	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	15	×	2,190	×	NV	)
Zinc	NA	=	(	4.61E+02	×	1.2	×	2	×	52	×	6	×	[	1	/	NA	+	1	/	1.32E+09	]	+	(	15	×	2,190	×	NV	)
Benzo(a)anthracene	NA	=	(	3.60E+00	×	1.2	×	2	×	52	×	6	×	[	1	/	NC	+	1	/	1.32E+09	]	+	(	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	=	(	7.10E+00	×	1.2	×	2	×	52	×	6	×	[	1	/	NC	+	1	/	1.32E+09	]	+	(	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	=	(	6.85E+00	×	1.2	×	2	×	52	×	6	×	[	1	/	NC	+	1	/	1.32E+09	]	+	(	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	=	(	1.93E+00	×	1.2	×	2	×	52	×	6	×	[	1	/	NC	+	1	/	1.32E+09	]	+	(	15	×	2,190	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	=	(	4.72E+00	×	1.2	×	2	×	52	×	6	×	[	1	/	NC	+	1	/	1.32E+09	]	+	(	15	×	2,190	×	NV	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Csoil – Soil Concentration
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VF – Volatilization Factor
PEF – Particulate Emission Factor
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment D

Table 12c
Recreational Scenario: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} \times \frac{(3.14 \times D_A \times T)^{1/2}}{(2 \times \rho_b \times D_A)} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} $(g/m^2\text{-}s)/(kg/m^3)$	π	D_A (cm^2/s)	T (s)	2	ρb (g/cm^3)	10^{-4} (m^2/cm^2)	VF (m^3/kg)
Benzo(a)anthracene	73.32	3.14	NC	1.89E+08	2	1.38	1.00E-04	NC
Benzo(a)pyrene	73.32	3.14	NC	1.89E+08	2	1.38	1.00E-04	NC
Benzo(b)fluoranthene	73.32	3.14	NC	1.89E+08	2	1.38	1.00E-04	NC
Benzo(k)fluoranthene	73.32	3.14	NC	1.89E+08	2	1.38	1.00E-04	NC
Indeno(1,2,3-cd)pyrene	73.32	3.14	NC	1.89E+08	2	1.38	1.00E-04	NC

Notes: *Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).*

VF – Volatilization Factor (m^3/kg) (calculated)

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source $(g/m^2\text{-}s)/(kg/m^3)$(*Value used is for Minneapolis, MN.*)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T – Exposure interval (s)

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated; PAHs are not considered volatile chemicals

Attachment D

Table 12d
Recreational Scenario: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical	VOC?	θa	Di	H'	θw	Dw	η	ρb	ρs	Kd	D_A
Units		(Lair /Lsoil)	(cm^2/s)	unitless	(Lwater /Lsoil)	(cm^2/s)	(Lpore /Lsoil)	(g/cm^3)	(g/cm^3)	(cm^3/g)	(cm^2/s)
Benzo(a)anthracene	No	3.29E-01	5.10E-02	4.91E-04	0.15	9.00E-06	4.79E-01	1.38	2.65	1.39E+03	NC
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Benzo(b)fluoranthene	No	3.29E-01	2.26E-02	2.69E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.82E+03	NC
Benzo(k)fluoranthene	No	3.29E-01	2.26E-02	2.39E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Indeno(1,2,3-cd)pyrene	No	3.29E-01	1.90E-02	1.42E-05	0.15	5.66E-06	4.79E-01	1.38	2.65	1.61E+04	NC

Notes:

D_A – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's Law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User's Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density
Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm^3 /g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)
VOC? – Volatile organic compounds; If no, an apparent diffusivity was not calculated.
NV – no value available
NC – not calculated

Attachment D

Table 13a
Risk Calculations
Adult Swimmer: Incidental Ingestion of Sediment Pathway – Carcinogenic Effects

$$Ing\text{-}Risk = \frac{(Csediment \times SFo \times CF \times EF \times ET \times ED \times SIR \times FI)}{(BW \times ATc)}$$

Equation	Ing - Risk	= (	Csediment	×	SFo	×	CF	×	EF	×	ET	×	ED	×	SIR	×	FI	) + (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		events/year		hour/event		years		mg/hour		unitless		kg		days	
Iron	NA	= (	2.70E+04	×	NV	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
Manganese	NA	= (	3.00E+02	×	NV	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
Vanadium	NA	= (	9.70E+00	×	NV	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
1-Methylnaphthalene	NA	= (	1.90E+01	×	NV	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	5.46E+02	×	NV	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
Acenaphthene	NA	= (	1.85E+02	×	NV	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
Benzo(a)anthracene	1.63E-09	= (	3.96E+01	×	7.30E-01	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
Benzo(a)pyrene	1.18E-08	= (	2.86E+01	×	7.30E+00	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
Benzo(b)fluoranthene	6.19E-10	= (	1.50E+01	×	7.30E-01	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
Benzo(k)fluoranthene	7.87E-11	= (	1.91E+01	×	7.30E-02	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
Chrysene	1.45E-11	= (	3.53E+01	×	7.30E-03	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
Dibenzo(a,h)anthracene	7.82E-10	= (	1.90E+00	×	7.30E+00	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
Fluoranthene	NA	= (	8.65E+01	×	NV	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
Fluorene	NA	= (	1.13E+02	×	NV	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	2.18E-10	= (	5.30E+00	×	7.30E-01	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
Naphthalene	NA	= (	5.73E+02	×	NV	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
Pyrene	NA	= (	1.10E+02	×	NV	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
Methylene chloride	5.49E-12	= (	1.30E+01	×	7.50E-03	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)
Xylenes (total)	NA	= (	1.03E+01	×	NV	×	0.000001	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csediment – Concentration in sediment
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Sediment Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable

Attachment D

Table 13b
Risk Calculations
Adult Swimmer: Incidental Ingestion of Sediment Pathway – Noncarcinogenic Effects

$$Ing\text{-}HQ = \frac{(Csediment \times CF \times EF \times ET \times ED \times SIR \times FI)}{(BW \times ATn \times RfDo)}$$

Equation	Ing - HQ	= (	Csediment	×	CF	×	EF	×	ET	×	ED	×	SIR	×	FI	) + (	BW	×	ATn	×	RfDo	)
Units	unitless		mg/kg		kg/mg		event/year		hours/event		years		mg/hour		unitless		kg		days		mg/kg-day	
Iron	1.18E-05	= (	2.70E+04	×	1E-06	×	12	×	1	×	30	×	0.280	×	1	) + (	70	×	10,950	×	3.0E-01	)
Manganese	8.45E-07	= (	3.00E+02	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	4.7E-02	)
Vanadium	1.28E-06	= (	9.70E+00	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	1.0E-03	)
1-Methylnaphthalene	NA	= (	1.90E+01	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	NV	)
2-Methylnaphthalene	1.80E-05	= (	5.46E+02	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	4.0E-03	)
Acenaphthene	4.05E-07	= (	1.85E+02	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	6.0E-02	)
Benzo(a)anthracene	NA	= (	3.96E+01	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	NV	)
Benzo(a)pyrene	NA	= (	2.86E+01	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.50E+01	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.91E+01	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	NV	)
Chrysene	NA	= (	3.53E+01	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.90E+00	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	NV	)
Fluoranthene	2.84E-07	= (	8.65E+01	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	4.0E-02	)
Fluorene	3.70E-07	= (	1.13E+02	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	4.0E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	5.30E+00	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	NV	)
Naphthalene	3.77E-06	= (	5.73E+02	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	2.0E-02	)
Pyrene	4.8E-07	= (	1.10E+02	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	3.0E-02	)
Methylene chloride	2.8E-08	= (	1.30E+01	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	6.0E-02	)
Xylenes (total)	6.8E-09	= (	1.03E+01	×	1E-06	×	12	×	1	×	30	×	0.28	×	1	) + (	70	×	10,950	×	2.0E-01	)

Notes:

Ing - HQ – Ingestion Hazard
Csediment – *Concentration in sediment*
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Sediment Ingestion Rate
ET – Exposure Time
FI – Fraction Ingested from Contaminated Source
BW – *Body Weight*
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose
NV – No toxicity value available for this pathway.
NA – Not Applicable

Attachment D

Table 14a
Risk Calculations
Adult Swimmer: Incidental Dermal Contact with Sediment Pathway – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csediment} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATc})}$$

Equation / Units	Derm - Risk unitless	= (	Csediment mg/kg	×	SFabs kg-day/mg	×	CF kg/mg	×	EF days/year	×	ED years	×	EV events/day	×	SA cm²	×	SSAF mg/cm²-event	×	ABSd unitless	) ÷ (	BW kg	×	ATc days	)
Iron	NA	= (	2.70E+04	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	NA	) ÷ (	70	×	25,550	)
Manganese	NA	= (	3.00E+02	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	NA	) ÷ (	70	×	25,550	)
Vanadium	NA	= (	9.70E+00	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	NA	) ÷ (	70	×	25,550	)
1-Methylnaphthalene	NA	= (	1.90E+01	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	5.46E+02	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.00E-01	) ÷ (	70	×	25,550	)
Acenaphthene	NA	= (	1.85E+02	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(a)anthracene	4.29E-06	= (	3.96E+01	×	7.30E-01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	3.10E-05	= (	2.86E+01	×	7.30E+00	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	1.63E-06	= (	1.50E+01	×	7.30E-01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	2.07E-07	= (	1.91E+01	×	7.30E-02	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Chrysene	3.83E-08	= (	3.53E+01	×	7.30E-03	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	2.06E-06	= (	1.90E+00	×	7.30E+00	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	8.65E+01	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	1.13E+02	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	5.74E-07	= (	5.30E+00	×	7.30E-01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	5.73E+02	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	1.10E+02	×	NV	×	1E-06	×	12		30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Methylene chloride	NA	= (	1.30E+01	×	7.50E-03	×	1E-06	×	12		30	×	1	×	5,672	×	1	×	NA	) ÷ (	70	×	25,550	)
Xylenes (total)	NA	= (	1.03E+01	×	NV	×	1E-06	×	12		30	×	1	×	5,672	×	1	×	NA	) ÷ (	70	×	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csediment – Concentration in Sediment
SFabs – Absorbed slope factor (SFo ÷ ABSgi)
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
SSAF – Sediment-to-skin Adherence Factor
ABSd – Dermal Sediment Absorption Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment D

Table 14b
Risk Calculations
Adult Swimmer: Incidental Dermal Contact with Sediment Pathway – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csediment} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATn} \times \text{RfDabs})}$$

Equation / Units	Derm - HQ unitless	=	Csediment mg/kg	×	CF kg/mg	×	EF days/year	×	ED years	×	EV events/day	×	SA cm^2	×	SSAF mg/cm^2-event	×	ABSd unitless	÷	BW kg	×	ATn days	×	RfDabs mg/kg-day
Iron	NA	=	2.70E+04	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	NA	÷	70	×	10,950	×	NV
Manganese	NA	=	3.00E+02	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	NA	÷	70	×	10,950	×	1.87E-03
Vanadium	NA	=	9.70E+00	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	NA	÷	70	×	10,950	×	2.60E-05
1-Methylnaphthalene	NA	=	1.90E+01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	NV
2-Methylnaphthalene	3.64E-02	=	5.46E+02	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.00E-01	÷	70	×	10,950	×	4.00E-03
Acenaphthene	1.07E-03	=	1.85E+02	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	6.00E-02
Benzo(a)anthracene	NA	=	3.96E+01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	NV
Benzo(a)pyrene	NA	=	2.86E+01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	NV
Benzo(b)fluoranthene	NA	=	1.50E+01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	NV
Benzo(k)fluoranthene	NA	=	1.91E+01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	NV
Chrysene	NA	=	3.53E+01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	NV
Dibenzo(a,h)anthracene	NA	=	1.90E+00	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	NV
Fluoranthene	7.49E-04	=	8.65E+01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	4.00E-02
Fluorene	9.75E-04	=	1.13E+02	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	4.00E-02
Indeno(1,2,3-cd)pyrene	NA	=	5.30E+00	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	NV
Naphthalene	9.92E-03	=	5.73E+02	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	2.00E-02
Pyrene	3.81E-05	=	1.10E+02	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	3.00E-02
Methylene chloride	NA	=	1.30E+01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	NA	÷	70	×	10,950	×	6.00E-02
Xylenes (total)	NA	=	1.03E+01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	NA	÷	70	×	10,950	×	2.00E-01

Notes:

Derm - HQ – Dermal Hazard Quotient
Csediment – Concentration in Sediment
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
ABSd – Dermal Sediment Absorption Factor
BW – Body Weight
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo ×ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.
SSAF – Sediment-to-skin Adherence Factor

Attachment D

Table 15a
Risk Calculations
Adolescent Swimmer: Incidental Ingestion of Sediment Pathway – Carcinogenic Effects

$$Ing\text{-}Risk = \frac{(Csediment \times SFo \times CF \times EF \times ET \times ED \times SIR \times FI)}{(BW \times ATc)}$$

Equation Units	Ing - Risk unitless	= (	Csediment mg/kg	×	SFo kg-day/mg	×	CF kg/mg	×	EF event/year	×	ET hours/event	×	ED years	×	SIR mg/hour	×	FI unitless	) + (	BW kg	×	ATc days	)
Iron	NA	= (	2.70E+04	×	NV	×	1.E-06	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
Manganese	NA	= (	3.00E+02	×	NV	×	1.E-06	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
Vanadium	NA	= (	9.70E+00	×	NV	×	1.E-06	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
1-Methylnaphthalene	NA	= (	1.90E+01	×	NV	×	1.E-06	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
2-Methylnaphthalene	NA	= (	5.46E+02	×	NV	×	1.E-06	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
Acenaphthene	NA	= (	1.85E+02	×	NV	×	1.E-06	×	12	×	1	×	12	×	0.00	×	1	) + (	47	×	25,550	)
Benzo(a)anthracene	9.70E-10	= (	3.96E+01	×	7.30E-01	×	1.E-06	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
Benzo(a)pyrene	7.01E-09	= (	2.86E+01	×	7.30E+00	×	1.E-06	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
Benzo(b)fluoranthene	3.69E-10	= (	1.50E+01	×	7.30E-01	×	1.E-06	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
Benzo(k)fluoranthene	4.69E-11	= (	1.91E+01	×	7.30E-02	×	1.E-06	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
Chrysene	8.66E-12	= (	3.53E+01	×	7.30E-03	×	1.E-06	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
Dibenzo(a,h)anthracene	4.66E-10	= (	1.90E+00	×	7.30E+00	×	1.E-06	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
Fluoranthene	NA	= (	8.65E+01	×	NV	×	1.E-06	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
Fluorene	NA	= (	1.13E+02	×	NV	×	1.E-06	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.30E-10	= (	5.30E+00	×	7.30E-01	×	1.E-06	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
Naphthalene	NA	= (	5.73E+02	×	NV	×	1.E-06	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
Pyrene	NA	= (	1.10E+02	×	NV	×	0.000001	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
Methylene chloride	3.27E-12	= (	1.30E+01	×	7.50E-03	×	0.000001	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)
Xylenes (total)	NA	= (	1.03E+01	×	NV	×	0.000001	×	12	×	1	×	12	×	0.28	×	1	) + (	47	×	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csediment – Concentration in sediment
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
ET – Exposure Time
ED – Exposure Duration
SIR – Sediment Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable

Attachment D

Table 15b
Risk Calculations
Adolescent Swimmer: Incidental Ingestion of Sediment Pathway – Noncarcinogenic Effects

$$\text{Ing - HQ} = \frac{(\text{Csediment} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation	Ing - HQ	= (	Csediment	×	CF	×	EF	×	ED	×	ET	×	SIR	×	FI	) + (	BW	×	ATn	×	RfDo	)
Units	unitless		mg/kg		kg/mg		events/year		years		hours/event		mg/hour		unitless		kg		days		mg/kg-day	
Iron	1.76E-05	= (	2.70E+04	×	1E-06	×	12	×	12	×	1	×	0.28	×	1.00	) + (	47	×	4,380	×	3.0E-01	)
Manganese	1.26E-06	= (	3.00E+02	×	1E-06	×	12	×	12	×	1	×	0.28	×	1.00	) + (	47	×	4,380	×	4.7E-02	)
Vanadium	1.90E-06	= (	9.70E+00	×	1E-06	×	12	×	12	×	1	×	0.28	×	1.00	) + (	47	×	4,380	×	1.0E-03	)
1-Methylnaphthalene	NA	= (	1.90E+01	×	1E-06	×	12	×	12	×	1	×	0.28	×	1.00	) + (	47	×	4,380	×	NV	)
2-Methylnaphthalene	2.67E-05	= (	5.46E+02	×	1E-06	×	12	×	12	×	1	×	0.28	×	1.00	) + (	47	×	4,380	×	4.0E-03	)
Acenaphthene	0.00E+00	= (	1.85E+02	×	1E-06	×	12	×	12	×	1	×	0.00	×	1.00	) + (	47	×	4,380	×	6.0E-02	)
Benzo(a)anthracene	NA	= (	3.96E+01	×	1E-06	×	12	×	12	×	1	×	0.28	×	1.00	) + (	47	×	4,380	×	NV	)
Benzo(a)pyrene	NA	= (	2.86E+01	×	1E-06	×	12	×	12	×	1	×	0.28	×	1.00	) + (	47	×	4,380	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.50E+01	×	1E-06	×	12	×	12	×	1	×	0.28	×	1.00	) + (	47	×	4,380	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.91E+01	×	1E-06	×	12	×	12	×	1	×	0.28	×	1.00	) + (	47	×	4,380	×	NV	)
Chrysene	NA	= (	3.53E+01	×	1E-06	×	12	×	12	×	1	×	0.28	×	1.00	) + (	47	×	4,380	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.90E+00	×	1E-06	×	12	×	12	×	1	×	0.28	×	1.00	) + (	47	×	4,380	×	NV	)
Fluoranthene	4.24E-07	= (	8.65E+01	×	1E-06	×	12	×	12	×	1	×	0.28	×	1.00	) + (	47	×	4,380	×	4.0E-02	)
Fluorene	5.51E-07	= (	1.13E+02	×	1E-06	×	12	×	12	×	1	×	0.28	×	1.00	) + (	47	×	4,380	×	4.0E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	5.30E+00	×	1E-06	×	12	×	12	×	1	×	0.28	×	1.00	) + (	47	×	4,380	×	NV	)
Naphthalene	5.61E-06	= (	5.73E+02	×	1E-06	×	12	×	12	×	1	×	0.28	×	1.00	) + (	47	×	4,380	×	2.0E-02	)
Pyrene	7.2E-07	= (	1.10E+02	×	1E-06	×	12	×	12		1	×	0.28	×	1.00	) + (	47	×	4,380	×	3.0E-02	)
Methylene chloride	4.2E-08	= (	1.30E+01	×	1E-06	×	12	×	12		1	×	0.28	×	1.00	) + (	47	×	4,380	×	6.0E-02	)
Xylenes (total)	1.0E-08	= (	1.03E+01	×	1E-06	×	12	×	12		1	×	0.28	×	1.00	) + (	47	×	4,380	×	2.0E-01	)

Notes:

Ing - HQ – Ingestion Hazard
Csediment – Concentration in sediment
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Sediment Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose

Attachment D

Table 16a
Risk Calculations
Adolescent Swimmer: Incidental Dermal Contact with Sediment Pathway – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csediment} \times \text{SFabs} \times CF \times EF \times ED \times EV \times SA \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATc})}$$

Equation / Units	Derm - Risk unitless	= (	Csediment mg/kg	×	SFabs kg-day/mg	×	CF kg/mg	×	EF days/year	×	ED years	×	EV events/day	×	SA cm²	×	SSAF mg/cm²-event	×	ABSd unitless	) ÷ (	BW kg	×	ATc days	)
Iron	NA	= (	2.70E+04	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	) ÷ (	47	×	25,550	)
Manganese	NA	= (	3.00E+02	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	) ÷ (	47	×	25,550	)
Vanadium	NA	= (	9.70E+00	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	) ÷ (	47	×	25,550	)
1-Methylnaphthalene	NA	= (	1.90E+01	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	25,550	)
2-Methylnaphthalene	NA	= (	5.46E+02	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.00E-01	) ÷ (	47	×	25,550	)
Acenaphthene	NA	= (	1.85E+02	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	25,550	)
Benzo(a)anthracene	1.82E-06	= (	3.96E+01	×	7.30E-01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	25,550	)
Benzo(a)pyrene	1.32E-05	= (	2.86E+01	×	7.30E+00	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	25,550	)
Benzo(b)fluoranthene	6.93E-07	= (	1.50E+01	×	7.30E-01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	25,550	)
Benzo(k)fluoranthene	8.80E-08	= (	1.91E+01	×	7.30E-02	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	25,550	)
Chrysene	1.63E-08	= (	3.53E+01	×	7.30E-03	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	25,550	)
Dibenzo(a,h)anthracene	8.75E-07	= (	1.90E+00	×	7.30E+00	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	25,550	)
Fluoranthene	NA	= (	8.65E+01	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	25,550	)
Fluorene	NA	= (	1.13E+02	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	2.44E-07	= (	5.30E+00	×	7.30E-01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	25,550	)
Naphthalene	NA	= (	5.73E+02	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	25,550	)
Pyrene	NA	= (	1.10E+02	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	25,550	)
Methylene chloride	NA	= (	1.30E+01	×	7.50E-03	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	) ÷ (	47	×	25,550	)
Xylenes (total)	NA	= (	1.03E+01	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	) ÷ (	47	×	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csediment – Concentration in sediment
SFabs – Absorbed slope factor (SFo + ABSgi)
CF – Conversion factor
EF – Exposure Frequency
ET – Exposure Time
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
SSAF – Sediment-to-skin Adherence Factor
ABSd – Dermal Sediment Absorption Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens

Attachment D

Table 16b
Risk Calculations
Adolescent Swimmer: Incidental Dermal Contact with Sediment Pathway – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csediment} \times EF \times CF \times ED \times EV \times SA \times SSAF \times ABSd)}{(BW \times ATn \times \text{RfDabs})}$$

Equation	Derm - HQ	= (	Csediment	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/kg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless		kg		days		mg/kg-day	
Iron	NA	= (	2.70E+04	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	) + (	47	×	4,380	×	NV	)
Manganese	NA	= (	3.00E+02	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	) + (	47	×	4,380	×	1.87E-03	)
Vanadium	NA	= (	9.70E+00	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	) + (	47	×	4,380	×	2.60E-05	)
1-Methylnaphthalene	NA	= (	1.90E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) + (	47	×	4,380	×	NV	)
2-Methylnaphthalene	3.86E-02	= (	5.46E+02	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.00E-01	) + (	47	×	4,380	×	4.00E-03	)
Acenaphthene	1.13E-03	= (	1.85E+02	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) + (	47	×	4,380	×	6.00E-02	)
Benzo(a)anthracene	NA	= (	3.96E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) + (	47	×	4,380	×	NV	)
Benzo(a)pyrene	NA	= (	2.86E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) + (	47	×	4,380	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.50E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) + (	47	×	4,380	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.91E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) + (	47	×	4,380	×	NV	)
Chrysene	NA	= (	3.53E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) + (	47	×	4,380	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.90E+00	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) + (	47	×	4,380	×	NV	)
Fluoranthene	7.96E-04	= (	8.65E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) + (	47	×	4,380	×	4.00E-02	)
Fluorene	1.04E-03	= (	1.13E+02	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) + (	47	×	4,380	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	5.30E+00	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) + (	47	×	4,380	×	NV	)
Naphthalene	1.05E-02	= (	5.73E+02	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) + (	47	×	4,380	×	2.00E-02	)
Pyrene	4.05E-05	= (	1.10E+02	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) + (	47	×	4,380	×	3.00E-02	)
Methylene chloride	NA	= (	1.30E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	) + (	47	×	4,380	×	6.00E-02	)
Xylenes (total)	NA	= (	1.03E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	) + (	47	×	4,380	×	2.00E-01	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csediment – Concentration in sediment
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
SSAF – Sediment-to-skin Adherence Factor
ABSd – Dermal Sediment Absorption Factor
BW – Body Weight
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo ×ABSgi)

Attachment D

Table 17a
Risk Calculations
Adult Wader: Incidental Ingestion of Sediment Pathway – Carcinogenic Effects

$$\text{Ing-Risk} = \frac{(\text{Csediment} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{ET} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATc})}$$

Equation / Units	Ing - Risk unitless	=	Csediment mg/kg	×	SFo kg-day/mg	×	CF kg/mg	×	EF events/year	×	ET hour/event	×	ED years	×	SIR mg/hour	×	FI unitless	÷	BW kg	×	ATc days
Iron	NA	=	2.70E+04	×	NV	×	1.E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	25,550
Manganese	NA	=	3.00E+02	×	NV	×	1.E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	25,550
Vanadium	NA	=	9.70E+00	×	NV	×	1.E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	25,550
1-Methylnaphthalene	NA	=	1.90E+01	×	NV	×	1.E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	25,550
2-Methylnaphthalene	NA	=	5.46E+02	×	NV	×	1.E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	25,550
Acenaphthene	NA	=	1.85E+02	×	NV	×	1.E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	25,550
Benzo(a)anthracene	3.26E-09	=	3.96E+01	×	7.30E-01	×	1.E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	25,550
Benzo(a)pyrene	2.35E-08	=	2.86E+01	×	7.30E+00	×	1.E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	25,550
Benzo(b)fluoranthene	1.24E-09	=	1.50E+01	×	7.30E-01	×	1.E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	25,550
Benzo(k)fluoranthene	1.57E-10	=	1.91E+01	×	7.30E-02	×	1.E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	25,550
Chrysene	2.91E-11	=	3.53E+01	×	7.30E-03	×	1.E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	25,550
Dibenzo(a,h)anthracene	1.56E-09	=	1.90E+00	×	7.30E+00	×	1.E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	25,550
Fluoranthene	NA	=	8.65E+01	×	NV	×	1.E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	25,550
Fluorene	NA	=	1.13E+02	×	NV	×	1.E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	25,550
Indeno(1,2,3-cd)pyrene	4.36E-10	=	5.30E+00	×	7.30E-01	×	1.E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	25,550
Naphthalene	NA	=	5.73E+02	×	NV	×	1.E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	25,550
Pyrene	NA	=	1.10E+02	×	NV	×	0.000001	×	12	×	2		30	×	0.28	×	1	÷	70	×	25,550
Methylene chloride	5.49E-12	=	1.30E+01	×	7.50E-03	×	0.000001	×	12	×	2		30	×	0.28	×	1	÷	70	×	25,550
Xylenes (total)	NA	=	1.03E+01	×	NV	×	0.000001	×	12	×	2		30	×	0.28	×	1	÷	70	×	25,550

Notes:

Ing - Risk – Ingestion risk
Csediment – Concentration in sediment
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Sediment Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable

Attachment D

Table 17b
Risk Calculations
Adult Wader: Incidental Ingestion of Sediment Pathway – Noncarcinogenic Effects

$$\text{Ing - HQ} = \frac{(\text{Csediment} \times \text{CF} \times \text{EF} \times \text{ET} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation / Units	Ing - HQ unitless	=	Csediment mg/kg	×	CF kg/mg	×	EF days/year	×	ET hours/day	×	ED years	×	SIR mg/hour	×	FI unitless	÷	BW kg	×	ATn days	×	RfDo mg/kg-day
Iron	2.37E-05	=	2.70E+04	×	1E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	10,950	×	3.0E-01
Manganese	8.45E-07	=	3.00E+02	×	1E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	10,950	×	4.7E-02
Vanadium	1.28E-06	=	9.70E+00	×	1E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	10,950	×	1.0E-03
1-Methylphenanthrene	NA	=	1.00E+00	×	1E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	10,950	×	NV
2-Methylnaphthalene	1.80E-05	=	5.46E+02	×	1E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	10,950	×	4.0E-03
Acenaphthene	2.19E-09	=	1.00E+00	×	1E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	10,950	×	6.0E-02
Benzo(a)anthracene	NA	=	3.96E+01	×	1E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	10,950	×	NV
Benzo(a)pyrene	NA	=	2.86E+01	×	1E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	10,950	×	NV
Benzo(b)fluoranthene	NA	=	1.50E+01	×	1E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	10,950	×	NV
Benzo(k)fluoranthene	NA	=	1.91E+01	×	1E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	10,950	×	NV
Chrysene	NA	=	1.00E+00	×	1E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	10,950	×	NV
Dibenzo(a,h)anthracene	NA	=	1.00E+00	×	1E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	10,950	×	NV
Fluoranthene	3.29E-09	=	1.00E+00	×	1E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	10,950	×	4.0E-02
Fluorene	3.29E-09	=	1.00E+00	×	1E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	10,950	×	4.0E-02
Indeno(1,2,3-cd)pyrene	NA	=	5.30E+00	×	1E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	10,950	×	NV
Naphthalene	3.77E-06	=	5.73E+02	×	1E-06	×	12	×	2	×	30	×	0.28	×	1	÷	70	×	10,950	×	2.0E-02
Pyrene	4.8E-07	=	1.10E+02	×	1E-06	×	12		2	×	30	×	0.28	×	1	÷	70	×	10,950	×	3.0E-02
Methylene chloride	2.8E-08	=	1.30E+01	×	1E-06	×	12		2	×	30	×	0.28	×	1	÷	70	×	10,950	×	6.0E-02
Xylenes (total)	6.8E-09	=	1.03E+01	×	1E-06	×	12		2	×	30	×	0.28	×	1	÷	70	×	10,950	×	2.0E-01

Notes:

Ing - HQ – Ingestion Hazard
Csediment – Concentration in sediment
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Sediment Ingestion Rate
ET – Exposure Time
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose
NV – No toxicity value available for this pathway.
NA – Not Applicable

Attachment D

Table 18a
Risk Calculations
Adult Wader: Incidental Dermal Contact with Sediment Pathway – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csediment} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATc})}$$

Equation / Units	Derm - Risk unitless	=	Csediment mg/kg	×	SFabs kg-day/mg	×	CF kg/mg	×	EF days/year	×	ED years	×	EV events/day	×	SA cm²	×	SSAF mg/cm²-event	×	ABSd unitless	) ÷ (	BW kg	×	ATc days	)
Iron	NA	= (	2.70E+04	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	NA	) ÷ (	70	×	25,550	)
Manganese	NA	= (	3.00E+02	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	NA	) ÷ (	70	×	25,550	)
Vanadium	NA	= (	9.70E+00	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	NA	) ÷ (	70	×	25,550	)
1-Methylnaphthalene	NA	= (	1.90E+01	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	5.46E+02	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.00E-01	) ÷ (	70	×	25,550	)
Acenaphthene	NA	= (	1.85E+02	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(a)anthracene	4.29E-06	= (	3.96E+01	×	7.30E-01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	3.10E-05	= (	2.86E+01	×	7.30E+00	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	1.63E-06	= (	1.50E+01	×	7.30E-01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	2.07E-07	= (	1.91E+01	×	7.30E-02	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Chrysene	3.83E-08	= (	3.53E+01	×	7.30E-03	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	2.06E-06	= (	1.90E+00	×	7.30E+00	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	8.65E+01	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	1.13E+02	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	5.74E-07	= (	5.30E+00	×	7.30E-01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	5.73E+02	×	NV	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	1.10E+02	×	NV	×	1E-06	×	12		30	×	1	×	5,672	×	1	×	1.30E-01	) ÷ (	70	×	25,550	)
Methylene chloride	NA	= (	1.30E+01	×	7.50E-03	×	1E-06	×	12		30	×	1	×	5,672	×	1	×	NA	) ÷ (	70	×	25,550	)
Xylenes (total)	NA	= (	1.03E+01	×	NV	×	1E-06	×	12		30	×	1	×	5,672	×	1	×	NA	) ÷ (	70	×	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csediment – Concentration in Sediment
SFabs – Absorbed slope factor (SFo ÷ ABSgi)
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
SSAF – Sediment-to-skin Adherence Factor
ABSd – Dermal Sediment Absorption Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment D

Table 18b
Risk Calculations
Adult Wader: Incidental Dermal Contact with Sediment Pathway – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csediment} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATn} \times \text{RfDabs})}$$

Equation / Units	Derm - HQ unitless	=	Csediment mg/kg	×	CF kg/mg	×	EF days/year	×	ED years	×	EV events/day	×	SA cm²	×	SSAF mg/cm²-event	×	ABSd unitless	÷	BW kg	×	ATn days	×	RfDabs mg/kg-day
Iron	NA	=	2.70E+04	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	NA	÷	70	×	10,950	×	NV
Manganese	NA	=	3.00E+02	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	NA	÷	70	×	10,950	×	1.87E-03
Vanadium	NA	=	9.70E+00	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	NA	÷	70	×	10,950	×	2.60E-05
1-Methylnaphthalene	NA	=	1.90E+01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	NV
2-Methylnaphthalene	3.64E-02	=	5.46E+02	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.00E-01	÷	70	×	10,950	×	4.00E-03
Acenaphthene	1.07E-03	=	1.85E+02	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	6.00E-02
Benzo(a)anthracene	NA	=	3.96E+01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	NV
Benzo(a)pyrene	NA	=	2.86E+01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	NV
Benzo(b)fluoranthene	NA	=	1.50E+01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	NV
Benzo(k)fluoranthene	NA	=	1.91E+01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	NV
Chrysene	NA	=	3.53E+01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	NV
Dibenzo(a,h)anthracene	NA	=	1.90E+00	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	NV
Fluoranthene	7.49E-04	=	8.65E+01	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	4.00E-02
Fluorene	9.75E-04	=	1.13E+02	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	4.00E-02
Indeno(1,2,3-cd)pyrene	NA	=	5.30E+00	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	NV
Naphthalene	9.92E-03	=	5.73E+02	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	2.00E-02
Pyrene	3.46E-07	=	1	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	1.30E-01	÷	70	×	10,950	×	3.00E-02
Methylene chloride	NA	=	1	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	NA	÷	70	×	10,950	×	6.00E-02
Xylenes (total)	NA	=	1	×	1E-06	×	12	×	30	×	1	×	5,672	×	1	×	NA	÷	70	×	10,950	×	2.00E-01

Notes:

Derm - HQ – Dermal Hazard Quotient
Csediment – Concentration in Sediment
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
ABSd – Dermal Sediment Absorption Factor
BW – Body Weight
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo ×ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.
SSAF – Sediment-to-skin Adherence Factor

Attachment D

Table 19a
Risk Calculations
Adolescent Wader: Incidental Ingestion of Sediment Pathway – Carcinogenic Effects

$$\text{Ing-Risk} = \frac{(\text{Csediment} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{ET} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATc})}$$

Equation / Units	Ing - Risk unitless	=	Csediment mg/kg	×	SFo kg-day/mg	×	CF kg/mg	×	EF event/year	×	ET hours/event	×	ED years	×	SIR mg/hour	×	FI unitless	÷	BW kg	×	ATc days
Iron	NA	=	2.70E+04	×	NV	×	1.E-06	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
Manganese	NA	=	3.00E+02	×	NV	×	1.E-06	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
Vanadium	NA	=	9.70E+00	×	NV	×	1.E-06	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
1-Methylnaphthalene	NA	=	1.90E+01	×	NV	×	1.E-06	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
2-Methylnaphthalene	NA	=	5.46E+02	×	NV	×	1.E-06	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
Acenaphthene	NA	=	1.85E+02	×	NV	×	1.E-06	×	12	×	2	×	12	×	0.00	×	1	÷	47	×	25,550
Benzo(a)anthracene	1.94E-09	=	3.96E+01	×	7.30E-01	×	1.E-06	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
Benzo(a)pyrene	1.40E-08	=	2.86E+01	×	7.30E+00	×	1.E-06	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
Benzo(b)fluoranthene	7.38E-10	=	1.50E+01	×	7.30E-01	×	1.E-06	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
Benzo(g,h,i)perylene	NA	=	1.00E+00	×	NV	×	1.E-06	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
Benzo(k)fluoranthene	9.37E-11	=	1.91E+01	×	7.30E-02	×	1.E-06	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
Chrysene	1.73E-11	=	3.53E+01	×	7.30E-03	×	1.E-06	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
Dibenzo(a,h)anthracene	9.31E-10	=	1.90E+00	×	7.30E+00	×	1.E-06	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
Fluoranthene	NA	=	8.65E+01	×	NV	×	1.E-06	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
Fluorene	NA	=	1.13E+02	×	NV	×	1.E-06	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
Indeno(1,2,3-cd)pyrene	2.60E-10	=	5.30E+00	×	7.30E-01	×	1.E-06	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
Naphthalene	NA	=	5.73E+02	×	NV	×	1.E-06	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
Pyrene	NA	=	1.10E+02	×	NV	×	0.000001	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
Methylene chloride	3.27E-12	=	1.30E+01	×	7.50E-03	×	0.000001	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550
Xylenes (total)	NA	=	1.03E+01	×	NV	×	0.000001	×	12	×	2	×	12	×	0.28	×	1	÷	47	×	25,550

Notes:

Ing - Risk – Ingestion risk
Csediment – Concentration in sediment
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
ET – Exposure Time
ED – Exposure Duration
SIR – Sediment Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable

Attachment D

Table 19b
Risk Calculations
Adolescent Wader: Incidental Ingestion of Sediment Pathway – Noncarcinogenic Effects

$$\text{Ing - HQ} = \frac{(\text{Csediment} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation	Ing - HQ	= (	Csediment	×	CF	×	EF	×	ED	×	ET	×	SIR	×	FI	) + (	BW	×	ATn	×	RfDo	)
Units	unitless		mg/kg		kg/mg		events/year		years		hours/event		mg/hour		unitless		kg		days		mg/kg-day	
Iron	3.53E-05	= (	2.70E+04	×	1E-06	×	12	×	12	×	2	×	0.28	×	1	) + (	47	×	4,380	×	3.0E-01	)
Manganese	2.52E-06	= (	3.00E+02	×	1E-06	×	12	×	12	×	2	×	0.28	×	1	) + (	47	×	4,380	×	4.7E-02	)
Vanadium	3.80E-06	= (	9.70E+00	×	1E-06	×	12	×	12	×	2	×	0.28	×	1	) + (	47	×	4,380	×	1.0E-03	)
1-Methylnaphthalene	NA	= (	1.90E+01	×	1E-06	×	12	×	12	×	2	×	0.28	×	1	) + (	47	×	4,380	×	NV	)
2-Methylnaphthalene	5.35E-05	= (	5.46E+02	×	1E-06	×	12	×	12	×	2	×	0.28	×	1	) + (	47	×	4,380	×	4.0E-03	)
Acenaphthene	0.00E+00	= (	1.85E+02	×	1E-06	×	12	×	12	×	2	×	0.00	×	1	) + (	47	×	4,380	×	6.0E-02	)
Benzo(a)anthracene	NA	= (	3.96E+01	×	1E-06	×	12	×	12	×	2	×	0.28	×	1	) + (	47	×	4,380	×	NV	)
Benzo(a)pyrene	NA	= (	2.86E+01	×	1E-06	×	12	×	12	×	2	×	0.28	×	1	) + (	47	×	4,380	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.50E+01	×	1E-06	×	12	×	12	×	2	×	0.28	×	1	) + (	47	×	4,380	×	NV	)
Benzo(g,h,i)perylene	NA	= (	1.00E+00	×	1E-06	×	12	×	12	×	2	×	0.28	×	1	) + (	47	×	4,380	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.91E+01	×	1E-06	×	12	×	12	×	2	×	0.28	×	1	) + (	47	×	4,380	×	NV	)
Chrysene	NA	= (	3.53E+01	×	1E-06	×	12	×	12	×	2	×	0.28	×	1	) + (	47	×	4,380	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.90E+00	×	1E-06	×	12	×	12	×	2	×	0.28	×	1	) + (	47	×	4,380	×	NV	)
Fluoranthene	8.47E-07	= (	8.65E+01	×	1E-06	×	12	×	12	×	2	×	0.28	×	1	) + (	47	×	4,380	×	4.0E-02	)
Fluorene	1.10E-06	= (	1.13E+02	×	1E-06	×	12	×	12	×	2	×	0.28	×	1	) + (	47	×	4,380	×	4.0E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	5.30E+00	×	1E-06	×	12	×	12	×	2	×	0.28	×	1	) + (	47	×	4,380	×	NV	)
Naphthalene	1.12E-05	= (	5.73E+02	×	1E-06	×	12	×	12	×	2	×	0.28	×	1	) + (	47	×	4,380	×	2.0E-02	)
Pyrene	7.2E-07	= (	1.10E+02	×	1E-06	×	12	×	12		2	×	0.28	×	1	) + (	47	×	4,380	×	3.0E-02	)
Methylene chloride	4.2E-08	= (	1.30E+01	×	1E-06	×	12	×	12		2	×	0.28	×	1	) + (	47	×	4,380	×	6.0E-02	)
Xylenes (total)	1.0E-08	= (	1.03E+01	×	1E-06	×	12	×	12		2	×	0.28	×	1	) + (	47	×	4,380	×	2.0E-01	)

Notes:

Ing - HQ – Ingestion Hazard
Csediment – Concentration in sediment
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Sediment Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose

Attachment D

Table 20a
Risk Calculations
Adolescent Wader: Incidental Dermal Contact with Sediment Pathway – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csediment} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATc})}$$

Equation	Derm - Risk	=	Csediment	×	SFabs	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	)	÷	(	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless				kg		days	
Iron	NA	=	2.70E+04	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	)	÷	(	47	×	25,550	)
Manganese	NA	=	3.00E+02	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	)	÷	(	47	×	25,550	)
Vanadium	NA	=	9.70E+00	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	)	÷	(	47	×	25,550	)
1-Methylnaphthalene	NA	=	1.90E+01	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	)	÷	(	47	×	25,550	)
2-Methylnaphthalene	NA	=	5.46E+02	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.00E-01	)	÷	(	47	×	25,550	)
Acenaphthene	NA	=	1.85E+02	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	)	÷	(	47	×	25,550	)
Benzo(a)anthracene	1.82E-06	=	3.96E+01	×	7.30E-01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	)	÷	(	47	×	25,550	)
Benzo(a)pyrene	1.32E-05	=	2.86E+01	×	7.30E+00	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	)	÷	(	47	×	25,550	)
Benzo(b)fluoranthene	6.93E-07	=	1.50E+01	×	7.30E-01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	)	÷	(	47	×	25,550	)
Benzo(g,h,i)perylene	NA	=	1.00E+00	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	)	÷	(	47	×	25,550	)
Benzo(k)fluoranthene	8.80E-08	=	1.91E+01	×	7.30E-02	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	)	÷	(	47	×	25,550	)
Chrysene	1.63E-08	=	3.53E+01	×	7.30E-03	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	)	÷	(	47	×	25,550	)
Dibenzo(a,h)anthracene	8.75E-07	=	1.90E+00	×	7.30E+00	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	)	÷	(	47	×	25,550	)
Fluoranthene	NA	=	8.65E+01	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	)	÷	(	47	×	25,550	)
Fluorene	NA	=	1.13E+02	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	)	÷	(	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	2.44E-07	=	5.30E+00	×	7.30E-01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	)	÷	(	47	×	25,550	)
Naphthalene	NA	=	5.73E+02	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	)	÷	(	47	×	25,550	)
Pyrene	NA	=	1.10E+02	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	)	÷	(	47	×	25,550	)
Methylene chloride	NA	=	1.30E+01	×	7.50E-03	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	)	÷	(	47	×	25,550	)
Xylenes (total)	NA	=	1.03E+01	×	NV	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	)	÷	(	47	×	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csediment – Concentration in sediment
SFabs – Absorbed slope factor (SFo + ABSgi)
CF – Conversion factor
EF – Exposure Frequency
ET – Exposure Time
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
SSAF – Sediment-to-skin Adherence Factor
ABSd – Dermal Sediment Absorption Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment D

Table 20b
Risk Calculations
Adolescent Wader: Incidental Dermal Contact with Sediment Pathway – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csediment} \times \text{EF} \times \text{CF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATn} \times \text{RfDabs})}$$

Equation Units	Derm - HQ unitless	= (	Csediment mg/kg	×	CF kg/mg	×	EF days/year	×	ED years	×	EV events/day	×	SA cm²	×	SSAF mg/cm²-event	×	ABSd unitless	) ÷ (	BW kg	×	ATn days	×	RfDabs mg/kg-day	)
Iron	NA	= (	2.70E+04	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	) ÷ (	47	×	4,380	×	NV	)
Manganese	NA	= (	3.00E+02	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	) ÷ (	47	×	4,380	×	1.87E-03	)
Vanadium	NA	= (	9.70E+00	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	) ÷ (	47	×	4,380	×	2.60E-05	)
1-Methylnaphthalene	NA	= (	1.90E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	4,380	×	NV	)
2-Methylnaphthalene	3.86E-02	= (	5.46E+02	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.00E-01	) ÷ (	47	×	4,380	×	4.00E-03	)
Acenaphthene	1.13E-03	= (	1.85E+02	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	4,380	×	6.00E-02	)
Benzo(a)anthracene	NA	= (	3.96E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	4,380	×	NV	)
Benzo(a)pyrene	NA	= (	2.86E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	4,380	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.50E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	4,380	×	NV	)
Benzo(g,h,i)perylene	NA	= (	1.00E+00	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	4,380	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.91E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	4,380	×	NV	)
Chrysene	NA	= (	3.53E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	4,380	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.90E+00	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	4,380	×	NV	)
Fluoranthene	7.96E-04	= (	8.65E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	4,380	×	4.00E-02	)
Fluorene	1.04E-03	= (	1.13E+02	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	4,380	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	5.30E+00	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	4,380	×	NV	)
Naphthalene	1.05E-02	= (	5.73E+02	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	4,380	×	2.00E-02	)
Pyrene	4.05E-05	= (	1.10E+02	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	1.30E-01	) ÷ (	47	×	4,380	×	3.00E-02	)
Methylene chloride	NA	= (	1.30E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	) ÷ (	47	×	4,380	×	6.00E-02	)
Xylenes (total)	NA	= (	1.03E+01	×	1E-06	×	12	×	12	×	1	×	4,046	×	1	×	NA	) ÷ (	47	×	4,380	×	2.00E-01	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csediment – Concentration in sediment
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
SSAF – Sediment-to-skin Adherence Factor
ABSd – Dermal Sediment Absorption Factor
BW – Body Weight
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo ×ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment D

Table 21a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Ingestion of Soil Pathway – Carcinogenic Effects

$$Ing\text{-}Risk = \frac{(Csoil \times SFo \times CF \times EF \times ED \times SIR \times FI)}{(BW \times ATc)}$$

Equation	Ing - Risk	= (	Csoil	×	SFo	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		mg/day		unitless		kg		days	
Inorganics																				
Arsenic	3.12E-07	= (	4.51E+00	×	1.50E+00	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Lead	NA	= (	9.58E+01	×	a	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Manganese	NA	= (	3.08E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Vanadium	NA	= (	3.15E+01	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
SVOCs																				
1-Methylnaphthalene	NA	= (	1.44E+03	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	1.60E+03	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25550	)
Acenaphthene	NA	= (	3.86E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	4.12E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Benzo(a)anthracene	5.74E-06	= (	1.71E+02	×	7.30E-01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	4.13E-05	= (	1.23E+02	×	7.30E+00	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	2.51E-06	= (	7.45E+01	×	7.30E-01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	3.11E-07	= (	9.23E+01	×	7.30E-02	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Chrysene	5.14E-08	= (	1.53E+02	×	7.30E-03	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	6.18E-06	= (	1.83E+01	×	7.30E+00	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	9.89E+01	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	2.82E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	2.88E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	2.26E-06	= (	6.72E+01	×	7.30E-01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	1.17E+03	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	3.95E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
VOCs																) ÷ (				
1,2,3-Trimethylbenzene	NA	= (	1.96E+01	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
1,2,4-Trichlorobenzene	NA	= (	2.64E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	4.21E+00	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	= (	1.97E+01	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Benzene	3.83E-08	= (	1.51E+01	×	5.50E-02	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)

Attachment D

Table 21a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Ingestion of Soil Pathway – Carcinogenic Effects

$$\text{Ing-Risk} = \frac{(\text{Csoil} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	= (	Csoil	×	SFo	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		mg/day		unitless		kg		days	
Ethylbenzene	NA	= (	5.04E+01	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
n-Butyl benzene	NA	= (	5.93E+01	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
p-Isopropyltoluene	NA	= (	2.30E+01	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
sec-Butyl benzene	NA	= (	5.02E+01	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Toluene	NA	= (	3.36E+01	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Xylenes (total)	NA	= (	2.35E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – Concentration in soil
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
VOC – Volatile organic compound
SIR – Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
SVOC – Semivolatile organic compound
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 21b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Ingestion of Soil Pathway – Noncarcinogenic Effects

$$\text{Ing - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation	Ing - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATn	×	RfDo [6]	)
Units	unitless		mg/kg		kg/mg		days/year		years		mg/day		unitless		kg		days		mg/kg-day	
Inorganics																				
Arsenic	4.9E-02	= (	4.51E+00	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	3.0E-04	)
Lead	NA	= (	9.58E+01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	a	)
Manganese	7.1E-03	= (	3.08E+02	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	1.4E-01	
Vanadium	1.5E-02	= (	3.15E+01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	7.0E-03	
SVOCs																				
1-Methylnaphthalene	6.6E-02	= (	1.44E+03	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	7.0E-02	)
2-Methylnaphthalene	1.3E+00	= (	1.60E+03	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	4.0E-03	)
Acenaphthene	2.1E-03	= (	3.86E+02	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	6.0E-01	)
Acenaphthylene	NA	= (	4.12E+02	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	NV	
Benzo(a)anthracene	NA	= (	1.71E+02	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	NV	)
Benzo(a)pyrene	NA	= (	1.23E+02	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	NV	)
Benzo(b)fluoranthene	NA	= (	7.45E+01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	NV	)
Benzo(k)fluoranthene	NA	= (	9.23E+01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	NV	)
Chrysene	NA	= (	1.53E+02	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.83E+01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	NV	)
Dibenzofuran	1.6E-01	= (	9.89E+01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	2.0E-03	)
Fluoranthene	2.3E-03	= (	2.82E+02	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	4.0E-01	)
Fluorene	2.3E-03	= (	2.88E+02	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	4.0E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (	6.72E+01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	NV	)
Naphthalene	1.9E-01	= (	1.17E+03	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	2.0E-02	)
Pyrene	4.3E-03	= (	3.95E+02	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	3.0E-01	)
VOCs																				
1,2,3-Trimethylbenzene	NA	= (	1.96E+01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	NV	
1,2,4-Trichlorobenzene	8.5E-02	= (	2.64E+02	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	1.0E-02	)
1,2,4-Trimethylbenzene	2.7E-04	= (	4.21E+00	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	5.0E-02	)
1,3,5-Trimethylbenzene	1.3E-04	= (	1.97E+01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	5.0E-01	)
Benzene	1.2E-02	= (	1.51E+01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	4.0E-03	)

Attachment D

Table 21b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Ingestion of Soil Pathway – Noncarcinogenic Effects

$$\text{Ing - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation / Units	Ing - HQ unitless	= (	Csoil mg/kg	×	CF kg/mg	×	EF days/year	×	ED years	×	SIR mg/day	×	FI unitless	) ÷ (	BW kg	×	ATn days	×	RfDo [b] mg/kg-day	)
Ethylbenzene	1.5E-03	= (	5.04E+01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	1.1E-01	)
n-Butyl benzene	4.8E-03	= (	5.93E+01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	4.0E-02	)
p-Isopropyltoluene	NA	= (	2.30E+01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	NV	
sec-Butyl benzene	4.1E-03	= (	5.02E+01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	4.0E-02	)
Toluene	5.4E-05	= (	3.36E+01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	2.0E+00	)
Xylenes (total)	2.1E-03	= (	2.35E+02	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	365	×	3.6E-01	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Concentration in Soil
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Soil Ingestion Rate
VOC – Volatile organic compound
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose
NV – No toxicity value available for this pathway.
NA – Not Applicable
SVOC – Semivolatile organic compound

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available. Toxicity criteria is presented in Attachment A, Table 1b.

Attachment D

Table 22a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Dermal Contact with Soil Pathway – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATc})}$$

Equation	Derm - Risk	= (	Csoil	×	SFabs	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless		kg		days	
Inorganics																								
Arsenic	1.73E-08	= (	4.51E+00	×	1.58E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	3.00E-02	) ÷ (	70	×	25,550	)
Lead	NA	= (	9.58E+01	×	a	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
Manganese	NA	= (	3.08E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
Vanadium	NA	= (	3.15E+01	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
SVOCs																								
1-Methylnaphthalene	NA	= (	1.44E+03	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	1.60E+03	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.00E-01	) ÷ (	70	×	25,550	)
Acenaphthene	NA	= (	3.86E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	4.12E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(a)anthracene	1.31E-06	= (	1.71E+02	×	7.30E-01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	9.41E-06	= (	1.23E+02	×	7.30E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	5.72E-07	= (	7.45E+01	×	7.30E-01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	7.09E-08	= (	9.23E+01	×	7.30E-02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Chrysene	1.17E-08	= (	1.53E+02	×	7.30E-03	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	1.41E-06	= (	1.83E+01	×	7.30E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	9.89E+01	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	2.82E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	2.88E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	5.16E-07	= (	6.72E+01	×	7.30E-01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	1.17E+03	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	3.95E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
VOCs																								
1,2,3-Trimethylbenzene	NA	= (	1.96E+01	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
1,2,4-Trichlorobenzene	NA	= (	2.64E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	4.21E+00	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	= (	1.97E+01	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)

Attachment D

Table 22a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Dermal Contact with Soil Pathway – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATc})}$$

Equation	Derm - Risk	= (	Csoil	×	SFabs	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless		kg		days	
Benzene	NA	= (	1.51E+01	×	5.50E-02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
Ethylbenzene	NA	= (	5.04E+01	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
n-Butyl benzene	NA	= (	5.93E+01	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
p-Isopropyltoluene	NA	= (	2.30E+01	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NV	) ÷ (	70	×	25,550	)
sec-Butyl benzene	NA	= (	5.02E+01	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
Toluene	NA	= (	3.36E+01	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
Xylenes (total)	NA	= (	2.35E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csoil – Concentration in Soil
SFabs – Absorbed slope factor (SFo + ABSgi)
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
VOC – Volatile organic compound
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 22b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Dermal Contact with Soil Pathway – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATn} \times \text{RfDabs})}$$

Equation	Derm - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) ÷ (	BW	×	ATn	×	RfDabs [b]	)
Units	unitless		mg/kg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless		kg		days		mg/kg-day	
Inorganics																								
Arsenic	2.69E-03	= (	4.51E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	3.00E-02	) + (	70	×	365	×	2.85E-04	)
Lead	NA	= (	9.58E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	a	)
Manganese	NA	= (	3.08E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	5.60E-03	
Vanadium	NA	= (	3.15E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	1.82E-04	
SVOCs																								
1-Methylnaphthalene	1.51E-02	= (	1.44E+03	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	7.00E-02	)
2-Methylnaphthalene	2.26E-01	= (	1.60E+03	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.00E-01	) + (	70	×	365	×	4.00E-03	)
Acenaphthene	4.74E-04	= (	3.86E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	6.00E-01	)
Acenaphthylene	NA	= (	4.12E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	
Benzo(a)anthracene	NA	= (	1.71E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Benzo(a)pyrene	NA	= (	1.23E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Benzo(b)fluoranthene	NA	= (	7.45E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Benzo(k)fluoranthene	NA	= (	9.23E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Chrysene	NA	= (	1.53E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.83E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Dibenzofuran	3.64E-02	= (	9.89E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	2.00E-03	)
Fluoranthene	5.20E-04	= (	2.82E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	4.00E-01	)
Fluorene	5.29E-04	= (	2.88E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	4.00E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (	6.72E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Naphthalene	4.30E-02	= (	1.17E+03	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	2.00E-02	)
Pyrene	9.71E-04	= (	3.95E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	3.00E-01	)
VOCs																								
1,2,3-Trimethylbenzene	NA	= (	1.96E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	NV	
1,2,4-Trichlorobenzene	NA	= (	2.64E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NV	) + (	70	×	365	×	NV	)
1,2,4-Trimethylbenzene	NA	= (	4.21E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	5.00E-02	)
1,3,5-Trimethylbenzene	NA	= (	1.97E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	5.00E-01	)
Benzene	NA	= (	1.51E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	4.00E-03	)
Ethylbenzene	NA	= (	5.04E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	1.10E-01	)
n-Butyl benzene	NA	= (	5.93E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	4.00E-02	)

Attachment D

Table 22b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Dermal Contact with Soil Pathway – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATn} \times \text{RfDabs})}$$

Equation / Units	Derm - HQ unitless	= (	Csoil mg/kg	×	CF kg/mg	×	EF days/year	×	ED years	×	EV events/day	×	SA cm²	×	SSAF mg/cm²-event	×	ABSd unitless	) ÷ (	BW kg	×	ATn days	×	RfDabs [b] mg/kg-day	)
p-Isopropyltoluene	NA	= (	2.30E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NV	) ÷ (	70	×	365	×	NV	
sec-Butyl benzene	NA	= (	5.02E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	365	×	4.00E-02	)
Toluene	NA	= (	3.36E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	365	×	2.00E+00	)
Xylenes (total)	NA	= (	2.35E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	365	×	3.57E-01	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Concentration in Soil
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
SSAF – Soil-to-skin Adherence Factor
ABSd – Dermal Soil Absorption Factor
BW – Body Weight
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo ×ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.
VOC – Volatile organic compound
SVOC – Semivolatile organic compound

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available. Toxicity criteria is presented in Attachment A, Table 1b.

Attachment D

Table 23a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Inhalation of Soil (Fugitive Emissions and Volatile Compounds) Pathway– Carcinogenic Effects

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times [(1/\text{VF}) + (1/\text{PEF})])}{(\text{BW} \times \text{ATc})}$$

Equation	Inh - Risk	=	(	Csoil	×	SFi	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	)	÷	(	BW	×	ATc	)
Units	unitless			mg/kg		kg-day/mg		m³/hour		hours/day		days/year		year					m³/kg				m³/kg					kg		days	
Inorganics																															
Arsenic	8.32E-09	=	(	4.51E+00	×	1.51E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Lead	NA	=	(	9.58E+01	×	a	×	1.5	×	8	×	250	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Manganese	NA	=	(	3.08E+02	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Vanadium	NA	=	(	3.15E+01	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
SVOCs																															
1-Methylnaphthalene	NA	=	(	1.44E+03	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	6.00E+03	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
2-Methylnaphthalene	NA	=	(	1.60E+03	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	5.68E+03	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Acenaphthene	NA	=	(	3.86E+02	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	1.10E+04	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Acenaphthylene	NA	=	(	4.12E+02	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	1.30E+04	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Benzo(a)anthracene	NA	=	(	1.71E+02	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Benzo(a)pyrene	4.62E-08	=	(	1.23E+02	×	3.08E+00	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Benzo(b)fluoranthene	NA	=	(	7.45E+01	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Benzo(k)fluoranthene	NA	=	(	9.23E+01	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Chrysene	NA	=	(	1.53E+02	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Dibenzo(a,h)anthracene	NA	=	(	1.83E+01	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Dibenzofuran	NA	=	(	9.89E+01	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	9.09E+03	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Fluoranthene	NA	=	(	2.82E+02	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Fluorene	NA	=	(	2.88E+02	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	1.67E+04	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	NA	=	(	6.72E+01	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Naphthalene	NA	=	(	1.17E+03	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	5.25E+03	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Pyrene	NA	=	(	3.95E+02	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	5.57E+04	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
VOCs																															
1,2,3-Trimethylbenzene	NA	=	(	1.96E+01	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	1.35E+03	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
1,2,4-Trichlorobenzene	NA	=	(	2.64E+02	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	2.62E+04	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	=	(	4.21E+00	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	9.98E+02	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	=	(	1.97E+01	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	8.26E+02	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Benzene	1.19E-06	=	(	1.51E+01	×	2.73E-02	×	1.5	×	8	×	250	×	1	×	[	1	/	5.83E+02	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Ethylbenzene	NA	=	(	5.04E+01	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	7.41E+02	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
n-Butyl benzene	NA	=	(	5.93E+01	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	7.70E+02	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
p-Isopropyltoluene	NA	=	(	2.30E+01	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	NV	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
sec-Butyl benzene	NA	=	(	5.02E+01	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	7.70E+02	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)

Attachment D

Table 23a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Inhalation of Soil (Fugitive Emissions and Volatile Compounds) Pathway– Carcinogenic Effects

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times [(1/\text{VF}) + (1/\text{PEF})])}{(\text{BW} \times \text{ATc})}$$

Equation	Inh - Risk	=	(	Csoil	×	SFi	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	)	÷	(	BW	×	ATc	)
Units	unitless			mg/kg		kg-day/mg		m³/hour		hours/day		days/year		year					m³/kg				m³/kg					kg		days	
Toluene	NA	=	(	3.36E+01	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	6.32E+02	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Xylenes (total)	NA	=	(	2.35E+02	×	NV	×	1.5	×	8	×	250	×	1	×	[	1	/	8.09E+02	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Concentration in Soil
SFi – Inhalation Slope Factor
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VOC – Volatile organic compound
VF – Volatilization Factor
PEF – Particulate Emission Factor (See Attachment G)
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
SVOC – Semivolatile organic compound
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 23b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Inhalation of Soil (Fugitive Emissions and Volatile Compounds) Pathway – Carcinogenic Effects

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BW} \times \text{ATn} \times \text{RfDi})}$$

Equation	Inh - HQ	=	(	Csoil	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	÷	(	BW	×	ATn	×	RfDi [(b)]	)
Units	unitless			mg/kg		m³/hour		hours/day		days/year		year					m³/kg				m³/kg				kg		days		mg/kg-day	
Inorganics																														
Arsenic	NA	=	(	4.51E+00	×	1.5	×	8	×	250	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Lead	NA	=	(	9.58E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	÷	(	70	×	365	×	a	)
Manganese	1.85E-01	=	(	3.08E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	÷	(	70	×	365	×	1.43E-05	
Vanadium	NA	=	(	3.15E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
SVOCs																														
1-Methylnaphthalene	NA	=	(	1.44E+03	×	1.5	×	8	×	250	×	1	×	[	1	/	6.00E+03	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
2-Methylnaphthalene	NA	=	(	1.60E+03	×	1.5	×	8	×	250	×	1	×	[	1	/	5.68E+03	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Acenaphthene	NA	=	(	3.86E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	1.10E+04	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
Acenaphthylene	NA	=	(	4.12E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	1.30E+04	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
Benzo(a)anthracene	NA	=	(	1.71E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Benzo(a)pyrene	NA	=	(	1.23E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Benzo(b)fluoranthene	NA	=	(	7.45E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Benzo(k)fluoranthene	NA	=	(	9.23E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
Chrysene	NA	=	(	1.53E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
Dibenzo(a,h)anthracene	NA	=	(	1.83E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Dibenzofuran	NA	=	(	9.89E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	9.09E+03	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Fluoranthene	NA	=	(	2.82E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
Fluorene	NA	=	(	2.88E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	1.67E+04	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
Indeno(1,2,3-cd)pyrene	NA	=	(	6.72E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Naphthalene	3.05E+01	=	(	1.17E+03	×	1.5	×	8	×	250	×	1	×	[	1	/	5.25E+03	+	1	/	1.37E+07	]	÷	(	70	×	365	×	8.57E-04	)
Pyrene	NA	=	(	3.95E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	5.57E+04	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
VOCs																														
1,2,3-Trimethylbenzene	NA	=	(	1.96E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	1.35E+03	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
1,2,4-Trichlorobenzene	1.04E+00	=	(	2.64E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	2.62E+04	+	1	/	1.37E+07	]	÷	(	70	×	365	×	1.14E-03	)
1,2,4-Trimethylbenzene	2.90E-01	=	(	4.21E+00	×	1.5	×	8	×	250	×	1	×	[	1	/	9.98E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	1.71E-03	)
1,3,5-Trimethylbenzene	1.65E-01	=	(	1.97E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	8.26E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	1.70E-02	)
Benzene	3.55E-01	=	(	1.51E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	5.83E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	8.57E-03	)
Ethylbenzene	2.76E-02	=	(	5.04E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	7.41E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	2.90E-01	
n-Butyl benzene	NA	=	(	5.93E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	7.70E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	

Attachment D

Table 23b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Inhalation of Soil (Fugitive Emissions and Volatile Compounds) Pathway – Carcinogenic Effects

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BW} \times \text{ATn} \times \text{RfDi})}$$

Equation	Inh - HQ	=	(	Csoil	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	÷	(	BW	×	ATn	×	RfDi [b]	)
Units	unitless			mg/kg		m³/hour		hours/day		days/year		year					m³/kg				m³/kg				kg		days		mg/kg-day	
p-Isopropyltoluene	NA	=	(	2.30E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	NV	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
sec-Butyl benzene	NA	=	(	5.02E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	7.70E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
Toluene	2.40E-02	=	(	3.36E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	6.32E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	2.60E-01	
Xylenes (total)	1.19E+00	=	(	2.35E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	8.09E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	2.86E-02	

Notes:

Inh - Risk – Inhalation Hazard Quotient
Csoil – Concentration in Soil
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VF – Volatilization Factor
VOC – Volatile organic compound
PEF – Particulate Emission Factor (See Attachment G)
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
SVOC – Semivolatile organic compound

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available. Toxicity criteria is presented in Attachment A, Table 1b.

Attachment D

Table 23c
Construction Worker: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} \times \frac{(3.14 \times D_A \times T)^{1/2}}{(2 \times \rho_b \times D_A)} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} (g/m^2-s)/(kg/m^2)	π	D_A (cm^2/s)	T (s)	2	ρb (g/cm^3)	10^{-4} (m^2/cm^2)	VF (m^2/kg)
1-Methylnaphthalene	73.32	3.14	1.94E-05	3.15E+07	2	1.38	1.00E-04	6.00E+03
2-Methylnaphthalene	73.32	3.14	2.17E-05	3.15E+07	2	1.38	1.00E-04	5.68E+03
Acenaphthene	73.32	3.14	5.82E-06	3.15E+07	2	1.38	1.00E-04	1.10E+04
Benzo(a)anthracene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Benzo(a)pyrene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Benzo(b)fluoranthene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Benzo(k)fluoranthene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Chrysene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Dibenzo(a,h)anthracene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Dibenzofuran	73.32	3.14	8.46E-06	3.15E+07	2	1.38	1.00E-04	9.09E+03
Fluoranthene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Fluorene	73.32	3.14	2.50E-06	3.15E+07	2	1.38	1.00E-04	1.67E+04
Indeno(1,2,3-cd)pyrene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Naphthalene	73.32	3.14	2.54E-05	3.15E+07	2	1.38	1.00E-04	5.25E+03
Pyrene	73.32	3.14	2.25E-07	3.15E+07	2	1.38	1.00E-04	5.57E+04
1,2,4-Trichlorobenzene	73.32	3.14	1.02E-06	3.15E+07	2	1.38	1.00E-04	2.62E+04
1,2,4-Trimethylbenzene	73.32	3.14	7.01E-04	3.15E+07	2	1.38	1.00E-04	9.98E+02
1,3,5-Trimethylbenzene	73.32	3.14	1.02E-03	3.15E+07	2	1.38	1.00E-04	8.26E+02
Benzene	73.32	3.14	2.05E-03	3.15E+07	2	1.38	1.00E-04	5.83E+02
Ethylbenzene	73.32	3.14	1.27E-03	3.15E+07	2	1.38	1.00E-04	7.41E+02
sec-Butyl benzene	73.32	3.14	1.18E-03	3.15E+07	2	1.38	1.00E-04	7.70E+02
Toluene	73.32	3.14	1.75E-03	3.15E+07	2	1.38	1.00E-04	6.32E+02
Xylenes (total)	73.32	3.14	1.07E-03	3.15E+07	2	1.38	1.00E-04	8.09E+02

Notes:
Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).
VF – Volatilization Factor (m^3/kg) (calculated)
Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source (g/m^2-s)/(kg/m^2)(Value used is for Minneapolis, MN.)
π – pi (3.14)
D_A – Apparent Diffusivity (cm^2/s)
T – Exposure interval (s)
ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)
NC – Not calculated

Attachment D

Table 23d
Construction Worker: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical	VOC?	θa	Di	H'	θw	Dw	η	ρb	ρs	Kd	D_A
Units		(Lair /Lsoil)	(cm^2/s)	unitless	(Lwater /Lsoil)	(cm^2/s)	(Lpore /Lsoil)	(g/cm^3)	(g/cm^3)	(cm^3/g)	(cm^2/s)
1-Methylnaphthalene	*Yes*	3.29E-01	6.31E-02	1.64E-02	0.15	7.13E-06	4.79E-01	1.38	2.65	3.75E+01	1.948E-05
2-Methylnaphthalene	*Yes*	3.29E-01	4.80E-02	2.12E-02	0.15	7.84E-06	4.79E-01	1.38	2.65	1.79E+01	2.166E-05
Acenaphthene	*Yes*	3.29E-01	4.21E-02	7.44E-03	0.15	7.69E-06	4.79E-01	1.38	2.65	3.67E+01	5.819E-06
Benzo(a)anthracene	No	3.29E-01	5.10E-02	4.91E-04	0.15	9.00E-06	4.79E-01	1.38	2.65	1.39E+03	NC
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Benzo(b)fluoranthene	No	3.29E-01	2.26E-02	2.69E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.82E+03	NC
Benzo(k)fluoranthene	No	3.29E-01	2.26E-02	2.39E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Chrysene	No	3.29E-01	2.48E-02	2.14E-04	0.15	6.21E-06	4.79E-01	1.38	2.65	1.42E+03	NC
Dibenzo(a,h)anthracene	No	3.29E-01	2.02E-02	5.03E-06	0.15	5.18E-06	4.79E-01	1.38	2.65	1.57E+04	NC
Dibenzofuran	*Yes*	3.29E-01	5.51E-02	8.71E-03	0.15	7.04E-06	4.79E-01	1.38	2.65	6.78E+01	8.463E-06
Fluoranthene	No	3.29E-01	3.02E-02	3.62E-04	0.15	6.35E-06	4.79E-01	1.38	2.65	4.25E+02	NC
Fluorene	*Yes*	3.29E-01	3.63E-02	3.93E-03	0.15	7.88E-06	4.79E-01	1.38	2.65	6.78E+01	2.499E-06
Indeno(1,2,3-cd)pyrene	No	3.29E-01	1.90E-02	1.42E-05	0.15	5.66E-06	4.79E-01	1.38	2.65	1.61E+04	NC
Naphthalene	*Yes*	3.29E-01	5.90E-02	1.80E-02	0.15	7.50E-06	4.79E-01	1.38	2.65	1.10E+01	2.537E-05
Pyrene	*Yes*	3.29E-01	2.72E-02	4.87E-04	0.15	7.24E-06	4.79E-01	1.38	2.65	4.16E+02	2.254E-07
1,2,4-Trichlorobenzene	NV	3.29E-01	3.00E-02	1.42E-03	0.15	8.23E-06	4.79E-01	1.38	2.65	1.07E+01	1.02E-06
1,2,4-Trimethylbenzene	*Yes*	3.29E-01	6.44E-02	2.52E-01	0.15	7.92E-06	4.79E-01	1.38	2.65	4.31E+00	7.01E-04
1,3,5-Trimethylbenzene	*Yes*	3.29E-01	6.02E-02	3.59E-01	0.15	8.67E-06	4.79E-01	1.38	2.65	4.22E+00	1.02E-03
Benzene	*Yes*	3.29E-01	8.80E-02	2.27E-01	0.15	9.80E-06	4.79E-01	1.38	2.65	9.93E-01	2.05E-03
Ethylbenzene	*Yes*	3.29E-01	7.50E-02	3.22E-01	0.15	7.80E-06	4.79E-01	1.38	2.65	3.11E+00	1.27E-03
sec-Butyl benzene	*Yes*	3.29E-01	5.76E-02	5.07E-01	0.15	6.75E-06	4.79E-01	1.38	2.65	1.25E+01	1.18E-03
Toluene	*Yes*	3.29E-01	8.70E-02	2.71E-01	0.15	8.60E-06	4.79E-01	1.38	2.65	1.61E+00	1.75E-03
Xylenes (total)	*Yes*	3.29E-01	7.14E-02	2.71E-01	0.15	9.34E-06	4.79E-01	1.38	2.65	2.66E+00	1.07E-03

Notes:

D_A – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's Law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User'S Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density
Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm^3/g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)
VOC? – Volatile organic compounds; If no an apparent diffusivity was not calculated.
NV – no value available
NC – not calculated

Attachment D

Table 23e
Calculation of Blood Lead Concentrations (PbBs) for Non-residential Receptors (Construction Workers)

Exposure Variable	PbB Equation[1] 1*	2**	Description of Exposure Variable	Units	Values for Non-Residential Exposure Scenario			
					Using Equation 1		Using Equation 2	
					GSDi = Hom	GSDi = Het	GSDi = Hom	GSDi = Het
PbS	X	X	Soil lead concentration (site-specific average concentration)	ug/g or ppm	88.74	88.74	88.74	88.74
$R_{fetal/maternal}$	X	X	Fetal/maternal PbB ratio	--	0.9	0.9	0.9	0.9
BKSF	X	X	Biokinetic Slope Factor	ug/dL per ug/day	0.4	0.4	0.4	0.4
GSD_i	X	X	Geometric standard deviation PbB	--	2.1	2.3	2.1	2.3
PbB_0	X	X	Baseline PbB	ug/dL	1.5	1.7	1.5	1.7
IR_S	X		*Soil ingestion rate (including soil-derived indoor dust)*	g/day	0.050	0.050	--	--
IR_{S+D}		X	Total ingestion rate of outdoor soil and indoor dust	g/day	--	--	0.050	0.050
W_S		X	Weighting factor; fraction of IR_{S+D} ingested as outdoor soil	--	--	--	1.0	1.0
K_{SD}		X	Mass fraction of soil in dust	--	--	--	0.7	0.7
$AF_{S,D}$	X	X	Absorption fraction (same for soil and dust)	--	0.12	0.12	0.12	0.12
$EF_{S,D}$	X	X	Exposure frequency (same for soil and dust)	days/yr	219	219	219	219
$AT_{S,D}$	X	X	Averaging time (same for soil and dust)	days/yr	365	365	365	365
PbB_{adult}	***PbB of adult worker, geometric mean***			**ug/dL**	**1.6**	**1.8**	**1.6**	**1.8**
$PbB_{fetal,\ 0.95}$	**95th percentile PbB among fetuses of adult workers**			**ug/dL**	**5.0**	**6.5**	**5.0**	**6.5**
PbB_t	**Target PbB level of concern (e.g., 10 ug/dL)**			**ug/dL**	**10.0**	**10.0**	**10.0**	**10.0**
$P(PbB_{fetal} > PbB_t)$	***Probability that fetal PbB > PbB_t, assuming lognormal distribution***			**%**	**0.5%**	**1.5%**	**0.5%**	**1.5%**

[1] Equation 1 does not apportion exposure between soil and dust ingestion (excludes W_S, K_{SD}).
When $IR_S = IR_{S+D}$ and $W_S = 1.0$, the equations yield the same $PbB_{fetal,0.95}$.

***Equation 1, based on Eq. 1, 2 in USEPA (1996).**

PbB_{adult} =	$(PbS*BKSF*IR_{S+D}*AF_{S,D}*EF_S/AT_{S,D}) + PbB_0$
$PbB_{fetal,\ 0.95}$ =	$PbB_{adult} * (GSD_i^{1.645} * R)$

****Equation 2, alternate approach based on Eq. 1, 2, and A-19 in USEPA (1996).**

PbB_{adult} =	$PbS*BKSF*([(IR_{S+D})*AF_S*EF_S*W_S]+[K_{SD}*(IR_{S+D})*(1-W_S)*AF_D*EF_D])/365+PbB_0$
$PbB_{fetal,\ 0.95}$ =	$PbB_{adult} * (GSD_i^{1.645} * R)$

Source: U.S. EPA (1996). Recommendations of the Technical Review Workgroup for Lead for an Interim Approach to Assessing Risks Associated with Adult Exposures to Lead in Soil

Attachment D

Table 24a
Risk Calculations: Reasonable Maximum Exposure
Industrial Worker: Incidental Ingestion of Soil Pathway – Carcinogenic Effects

$$\text{Ing-Risk} = \frac{(\text{Csoil} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	= (	Csoil	×	SFo	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		mg/day		unitless		kg		days	
Inorganics																				
Arsenic	9.58E-07	= (	3.65E+00	×	1.50E+00	×	1E-06	×	250	×	25	×	50	×	1	) ÷ (	70	×	25,550	)
SVOCs																				
Benzo(a)pyrene	2.31E-07	= (	1.81E-01	×	7.30E+00	×	1E-06	×	250	×	25	×	50	×	1	) ÷ (	70	×	25,550	)

Notes:

ATc – Averaging Time for Carcinogens
BW – Body Weight
CF – Unit Conversion Factor
Csoil – Soil Concentration
ED – Exposure Duration
EF – Exposure Frequency
FI – Fraction Ingested from Contaminated Source
Ing - Risk – Ingestion risk
SFo – Oral Slope Factor
SIR – Soil Ingestion Rate
SVOC – Semivolatile organic compound

Attachment D

Table 24b
Risk Calculations: Reasonable Maximum Exposure
Industrial Worker: Incidental Ingestion of Soil Pathway – Noncarcinogenic Effects

$$\text{Ing - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation	Ing - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATn	×	RfDo	)
Units	unitless		mg/kg		kg/mg		days/year		years		mg/day		unitless		kg		days		mg/kg-day	
Inorganics																				
Arsenic	6.0E-03	= (	3.65E+00	×	1E-06	×	250	×	25	×	50	×	1	) ÷ (	70	×	9,125	×	3.0E-04	)
SVOCs																				
Benzo(a)pyrene	NA	= (	1.81E-01	×	1E-06	×	250	×	25	×	50	×	1	) ÷ (	70	×	9,125	×	NV	)

Notes:

ATn – Averaging Time for Noncarcinogens
BW – Body Weight
CF – Unit Conversion Factor
Csoil – Soil Concentration
ED – Exposure Duration
EF – Exposure Frequency
FI – Fraction Ingested from Contaminated Source
Ing - HQ – Ingestion Hazard
NA – Not Applicable
NV – No toxicity value available for this pathway.
RfDo – Oral reference dose
SIR – Soil Ingestion Rate
SVOC – Semiviolatile organic compound

Attachment D

Table 25a
Risk Calculations: Reasonable Maximum Exposure
Industrial Worker: Dermal Contact with Soil Pathway – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATc})}$$

Equation	Derm - Risk	= (	Csoil	×	SFabs	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless		kg		days	
Inorganics																								
Arsenic	2.00E-07	= (	3.65E+00	×	1.58E+00	×	1E-06	×	250	×	25	×	1	×	3,300	×	0.1	×	3.00E-02	) ÷ (	70	×	25,550	)
SVOCs																								
Benzo(a)pyrene	NA	= (	1.81E-01	×	NV	×	1E-06	×	250	×	25	×	1	×	3,300	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)

Notes:

ABSd – Dermal Soil Absorption Factor
ATc – Averaging Time for Carcinogens
BW – Body Weight
CF – Conversion factor
Csoil – Soil Concentration
Derm - Risk – Dermal Risk
ED – Exposure Duration
EF – Exposure Frequency
EV – Event Frequency
SA – Skin Surface Area
SFabs – Absorbed slope factor (SFo + ABSgi)
SSAF – Soil-to-skin Adherence Factor
SVOC – Semivolatile organic compound

Attachment D

Table 25b
Risk Calculations: Reasonable Maximum Exposure
Industrial Worker: Dermal Contact with Soil Pathway – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATn} \times \text{RfDabs})}$$

Equation / Units	Derm - HQ = (Csoil	× CF	× EF	× ED	× EV	× SA	× SSAF	× ABSd) ÷ (BW	× ATn	× RfDabs)
	unitless = (mg/kg	kg/mg	days/year	years	events/day	cm^2	mg/cm^2-event	unitless) ÷ (kg	days	mg/kg-day)
Inorganics											
Arsenic	1.24E-03 = (3.65E+00	× 1E-06	× 250	× 25	× 1	× 3,300	× 0.1	× 3.00E-02) ÷ (70	× 9,125	× 2.85E-04)
SVOCs											
Benzo(a)pyrene	NA = (1.81E-01	× 1E-06	× 250	× 25	× 1	× 3,300	× 0.1	× 1.30E-01) ÷ (70	× 9,125	× NV)

Notes:

ABSd – Dermal Soil Absorption Factor
ATn – Averaging Time for noncarcinogens
BW – Body Weight
CF – Conversion factor
Csoil – Soil Concentration
Derm - HQ – Dermal Hazard Quotient
ED – Exposure Duration
EF – Exposure Frequency
EV – Event Frequency
NA – Not Applicable
NV – No toxicity value available for this pathway.
RfDabs – Absorbed reference dose (RfDo ×ABSgi)
SA – Skin Surface Area
SSAF – Soil-to-skin Adherence Factor
SVOC – Semivolatile organic compound

Attachment D

Table 26a
Risk Calculations: Reasonable Maximum Exposure
Industrial Worker: Inhalation of Soil-derived Chemicals Pathway– Carcinogenic Effects

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times [(1/\text{VF}) + (1/\text{PEF})])}{(\text{BW} \times \text{ATc})}$$

Equation	Inh - Risk	= (	Csoil	×	SFi	×	IR	×	ET	×	EF	×	ED	× [	1	/	VF	+	1	/	PEF	]) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		m³/hour		hours/day		days/year		year				m³/kg				m³/kg		kg		days	
Inorganics																										
Arsenic	3.03E-10	= (	3.65E+00	×	1.51E+01	×	1	×	8	×	250	×	25	× [	1	/	NA	+	1	/	5.07E+09	]) ÷ (	70	×	25,550	)
SVOCs																										
Benzo(a)pyrene	3.07E-12	= (	1.81E-01	×	3.08E+00	×	1	×	8	×	250	×	25	× [	1	/	NC	+	1	/	5.07E+09	]) ÷ (	70	×	25,550	)

Notes:

ATc – Averaging Time for Carcinogens
BW – Body Weight
Csoil – Soil Concentration
ED – Exposure duration
EF – Exposure frequency
ET – Exposure Time
Inh - Risk – Inhalation Risk
IR – Inhalation Rate
NA – Not Applicable
NC – Not Calculated
PEF – Particulate Emission Factor
SFi – Inhalation Slope Factor
SVOC – Semivolatile organic compound
VF – Volatilization Factor

Attachment D

Table 26b
Risk Calculations: Reasonable Maximum Exposure
Industrial Worker: Inhalation of Soil-derived Chemicals Pathway – Noncarcinogenic Effects

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BW} \times \text{ATn} \times \text{RfDi})}$$

Equation	Inh - HQ	=	(	Csoil	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	÷	(	BW	×	ATn	×	RfDi	)
Units	unitless			mg/kg		m³/hour		hours/day		days/year		year					m³/kg				m³/kg				kg		days		mg/kg-day	
Inorganics																														
Arsenic	NA	=	(	3.65E+00	×	1	×	8	×	250	×	25	×	[	1	/	NA	+	1	/	5.07E+09	]	÷	(	70	×	9,125	×	NV	)
SVOCs																														
Benzo(a)pyrene	NA	=	(	1.81E-01	×	1	×	8	×	250	×	25	×	[	1	/	NC	+	1	/	5.07E+09	]	÷	(	70	×	9,125	×	NV	)

Notes:

ATn – Averaging Time for Noncarcinogens
BW – Body Weight
Csoil – Soil Concentration
ED – Exposure duration
EF – Exposure frequency
ET – Exposure Time
Inh - Risk – Inhalation Hazard Quotient
IR – Inhalation Rate
NA – Not Applicable
NC – Not Calculated
NV – No toxicity value available for this pathway.
PEF – Particulate Emission Factor
RfDi – Inhalation Reference Dose
SVOC – Semivolatile organic compound
VF – Volatilization Factor

Attachment D

Table 26c
Industrial Worker: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} \times \frac{(3.14 \times D_A \times T)^{1/2}}{(2 \times \rho_b \times D_A)} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} $(g/m^2\text{-}s)/(kg/m^3)$	π	D_A (cm^2/s)	T (s)	2	ρb (g/cm^3)	10^{-4} (m^2/cm^2)	VF (m^2/kg)
Benzo(a)pyrene	73.32	3.14	NC	7.88E+08	2	1.38	1.00E-04	NC

Notes:

Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

VF – Volatilization Factor (m^3/kg) (calculated)

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source $(g/m^2\text{-}s)/(kg/m^3)$(Value used is for Minneapolis, MN.)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T – Exposure interval (s)

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated; PAHs are not considered volatile chemicals

Attachment D

Table 26d
Industrial Worker: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical Units	VOC?	θa (Lair /Lsoil)	Di (cm^2/s)	H' unitless	θw (Lwater /Lsoil)	Dw (cm^2/s)	η (Lpore /Lsoil)	ρb (g/cm^3)	ρs (g/cm^3)	Kd (cm^3/g)	D_A (cm^2/s)
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC

Notes:

D_A – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's Law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User's Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density
Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm^3/g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)
VOC? – Volatile organic compounds; If no, an apparent diffusivity was not calculated.
NV – No value available
NC – not calculated

Attachment D

Table 27a
Risk Calculations: Reasonable Maximum Exposure
Industrial Worker: Inhalation of Chemicals in Indoor Air Pathway– Carcinogenic Effects

$$\text{Inh - Risk} = \frac{(\text{Cair} \times \text{SFi} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED})}{(\text{BW} \times \text{ATc})}$$

Equation	Inh - Risk	= (	Cair	×	SFi	×	IR	×	ET	×	EF	×	ED	) ÷ (	BW	×	ATc	)
Units	unitless		mg/m³		kg-day/mg		m³/hour		hours/day		days/year		year		kg		days	
1,2,4-Trimethylbenzene	NA	= (	3.88E-02	×	NV	×	1	×	8	×	250	×	25	) ÷ (	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	= (	9.32E-03	×	NV	×	1	×	8	×	250	×	25	) ÷ (	70	×	25,550	)
1,4-Dichlorobenzene	NA	= (	9.62E-01	×	NV	×	1	×	8	×	250	×	25	) ÷ (	70	×	25,550	)
Benzene	2.92E-05	= (	3.83E-02	×	2.73E-02	×	1	×	8	×	250	×	25	) ÷ (	70	×	25,550	)
Carbon tetrachloride	1.57E-05	= (	1.07E-02	×	5.25E-02	×	1	×	8	×	250	×	25	) ÷ (	70	×	25,550	)
Methylene chloride	2.24E-07	= (	4.86E-03	×	1.65E-03	×	1	×	8	×	250	×	25	) ÷ (	70	×	25,550	)
Trichloroethylene	3.53E-05	= (	3.16E-03	×	4.00E-01	×	1	×	8	×	250	×	25	) ÷ (	70	×	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Cair – Air Concentration
SFi – Inhalation Slope Factor
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable

Attachment D

Table 27b
Risk Calculations: Reasonable Maximum Exposure
Industrial Worker: Inhalation of Chemicals in Indoor Air Pathway – Carcinogenic Effects

$$\text{Inh - HQ} = \frac{(\text{Cair} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED})}{(\text{BW} \times \text{ATn} \times \text{RfDi})}$$

Equation	Inh - HQ	= (	Cair	×	IR	×	ET	×	EF	×	ED	)) + (	BW	×	ATn	×	RfDi	)
Units	unitless		mg/m³		m³/day		hours/day		days/year		year		kg		days		mg/kg-day	
1,2,4-Trimethylbenzene	1.77E+00	= (	3.88E-02	×	1	×	8	×	250	×	25	) + (	70	×	9,125	×	1.71E-03	)
1,3,5-Trimethylbenzene	4.27E-01	= (	9.32E-03	×	1	×	8	×	250	×	25	) + (	70	×	9,125	×	1.71E-03	)
1,4-Dichlorobenzene	3.29E-01	= (	9.62E-01	×	1	×	8	×	250	×	25	) + (	70	×	9,125	×	2.29E-01	)
Benzene	3.50E-01	= (	3.83E-02	×	1	×	8	×	250	×	25	) + (	70	×	9,125	×	8.57E-03	)
Carbon tetrachloride	NA	= (	1.07E-02	×	1	×	8	×	250	×	25	) + (	70	×	9,125	×	NV	)
Methylene chloride	4.44E-04	= (	4.86E-03	×	1	×	8	×	250	×	25	) + (	70	×	9,125	×	8.57E-01	)
Trichloroethylene	2.17E-02	= (	3.16E-03	×	1	×	8	×	250	×	25	) + (	70	×	9,125	×	1.14E-02	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Cair – Air Concentration
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose
NV – No toxicity value available for this pathway.
NA – Not Applicable

Attachment D

Table 28a
Risk Calculations: Reasonable Maximum Exposure
Maintenance Worker: Incidental Ingestion of Soil Pathway – Carcinogenic Effects

$$Ing\text{-}Risk = \frac{(Csoil \times SFo \times CF \times EF \times ED \times SIR \times FI)}{(BW \times ATc)}$$

Equation	Ing - Risk	= (	Csoil	×	SFo	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		mg/day		unitless		kg		days	
Arsenic	1.15E-07	= (	4.99E+00	×	1.50E+00	×	1E-06	×	22	×	25	×	100	×	0.5	) ÷ (	70	×	25,550	)
Lead	NA	= (	9.51E+01	×	a	×	1E-06	×	22	×	25	×	100	×	0.5	) ÷ (	70	×	25,550	)
Benzo(a)anthracene	3.17E-08	= (	2.83E+00	×	7.30E-01	×	1E-06	×	22	×	25	×	100	×	0.5	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	6.37E-07	= (	5.68E+00	×	7.30E+00	×	1E-06	×	22	×	25	×	100	×	0.5	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	5.89E-08	= (	5.25E+00	×	7.30E-01	×	1E-06	×	22	×	25	×	100	×	0.5	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	4.06E-08	= (	3.62E+00	×	7.30E-01	×	1E-06	×	22	×	25	×	100	×	0.5	) ÷ (	70	×	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – Soil Concentration
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 28b
Risk Calculations: Reasonable Maximum Exposure
Maintenance Worker: Incidental Ingestion of Soil Pathway – Noncarcinogenic Effects

$$\text{Ing - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation	Ing - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATn	×	RfDo	)
Units	unitless		mg/kg		kg/mg		days/year		years		mg/day		unitless		kg		days		mg/kg-day	
Arsenic	7.2E-04	= (	4.99E+00	×	1E-06	×	22	×	25	×	100	×	0.5	) ÷ (	70	×	9,125	×	3.0E-04	)
Lead	NA	= (	9.51E+01	×	1E-06	×	22	×	25	×	100	×	0.5	) ÷ (	70	×	9,125	×	a	)
Benzo(a)anthracene	NA	= (	2.83E+00	×	1E-06	×	22	×	25	×	100	×	0.5	) ÷ (	70	×	9,125	×	NV	)
Benzo(a)pyrene	NA	= (	5.68E+00	×	1E-06	×	22	×	25	×	100	×	0.5	) ÷ (	70	×	9,125	×	NV	)
Benzo(b)fluoranthene	NA	= (	5.25E+00	×	1E-06	×	22	×	25	×	100	×	0.5	) ÷ (	70	×	9,125	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	= (	3.62E+00	×	1E-06	×	22	×	25	×	100	×	0.5	) ÷ (	70	×	9,125	×	NV	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose
NV – No toxicity value available for this pathway.
NA – Not Applicable
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 29a
Risk Calculations: Reasonable Maximum Exposure
Maintenance Worker: Incidental Dermal Contact with Soil Pathway – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATc})}$$

Equation	Derm - Risk	= (	Csoil	×	SFabs	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless		kg		days	
Arsenic	2.40E-08	= (	4.99E+00	×	1.58E+00	×	1E-06	×	22	×	25	×	1	×	3,300	×	0.1	×	3.00E-02	) ÷ (	70	×	25,550	)
Lead	NA	= (	9.51E+01	×	a	×	1E-06	×	22	×	25	×	1	×	3,300	×	0.1	×	NA	) ÷ (	70	×	25,550	)
Benzo(a)anthracene	2.72E-08	= (	2.83E+00	×	7.30E-01	×	1E-06	×	22	×	25	×	1	×	3,300	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	5.47E-07	= (	5.68E+00	×	7.30E+00	×	1E-06	×	22	×	25	×	1	×	3,300	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	5.05E-08	= (	5.25E+00	×	7.30E-01	×	1E-06	×	22	×	25	×	1	×	3,300	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	3.48E-08	= (	3.62E+00	×	7.30E-01	×	1E-06	×	22	×	25	×	1	×	3,300	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csoil – Soil Concentration
SFabs – Absorbed slope factor (SFo + ABSgi)
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
SSAF – Soil-to-skin Adherence Factor
ABSd – Dermal Soil Absorption Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 29b
Risk Calculations: Reasonable Maximum Exposure
Maintenance Worker: Incidental Dermal Contact with Soil Pathway – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATn} \times \text{RfDabs})}$$

Equation	Derm - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/kg		kg/mg		days/year		years		events/day		cm^2		mg/cm^2-event		unitless		kg		days		mg/kg-day	
Arsenic	1.49E-04	= (	4.99E+00	×	1E-06	×	22	×	25	×	1	×	3,300	×	0.1	×	3.00E-02	) ÷ (	70	×	9,125	×	2.85E-04	)
Lead	NA	= (	9.51E+01	×	1E-06	×	22	×	25	×	1	×	3,300	×	0.1	×	NA	) ÷ (	70	×	9,125	×	a	)
Benzo(a)anthracene	NA	= (	2.83E+00	×	1E-06	×	22	×	25	×	1	×	3,300	×	0.1	×	1.30E-01	) ÷ (	70	×	9,125	×	NV	)
Benzo(a)pyrene	NA	= (	5.68E+00	×	1E-06	×	22	×	25	×	1	×	3,300	×	0.1	×	1.30E-01	) ÷ (	70	×	9,125	×	NV	)
Benzo(b)fluoranthene	NA	= (	5.25E+00	×	1E-06	×	22	×	25	×	1	×	3,300	×	0.1	×	1.30E-01	) ÷ (	70	×	9,125	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	= (	3.62E+00	×	1E-06	×	22	×	25	×	1	×	3,300	×	0.1	×	1.30E-01	) ÷ (	70	×	9,125	×	NV	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Soil Concentration
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
ABSd – Dermal Soil Absorption Factor
BW – Body Weight
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo ×ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.
SSAF – Soil-to-skin Adherence Factor
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 30a
Risk Calculations: Reasonable Maximum Exposure
Maintenance Worker: Incidental Inhalation of Soil (Fugitive Emissions and Volatile Compounds) Pathway– Carcinogenic Effects

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times [(1/\text{VF}) + (1/\text{PEF})])}{(\text{BW} \times \text{ATc})}$$

Equation	Inh - Risk	=	(	Csoil	×	SFi	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	)	+	(	BW	×	ATc	)
Units	unitless			mg/kg		kg-day/mg		m³/hour		hours/day		days/year		year					m³/kg				m³/kg					kg		days	
Arsenic	6.98E-11	=	(	4.99E+00	×	1.51E+01	×	1.5	×	8	×	22	×	25	×	[	1	/	NA	+	1	/	3.97E+09	]	)	+	(	70	×	25,550	)
Lead	NA	=	(	9.51E+01	×	a	×	1.5	×	8	×	22	×	25	×	[	1	/	NA	+	1	/	3.97E+09	]	)	+	(	70	×	25,550	)
Benzo(a)anthracene	NA	=	(	2.83E+00	×	NV	×	1.5	×	8	×	22	×	25	×	[	1	/	NC	+	1	/	3.97E+09	]	)	+	(	70	×	25,550	)
Benzo(a)pyrene	1.63E-11	=	(	5.68E+00	×	3.08E+00	×	1.5	×	8	×	22	×	25	×	[	1	/	NC	+	1	/	3.97E+09	]	)	+	(	70	×	25,550	)
Benzo(b)fluoranthene	NA	=	(	5.25E+00	×	NV	×	1.5	×	8	×	22	×	25	×	[	1	/	NC	+	1	/	3.97E+09	]	)	+	(	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	NA	=	(	3.62E+00	×	NV	×	1.5	×	8	×	22	×	25	×	[	1	/	NC	+	1	/	3.97E+09	]	)	+	(	70	×	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Soil Concentration
SFi – Inhalation Slope Factor
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VF – Volatilization Factor
PEF – Particulate Emission Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 30b
Risk Calculations: Reasonable Maximum Exposure
Maintenance Worker: Incidental Inhalation of Soil (Fugitive Emissions and Volatile Compounds) Pathway – Carcinogenic Effects

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BW} \times \text{ATn} \times \text{RfDi})}$$

Equation	Inh - HQ	= (	Csoil	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	÷ (	BW	×	ATn	×	RfDi	)
Units	unitless		mg/kg		m³/hour		hours/day		days/year		year					m³/kg				m³/kg			kg		days		mg/kg-day	
Arsenic	NA	= (	4.99E+00	×	1.5	×	8	×	22	×	25	×	[	1	/	NA	+	1	/	3.97E+09	]	÷ (	70	×	9,125	×	NV	)
Lead	NA	= (	9.51E+01	×	1.5	×	8	×	22	×	25	×	[	1	/	NA	+	1	/	3.97E+09	]	÷ (	70	×	9125	×	a	)
Benzo(a)anthracene	NA	= (	2.83E+00	×	1.5	×	8	×	22	×	25	×	[	1	/	NC	+	1	/	3.97E+09	]	÷ (	70	×	9125	×	NV	)
Benzo(a)pyrene	NA	= (	5.68E+00	×	1.5	×	8	×	22	×	25	×	[	1	/	NC	+	1	/	3.97E+09	]	÷ (	70	×	9125	×	NV	)
Benzo(b)fluoranthene	NA	= (	5.25E+00	×	1.5	×	8	×	22	×	25	×	[	1	/	NC	+	1	/	3.97E+09	]	÷ (	70	×	9125	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	= (	3.62E+00	×	1.5	×	8	×	22	×	25	×	[	1	/	NC	+	1	/	3.97E+09	]	÷ (	70	×	9125	×	NV	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Csoil – Soil Concentration
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VF – Volatilization Factor
PEF – Particulate Emission Factor
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment D

Table 30c
Maintenance Worker: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} \times \frac{(3.14 \times D_A \times T)^{1/2}}{(2 \times \rho_b \times D_A)} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} $(g/m^2\text{-}s)/(kg/m^3)$	π	D_A (cm^2/s)	T (s)	2	ρb (g/cm^3)	10^{-4} (m^2/cm^2)	VF (m^2/kg)
Benzo(a)anthracene	73.32	3.14	NC	7.88E+08	2	1.38	1.00E-04	NC
Benzo(a)pyrene	73.32	3.14	NC	7.88E+08	2	1.38	1.00E-04	NC
Benzo(b)fluoranthene	73.32	3.14	NC	7.88E+08	2	1.38	1.00E-04	NC
Indeno(1,2,3-cd)pyrene	73.32	3.14	NC	7.88E+08	2	1.38	1.00E-04	NC

Notes:

Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

VF – Volatilization Factor (m^3/kg) (calculated)

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source $(g/m^2\text{-}s)/(kg/m^3)$(Value used is for Minneapolis, MN.)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T – Exposure interval (s)

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated

Attachment D

Table 30d
Maintenance Worker: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical Units	VOC?	θa (Lair /Lsoil)	Di (cm²/s)	H' unitless	θw (Lwater /Lsoil)	Dw (cm²/s)	η (Lpore /Lsoil)	ρb (g/cm³)	ρs (g/cm³)	Kd (cm³/g)	D_A (cm²/s)
Benzo(a)anthracene	No	3.29E-01	5.10E-02	4.91E-04	0.15	9.00E-06	4.79E-01	1.38	2.65	1.39E+03	NC
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Benzo(b)fluoranthene	No	3.29E-01	2.26E-02	2.69E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.82E+03	NC
Indeno(1,2,3-cd)pyrene	No	3.29E-01	1.90E-02	1.42E-05	0.15	5.66E-06	4.79E-01	1.38	2.65	1.61E+04	NC

Notes:

D_A – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's Law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User'S Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density
Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm³ /g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)

Attachment D

Table 30e

Calculation of Blood Lead Concentrations (PbBs) for Non-residential Receptors (Maintenance Workers)

Exposure Variable	PbB Equation[1] 1*	2**	Description of Exposure Variable	Units	Values for Non-Residential Exposure Scenario			
					Using Equation 1		Using Equation 2	
					GSDi = Hom	GSDi = Het	GSDi = Hom	GSDi = Het
PbS	X	X	Soil lead concentration	ug/g or ppm	99.31	99.31	99.31	99.31
$R_{fetal/maternal}$	X	X	Fetal/maternal PbB ratio	--	0.9	0.9	0.9	0.9
BKSF	X	X	Biokinetic Slope Factor	ug/dL per ug/day	0.4	0.4	0.4	0.4
GSD_i	X	X	Geometric standard deviation PbB	--	2.1	2.3	2.1	2.3
PbB_0	X	X	Baseline PbB	ug/dL	1.5	1.7	1.5	1.7
IR_S	X		Soil ingestion rate (including soil-derived indoor dust)	g/day	0.050	0.050	--	--
IR_{S+D}		X	Total ingestion rate of outdoor soil and indoor dust	g/day	--	--	0.050	0.050
W_S		X	Weighting factor; fraction of IR_{S+D} ingested as outdoor soil	--	--	--	1.0	1.0
K_{SD}		X	Mass fraction of soil in dust	--	--	--	0.7	0.7
$AF_{S,D}$	X	X	Absorption fraction (same for soil and dust)	--	0.12	0.12	0.12	0.12
$EF_{S,D}$	X	X	Exposure frequency (same for soil and dust)	days/yr	219	219	219	219
$AT_{S,D}$	X	X	Averaging time (same for soil and dust)	days/yr	365	365	365	365
PbB_{adult}	**PbB of adult worker, geometric mean**			**ug/dL**	**1.6**	**1.8**	**1.6**	**1.8**
$PbB_{fetal,\ 0.95}$	**95th percentile PbB among fetuses of adult workers**			**ug/dL**	**5.0**	**6.5**	**5.0**	**6.5**
PbB_t	**Target PbB level of concern (e.g., 10 ug/dL)**			**ug/dL**	**10.0**	**10.0**	**10.0**	**10.0**
$P(PbB_{fetal} > PbB_t)$	**Probability that fetal PbB > PbB_t, assuming lognormal distribution**			**%**	**0.5%**	**1.6%**	**0.5%**	**1.6%**

[1] Equation 1 does not apportion exposure between soil and dust ingestion (excludes W_S, K_{SD}).
When $IR_S = IR_{S+D}$ and $W_S = 1.0$, the equations yield the same $PbB_{fetal,0.95}$.

***Equation 1, based on Eq. 1, 2 in USEPA (1996).**

PbB_{adult} =	$(PbS*BKSF*IR_{S+D}*AF_{S,D}*EF_S/AT_{S,D}) + PbB_0$
$PbB_{fetal,\ 0.95}$ =	$PbB_{adult} * (GSD_i^{1.645} * R)$

****Equation 2, alternate approach based on Eq. 1, 2, and A-19 in USEPA (1996).**

PbB_{adult} =	$PbS*BKSF*([(IR_{S+D})*AF_S*EF_S*W_S]+[K_{SD}*(IR_{S+D})*(1-W_S)*AF_D*EF_D])/365+PbB_0$
$PbB_{fetal,\ 0.95}$ =	$PbB_{adult} * (GSD_i^{1.645} * R)$

Source: U.S. EPA (1996). Recommendations of the Technical Review Workgroup for Lead for an Interim Approach to Assessing Risks Associated with Adult Exposures to Lead in Soil

Attachment D

Table 31a
Risk Calculations: Reasonable Maximum Exposure
Subsistence Fisher – Adult: Ingestion of Fish Pathway – Carcinogenic Effects

$$\text{Ing-Risk} = \frac{(\text{Cfish} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{FIR} \times \text{FI})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	= (	Cfish	×	SFo	×	EF	×	ED	×	FIR	×	FI	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		events/year		years		kg/event		unitless		kg		days	
Shorthead Redhorse and Walleye																		
1-Methylnaphthalene	NA	= (	6.200E-01	×	NV	×	350	×	30	×	0.081	×	1	) ÷ (	70	×	25,550	)
Smelt																		
Benzo(a)anthracene	5.90E-05	= (	1.70E-01	×	7.30E-01	×	350	×	30	×	0.081	×	1	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	5.21E-05	= (	1.50E-02	×	7.30E+00	×	350	×	30	×	0.081	×	1	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	6.60E-06	= (	1.90E-02	×	7.30E-01	×	350	×	30	×	0.081	×	1	) ÷ (	70	×	25,550	)
Benzo(e)pyrene	NA	= (	9.80E-03	×	NV	×	350	×	30	×	0.081	×	1	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	9.03E-06	= (	2.60E-03	×	7.30E+00	×	350	×	30	×	0.081	×	1	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	2.64E-06	= (	7.60E-03	×	7.30E-01	×	350	×	30	×	0.081	×	1	) ÷ (	70	×	25,550	)

Notes:

Ing - Risk – Ingestion risk
Cfish – Concentration in fish
SFo – Oral Slope Factor
EF – Exposure Frequency
ED – Exposure Duration
FIR – Fish Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable

Attachment D

Table 31b
Risk Calculations: Reasonable Maximum Exposure
Subsistence Fisher – Adult: Ingestion of Fish Pathway – Noncarcinogenic Effects

$$\text{Ing - HQ} = \frac{(\text{Cfish} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{FIR} \times \text{FI})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation	Ing - HQ	= (	Cfish	×	EF	×	ED	×	FIR	×	FI	) ÷ (	BW	×	ATn	×	RfDo	)
Units	unitless		mg/kg		events/year		years		kg/event		unitless		kg		days		mg/kg-day	
Shorthead Redhorse & Walleye																		
1-Methylnaphthalene	9.8E-03	= (	6.20E-01	×	350	×	30	×	0.081	×	1	) ÷ (	70	×	10,950	×	7.0E-02	)
Smelt																		
Benzo(a)anthracene	NA	= (	1.70E-01	×	350	×	30	×	0.081	×	1	) ÷ (	70	×	10,950	×	NV	)
Benzo(a)pyrene	NA	= (	1.50E-02	×	350	×	30	×	0.081	×	1	) ÷ (	70	×	10,950	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.90E-02	×	350	×	30	×	0.081	×	1	) ÷ (	70	×	10,950	×	NV	)
Benzo(e)pyrene	NA	= (	9.80E-03	×	350	×	30	×	0.081	×	1	) ÷ (	70	×	10,950	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.60E-03	×	350	×	30	×	0.081	×	1	) ÷ (	70	×	10,950	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	= (	7.60E-03	×	350	×	30	×	0.081	×	1	) ÷ (	70	×	10,950	×	NV	)

Notes:

Ing - HQ – Ingestion Hazard
Cfish – Concentration in fish
EF – Exposure Frequency
ED – Exposure Duration
FIR – Fish Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose
NV – No toxicity value available for this pathway.
NA – Not Applicable

ATTACHMENT E

Estimates of Carcinogenic and Noncarcinogenic Risk – CTE Scenario

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Attachment E

Table 1a
Risk Calculations: Central Tendency Evaluation
Residential Adult and Child (0-10 feet): Incidental Ingestion of Soil Pathway – Carcinogenic Effects

$$\text{Ing-Risk} = \frac{(\text{Csoil} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIRadj} \times \text{FI})}{\text{ATc}}$$

Equation / Units	Ing - Risk unitless	= (	Csoil mg/kg	×	SFo kg-day/mg	×	CF kg/mg	×	EF days/year	×	SIRadj mg-yr/kg-day	×	FI unitless	) ÷ (	ATc days	)
Arsenic	4.10E-06	= (	4.30E+00	×	1.50E+00	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Lead	NA	= (	9.05E+01	×	a	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Thallium	NA	= (	7.83E-01	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25550	)
1-Methylnaphthalene	NA	= (	7.53E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
2-Methylnaphthalene	NA	= (	8.05E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Acenaphthene	NA	= (	2.18E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Benzo(a)anthracene	6.79E-06	= (	1.46E+01	×	7.30E-01	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Benzo(a)pyrene	5.70E-05	= (	1.23E+01	×	7.30E+00	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Benzo(b)fluoranthene	6.05E-06	= (	1.30E+01	×	7.30E-01	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Benzo(k)fluoranthene	2.95E-07	= (	6.35E+00	×	7.30E-02	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Chrysene	6.51E-08	= (	1.40E+01	×	7.30E-03	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Dibenzo(a,h)anthracene	9.42E-06	= (	2.03E+00	×	7.30E+00	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Dibenzofuran	NA	= (	4.67E+00	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Fluoranthene	NA	= (	3.67E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Fluorene	NA	= (	2.54E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Indeno(1,2,3-cd)pyrene	1.59E-06	= (	3.44E+00	×	7.30E-01	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Naphthalene	NA	= (	1.21E+02	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Phenanthrene	NA	= (	7.94E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Pyrene	NA	= (	4.92E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
1,2,4-Trichlorobenzene	NA	= (	1.54E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	3.77E+00	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	6.88E+00	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Benzene	2.94E-07	= (	8.40E+00	×	5.50E-02	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Xylenes (total)	NA	= (	2.33E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – Soil Concentration
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
SIRadj – Age-adjusted Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment E

Table 1b
Risk Calculations: Central Tendency Evaluation
Residential Child (0-10 feet): Incidental Ingestion of Soil Pathway – Noncarcinogenic Effects

$$Ing\text{-}HQ = \frac{(Csoil \times CF \times EF \times EDc \times SIRc \times FI)}{(BWc \times ATn \times RfDo)}$$

Equation	Ing - HQ	= (	Csoil	×	CF	×	EF	×	EDc	×	SIRc	×	FI	) + (	BWc	×	ATn	×	RfDo [b]	)
Units	unitless		mg/kg		kg/mg		days/year		years		mg/day		unitless		kg		days		mg/kg-day	
Arsenic	9.16E-02	= (	4.30E+00	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	3.0E-04	)
Lead	NA	= (	9.05E+01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	a	)
Thallium	6.26E-02	= (	7.83E-01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	8.0E-05	)
1-Methylnaphthalene	6.88E-03	= (	7.53E+01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	7.0E-02	)
2-Methylnaphthalene	1.29E-01	= (	8.05E+01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	4.0E-03	)
Acenaphthene	2.32E-03	= (	2.18E+01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	6.0E-02	)
Benzo(a)anthracene	NA	= (	1.46E+01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	= (	1.23E+01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.30E+01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	= (	6.35E+00	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	NV	)
Chrysene	NA	= (	1.40E+01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.03E+00	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	NV	)
Dibenzofuran	1.49E-02	= (	4.67E+00	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	2.0E-03	)
Fluoranthene	5.87E-03	= (	3.67E+01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	4.0E-02	)
Fluorene	4.05E-03	= (	2.54E+01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	4.0E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	3.44E+00	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	NV	)
Naphthalene	1.55E-02	= (	1.21E+02	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	5.0E-02	)
Phenanthrene	NA	= (	7.94E+01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	NV	)
Pyrene	1.05E-03	= (	4.92E+01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	3.0E-01	)
1,2,4-Trichlorobenzene	9.87E-03	= (	1.54E+01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	1.0E-02	)
1,2,4-Trimethylbenzene	4.82E-04	= (	3.77E+00	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	5.0E-02	)
1,3,5-Trimethylbenzene	8.80E-04	= (	6.88E+00	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	5.0E-02	)
Benzene	1.34E-02	= (	8.40E+00	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	4.0E-03	)
Xylenes (total)	1.86E-03	= (	2.33E+01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	8.0E-02	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
EDc – Exposure Duration, child
SIRc – Soil Ingestion Rate, child
FI – Fraction Ingested from Contaminated Source
BWc – Body Weight, child
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment E

Table 2a
Risk Calculations: Central Tendency Evaluation
Residential Adult and Child (0-10 feet): Dermal Contact with Soil Pathway – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(Csoil \times SFabs \times CF \times EF \times EV \times SCRadj \times ABSd)}{ATc}$$

Equation	Derm - Risk	= (	Csoil	×	SFabs	×	CF	×	EF	×	EV	×	SCRadj	×	ABSd	) ÷ (	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		events/day		mg-yr/kg-event		unitless		days	
Arsenic	1.45E-07	= (	4.30E+00	×	1.58E+00	×	1E-06	×	350	×	1	×	52.1	×	3.00E-02	) ÷ (	25,550	)
Lead	NA	= (	9.05E+01	×	a	×	1E-06	×	350	×	1	×	52.1	×	NA	) ÷ (	25,550	)
Thallium	NA	= (	7.83E-01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	NA	) ÷ (	25,550	)
1-Methylnaphthalene	NA	= (	7.53E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
2-Methylnaphthalene	NA	= (	8.05E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.00E-01	) ÷ (	25,550	)
Acenaphthene	NA	= (	2.18E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Benzo(a)anthracene	9.91E-07	= (	1.46E+01	×	7.30E-01	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Benzo(a)pyrene	8.31E-06	= (	1.23E+01	×	7.30E+00	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Benzo(b)fluoranthene	8.83E-07	= (	1.30E+01	×	7.30E-01	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Benzo(k)fluoranthene	4.31E-08	= (	6.35E+00	×	7.30E-02	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Chrysene	9.50E-09	= (	1.40E+01	×	7.30E-03	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Dibenzo(a,h)anthracene	1.37E-06	= (	2.03E+00	×	7.30E+00	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Dibenzofuran	NA	= (	4.67E+00	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Fluoranthene	NA	= (	3.67E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Fluorene	NA	= (	2.54E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Indeno(1,2,3-cd)pyrene	2.33E-07	= (	3.44E+00	×	7.30E-01	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Naphthalene	NA	= (	1.21E+02	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Phenanthrene	NA	= (	7.94E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Pyrene	NA	= (	4.92E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
1,2,4-Trichlorobenzene	NA	= (	1.54E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	NV	) ÷ (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	3.77E+00	×	NV	×	1E-06	×	350	×	1	×	52.1	×	NA	) ÷ (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	6.88E+00	×	NV	×	1E-06	×	350	×	1	×	52.1	×	NA	) ÷ (	25,550	)
Benzene	NA	= (	8.40E+00	×	5.50E-02	×	1E-06	×	350	×	1	×	52.1	×	NA	) ÷ (	25,550	)
Xylenes (total)	NA	= (	2.33E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	NA	) ÷ (	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csoil – Soil Concentration
SFabs – Absorbed slope factor (SFo + ABSgi)
CF – *Unit Conversion Factor*
EF – Exposure Frequency
EV – Event Frequency
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.
SCRadj – Age-adjusted Soil Contact Rate
ABSd – Dermal Soil Absorption Factor
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment E

Table 2b
Risk Calculations: Central Tendency Evaluation
Residential Child (0-10 feet): Dermal Contact with Soil Pathway – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{EDc} \times \text{EV} \times \text{SAc} \times \text{AFc} \times \text{ABSd})}{(\text{BWc} \times \text{ATn} \times \text{RfDabs})}$$

Equation / Units	Derm - HQ unitless	= (	Csoil mg/kg	×	CF kg/mg	×	EF days/year	×	EDc years	×	EV events/day	×	SAc cm²	×	AFc mg/cm²-event	×	ABSd unitless	) ÷ (	BWc kg	×	ATn days	×	RfDabs [b] mg/kg-day	)
Arsenic	3.24E-03	= (	4.30E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	3.00E-02	) ÷ (	15	×	2,190	×	2.85E-04	)
Lead	NA	= (	9.05E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	NA	) ÷ (	15	×	2,190	×	a	)
Thallium	NA	= (	7.83E-01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	NA	) ÷ (	15	×	2,190	×	8.00E-05	)
1-Methylnaphthalene	1.00E-03	= (	7.53E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	7.00E-02	)
2-Methylnaphthalene	1.44E-02	= (	8.05E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.00E-01	) ÷ (	15	×	2,190	×	4.00E-03	)
Acenaphthene	3.38E-04	= (	2.18E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	6.00E-02	)
Benzo(a)anthracene	NA	= (	1.46E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	= (	1.23E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.30E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	= (	6.35E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Chrysene	NA	= (	1.40E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.03E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Dibenzofuran	2.17E-03	= (	4.67E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	2.00E-03	)
Fluoranthene	8.55E-04	= (	3.67E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	4.00E-02	)
Fluorene	5.90E-04	= (	2.54E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	3.44E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Naphthalene	2.26E-03	= (	1.21E+02	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	5.00E-02	)
Phenanthrene	NA	= (	7.94E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Pyrene	1.53E-04	= (	4.92E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	3.00E-01	)
1,2,4-Trichlorobenzene	NA	= (	1.54E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	NV	) ÷ (	15	×	2,190	×	NV	)
1,2,4-Trimethylbenzene	NA	= (	3.77E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	NA	) ÷ (	15	×	2,190	×	5.00E-02	)
1,3,5-Trimethylbenzene	NA	= (	6.88E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	NA	) ÷ (	15	×	2,190	×	5.00E-02	)
Benzene	NA	= (	8.40E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	NA	) ÷ (	15	×	2,190	×	4.00E-03	)
Xylenes (total)	NA	= (	2.33E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	NA	) ÷ (	15	×	2,190	×	8.00E-02	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
EDc – Exposure Duration, child
EV – Event Frequency
SAc – Skin Surface Area, child
AFc – Soil-to-skin Adherence Factor, child
ABSd – Dermal Soil Absorption Factor
BWc – Body Weight, child
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo × ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment E

Table 3a
Risk Calculations: Central Tendency Evaluation
Residential Adult and Child (0-10 feet): Inhalation of Soil-derived Chemicals Pathway– Carcinogenic Effects

$$Inh\text{ - }Risk = \frac{(Csoil \times SFi \times EF \times SInhRadj \times [(1/VF) + (1/PEF)])}{ATc}$$

Equation / Units	Inh - Risk unitless	= (	Csoil mg/kg	×	SFi kg-day/mg	×	EF days/year	×	SInhRadj m3-yr/kg-day	× [1 /	VF_{adult} m^3/kg	+ 1 /	PEF m^3/kg	]) ÷ (	ATc days	)
Arsenic	NA	= (	4.30E+00	×	1.51E+01	×	350	×	4.58	× [1 /	NA	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Lead	NA	= (	9.05E+01	×	a	×	350	×	4.58	× [1 /	NA	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Thallium	NA	= (	7.83E-01	×	NV	×	350	×	4.58	× [1 /	NA	+ 1 /	6.58E+09	]) ÷ (	25,550	)
1-Methylnaphthalene	NA	= (	7.53E+01	×	NV	×	350	×	4.58	× [1 /	5.41E+04	+ 1 /	6.58E+09	]) ÷ (	25,550	)
2-Methylnaphthalene	NA	= (	8.05E+01	×	NV	×	350	×	4.58	× [1 /	3.77E+04	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Acenaphthene	NA	= (	2.18E+01	×	NV	×	350	×	4.58	× [1 /	9.73E+04	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Benzo(a)anthracene	NA	= (	1.46E+01	×	NV	×	350	×	4.58	× [1 /	NC	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Benzo(a)pyrene	3.61E-10	= (	1.23E+01	×	3.08E+00	×	350	×	4.58	× [1 /	NC	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Benzo(b)fluoranthene	NA	= (	1.30E+01	×	NV	×	350	×	4.58	× [1 /	NC	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Benzo(k)fluoranthene	NA	= (	6.35E+00	×	NV	×	350	×	4.58	× [1 /	NC	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Chrysene	NA	= (	1.40E+01	×	NV	×	350	×	4.58	× [1 /	NC	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Dibenzo(a,h)anthracene	NA	= (	2.03E+00	×	NV	×	350	×	4.58	× [1 /	NC	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Dibenzofuran	NA	= (	4.67E+00	×	NV	×	350	×	4.58	× [1 /	1.07E+05	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Fluoranthene	NA	= (	3.67E+01	×	NV	×	350	×	4.58	× [1 /	NC	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Fluorene	NA	= (	2.54E+01	×	NV	×	350	×	4.58	× [1 /	1.95E+05	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Indeno(1,2,3-cd)pyrene	NA	= (	3.44E+00	×	NV	×	350	×	4.58	× [1 /	NC	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Naphthalene	NA	= (	1.21E+02	×	NV	×	350	×	4.58	× [1 /	2.91E+04	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Phenanthrene	NA	= (	7.94E+01	×	NV	×	350	×	4.58	× [1 /	4.16E+05	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Pyrene	NA	= (	4.92E+01	×	NV	×	350	×	4.58	× [1 /	1.56E+06	+ 1 /	6.58E+09	]) ÷ (	25,550	)
1,2,4-Trichlorobenzene	NA	= (	1.54E+01	×	NV	×	350	×	4.58	× [1 /	2.23E+04	+ 1 /	6.58E+09	]) ÷ (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	3.77E+00	×	NV	×	350	×	4.58	× [1 /	4.71E+03	+ 1 /	6.58E+09	]) ÷ (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	6.88E+00	×	NV	×	350	×	4.58	× [1 /	4.06E+03	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Benzene	1.01E-15	= (	8.40E+00	×	2.73E-02	×	350	×	4.58	× [1 /	2.16E+03	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Xylenes (total)	NA	= (	2.33E+01	×	NV	×	350	×	4.58	× [1 /	3.43E+03	+ 1 /	6.58E+09	]) ÷ (	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Soil Concentration
SFi – Inhalation Slope Factor
EF – Exposure frequency
SInhRadj – Age-adjusted Soil Inhalation Rate
VF_{adult} – Volatilization Factor (adult)
PEF – Particulate Emission Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment E

Table 3b
Risk Calculations: Central Tendency Evaluation
Residential Child (0-10 feet): Inhalation of Soil-derived Pathway – Noncarcinogenic Effects

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{InhRc} \times \text{EF} \times \text{EDc} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BWc} \times \text{ATn} \times \text{RfDi})}$$

Equation / Units	Inh - HQ unitless	=	Csoil mg/kg	×	InhRc m³/day	×	EF days/year	×	EDc year	×	[	1	/	VF_{child} m³/kg	+	1	/	PEF m³/kg	]	+	BWc kg	×	ATn days	×	RfDi [b] mg/kg-day	)
Arsenic	NA	=	4.30E+00	×	7.2	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
Lead	NA	=	9.05E+01	×	7.2	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	+	15	×	2,190	×	a	)
Thallium	NA	=	7.83E-01	×	7.2	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
1-Methylnaphthalene	NA	=	7.53E+01	×	7.2	×	350	×	6	×	[	1	/	4.42E+04	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
2-Methylnaphthalene	NA	=	8.05E+01	×	7.2	×	350	×	6	×	[	1	/	3.08E+04	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
Acenaphthene	NA	=	2.18E+01	×	7.2	×	350	×	6	×	[	1	/	7.94E+04	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
Benzo(a)anthracene	NA	=	1.46E+01	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	=	1.23E+01	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	=	1.30E+01	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	=	6.35E+00	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
Chrysene	NA	=	1.40E+01	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	=	2.03E+00	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
Dibenzofuran	NA	=	4.67E+00	×	7.2	×	350	×	6	×	[	1	/	8.71E+04	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
Fluoranthene	NA	=	3.67E+01	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
Fluorene	NA	=	2.54E+01	×	7.2	×	350	×	6	×	[	1	/	1.60E+05	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	=	3.44E+00	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
Naphthalene	2.74E+00	=	1.21E+02	×	7.2	×	350	×	6	×	[	1	/	2.37E+04	+	1	/	6.58E+09	]	+	15	×	2,190	×	8.57E-04	)
Phenanthrene	NA	=	7.94E+01	×	7.2	×	350	×	6	×	[	1	/	3.40E+05	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
Pyrene	NA	=	4.92E+01	×	7.2	×	350	×	6	×	[	1	/	1.27E+06	+	1	/	6.58E+09	]	+	15	×	2,190	×	NV	)
1,2,4-Trichlorobenzene	3.42E-01	=	1.54E+01	×	7.2	×	350	×	6	×	[	1	/	1.82E+04	+	1	/	6.58E+09	]	+	15	×	2,190	×	1.14E-03	)
1,2,4-Trimethylbenzene	2.64E-01	=	3.77E+00	×	7.2	×	350	×	6	×	[	1	/	3.85E+03	+	1	/	6.58E+09	]	+	15	×	2,190	×	1.71E-03	)
1,3,5-Trimethylbenzene	5.59E-01	=	6.88E+00	×	7.2	×	350	×	6	×	[	1	/	3.31E+03	+	1	/	6.58E+09	]	+	15	×	2,190	×	1.71E-03	)
Benzene	2.56E-01	=	8.40E+00	×	7.2	×	350	×	6	×	[	1	/	1.76E+03	+	1	/	6.58E+09	]	+	15	×	2,190	×	8.57E-03	)
Xylenes (total)	1.34E-01	=	2.33E+01	×	7.2	×	350	×	6	×	[	1	/	2.80E+03	+	1	/	6.58E+09	]	+	15	×	2,190	×	2.86E-02	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Csoil – Soil Concentration
InhRc – Inhalation Rate, child
EF – Exposure frequency
EDc – Exposure duration, child
VF_{child} – Volatilization Factor (child)
PEF – Particulate Emission Factor
BWc – Body Weight, child
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment E

Table 3c
Residential Scenario: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} \times \frac{(3.14 \times D_A \times T)^{1/2}}{(2 \times \rho_b \times D_A)} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} $(g/m^2\text{-}s)/(kg/m^3)$	π	D_A (cm^2/s)	T_{adult} (s)	T_{child} (s)	2	pb (g/cm^3)	10^{-4} (m^3/cm^3)	VFadult (m^3/kg)	VFchild (m^3/kg)
1-Methylnaphthalene	73.32	3.14	2.15E-06	2.84E+08	1.89E+08	2	1.38	1.00E-04	5.41E+04	4.42E+04
2-Methylnaphthalene	73.32	3.14	4.42E-06	2.84E+08	1.89E+08	2	1.38	1.00E-04	3.77E+04	3.08E+04
Acenaphthene	73.32	3.14	6.65E-07	2.84E+08	1.89E+08	2	1.38	1.00E-04	9.73E+04	7.94E+04
Benzo(a)anthracene	73.32	3.14	NC	2.84E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Benzo(a)pyrene	73.32	3.14	NC	2.84E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Benzo(b)fluoranthene	73.32	3.14	NC	2.84E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Benzo(k)fluoranthene	73.32	3.14	NC	2.84E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Chrysene	73.32	3.14	NC	2.84E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Dibenzo(a,h)anthracene	73.32	3.14	NC	2.84E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Dibenzofuran	73.32	3.14	5.52E-07	2.84E+08	1.89E+08	2	1.38	1.00E-04	1.07E+05	8.71E+04
Fluoranthene	73.32	3.14	NC	2.84E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Fluorene	73.32	3.14	1.65E-07	2.84E+08	1.89E+08	2	1.38	1.00E-04	1.95E+05	1.60E+05
Indeno(1,2,3-cd)pyrene	73.32	3.14	NC	2.84E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Naphthalene	73.32	3.14	7.45E-06	2.84E+08	1.89E+08	2	1.38	1.00E-04	2.91E+04	2.37E+04
Phenanthrene	73.32	3.14	3.63E-08	2.84E+08	1.89E+08	2	1.38	1.00E-04	4.16E+05	3.40E+05
Pyrene	73.32	3.14	2.58E-09	2.84E+08	1.89E+08	2	1.38	1.00E-04	1.56E+06	1.27E+06
1,2,4-Trichlorobenzene	73.32	3.14	1.26E-05	2.84E+08	1.89E+08	2	1.38	1.00E-04	2.23E+04	1.82E+04
1,2,4-Trimethylbenzene	73.32	3.14	2.83E-04	2.84E+08	1.89E+08	2	1.38	1.00E-04	4.71E+03	3.85E+03
1,3,5-Trimethylbenzene	73.32	3.14	3.82E-04	2.84E+08	1.89E+08	2	1.38	1.00E-04	4.06E+03	3.31E+03
Benzene	73.32	3.14	1.35E-03	2.84E+08	1.89E+08	2	1.38	1.00E-04	2.16E+03	1.76E+03
Xylenes (total)	73.32	3.14	5.33E-04	2.84E+08	1.89E+08	2	1.38	1.00E-04	3.43E+03	2.80E+03

Notes:

Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

VF_{adult} – Volatilization Factor (adult) - calculated

VF_{child} – Volatilization Factor (child) - calculated

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source $(g/m^2\text{-}s)/(kg/m^3)$(Value used is for Minneapolis, MN.)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T_{adult} – Exposure interval for adults (s)

T_{child} – Exposure interval for child (s)

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated; PAHs are not considered volatile chemicals

Attachment E

Table 3d
Residential Scenario: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical Units	VOC?	θa (Lair /Lsoil)	Di (cm^2/s)	H' unitless	θw (Lwater /Lsoil)	Dw (cm^2/s)	η (Lpore /Lsoil)	ρb (g/cm^3)	ρs (g/cm^3)	Kd (cm^3/g)	D_A (cm^2/s)
1-Methylnaphthalene	Yes	3.29E-01	6.31E-02	1.64E-02	0.15	7.13E-06	4.79E-01	1.38	2.65	3.75E+01	2.15E-06
2-Methylnaphthalene	Yes	3.29E-01	4.80E-02	2.12E-02	0.15	7.84E-06	4.79E-01	1.38	2.65	1.79E+01	4.42E-06
Acenaphthene	Yes	3.29E-01	4.21E-02	7.44E-03	0.15	7.69E-06	4.79E-01	1.38	2.65	3.67E+01	6.65E-07
Benzo(a)anthracene	No	3.29E-01	5.10E-02	4.91E-04	0.15	9.00E-06	4.79E-01	1.38	2.65	1.39E+03	NC
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Benzo(b)fluoranthene	No	3.29E-01	2.26E-02	2.69E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.82E+03	NC
Benzo(k)fluoranthene	No	3.29E-01	2.26E-02	2.39E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Chrysene	No	3.29E-01	2.48E-02	2.14E-04	0.15	6.21E-06	4.79E-01	1.38	2.65	1.42E+03	NC
Dibenzo(a,h)anthracene	No	3.29E-01	2.02E-02	5.03E-06	0.15	5.18E-06	4.79E-01	1.38	2.65	1.57E+04	NC
Dibenzofuran	Yes	3.29E-01	5.51E-02	8.71E-03	0.15	7.04E-06	4.79E-01	1.38	2.65	6.78E+01	5.52E-07
Fluoranthene	No	3.29E-01	3.02E-02	3.62E-04	0.15	6.35E-06	4.79E-01	1.38	2.65	4.25E+02	NC
Fluorene	Yes	3.29E-01	3.63E-02	3.93E-03	0.15	7.88E-06	4.79E-01	1.38	2.65	6.78E+01	1.65E-07
Indeno(1,2,3-cd)pyrene	No	3.29E-01	1.90E-02	1.42E-05	0.15	5.66E-06	4.79E-01	1.38	2.65	1.61E+04	NC
Naphthalene	Yes	3.29E-01	5.90E-02	1.80E-02	0.15	7.50E-06	4.79E-01	1.38	2.65	1.10E+01	7.45E-06
Phenanthrene	Yes	3.29E-01	3.33E-02	1.73E-03	0.15	7.47E-06	4.79E-01	1.38	2.65	1.25E+02	3.63E-08
Pyrene	Yes	3.29E-01	2.72E-02	4.87E-04	0.15	7.24E-06	4.79E-01	1.38	2.65	4.16E+02	2.58E-09
1,2,3-Trimethylbenzene	NV	3.29E-01	6.77E-02	1.33E-01	0.15	7.41E-06	4.79E-01	1.38	2.65	3.53E+00	1.91E-04
1,2,4-Trichlorobenzene	Yes	3.29E-01	3.00E-02	5.82E-02	0.15	8.23E-06	4.79E-01	1.38	2.65	1.07E+01	1.26E-05
1,2,4-Trimethylbenzene	Yes	3.29E-01	6.44E-02	2.52E-01	0.15	7.92E-06	4.79E-01	1.38	2.65	4.31E+00	2.83E-04
1,3,5-Trimethylbenzene	Yes	3.29E-01	6.02E-02	3.59E-01	0.15	8.67E-06	4.79E-01	1.38	2.65	4.22E+00	3.82E-04
Benzene	Yes	3.29E-01	8.80E-02	2.27E-01	0.15	9.80E-06	4.79E-01	1.38	2.65	9.93E-01	1.35E-03
Xylenes (total)	Yes	3.29E-01	7.14E-02	2.71E-01	0.15	9.34E-06	4.79E-01	1.38	2.65	2.66E+00	5.33E-04

Notes:

D_A – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
pb – dry soil bulk density based on soil type of silty clay. Value obtained from *User'S Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ps – soil particle density
Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm^3 /g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)
VOC? – Volatile organic compounds; If no, an apparent diffusivity was not calculated.
NV – no value available
NC – not calculated

Attachment F

Table 4a
Risk Calculations: Central Tendency Evaluation
Residential Adult and Child: Incidental Ingestion of Soil Pathway (0-3 feet) – Carcinogenic Effects

$$\text{Ing-Risk} = \frac{(\text{Csoil} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{SIRadj} \times \text{FI})}{\text{ATc}}$$

Equation	Ing - Risk	= (	Csoil	×	SFo	×	CF	×	EF	×	SIRadj	×	FI	) ÷ (	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		mg-yr/kg-day		unitless		days	
Arsenic	2.83E-06	= (	2.97E+00	×	1.50E+00	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Lead	NA	= (	1.76E+02	×	a	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
1-Methylnaphthalene	NA	= (	7.21E+00	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Benzo(a)anthracene	2.68E-06	= (	5.77E+00	×	7.30E-01	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Benzo(a)pyrene	3.24E-05	= (	6.97E+00	×	7.30E+00	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Benzo(b)fluoranthene	2.84E-06	= (	6.12E+00	×	7.30E-01	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Benzo(k)fluoranthene	9.19E-08	= (	1.98E+00	×	7.30E-02	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Dibenzo(a,h)anthracene	1.83E-06	= (	3.95E-01	×	7.30E+00	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Fluoranthene	NA	= (	1.12E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Indeno(1,2,3-cd)pyrene	7.17E-07	= (	1.54E+00	×	7.30E-01	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Naphthalene	NA	= (	2.82E+00	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Pyrene	NA	= (	1.91E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	6.13E-01	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	2.33E-01	×	NV	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)
Benzene	3.12E-08	= (	8.92E-01	×	5.50E-02	×	1E-06	×	350	×	46.43	×	1	) ÷ (	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – Soil Concentration
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
SIRadj – Age-adjusted Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment F

Table 4b
Risk Calculations: Central Tendency Evaluation
Residential Child: Incidental Ingestion of Soil Pathway (0-3 feet) – Noncarcinogenic Effects

$$Ing\text{-}HQ = \frac{(Csoil \times CF \times EF \times EDc \times SIRc \times FI)}{(BWc \times ATn \times RfDo)}$$

Equation																						
Units	Ing - HQ unitless	=	(	Csoil mg/kg	×	CF kg/mg	×	EF days/year	×	EDc years	×	SIRc mg/day	×	FI unitless	)	÷	(	BWc kg	×	ATn days	×	RfDo [b] mg/kg-day	)
Arsenic	6.33E-02	=	(	2.97E+00	×	1E-06	×	350	×	6	×	100	×	1	)	÷	(	15	×	2,190	×	3.0E-04	)
Lead	NA	=	(	1.76E+02	×	1E-06	×	350	×	6	×	100	×	1	)	÷	(	15	×	2,190	×	a	)
1-Methylnaphthalene	6.58E-04	=	(	7.21E+00	×	1E-06	×	350	×	6	×	100	×	1	)	÷	(	15	×	2,190	×	7.0E-02	)
Benzo(a)anthracene	NA	=	(	5.77E+00	×	1E-06	×	350	×	6	×	100	×	1	)	÷	(	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	=	(	6.97E+00	×	1E-06	×	350	×	6	×	100	×	1	)	÷	(	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	=	(	6.12E+00	×	1E-06	×	350	×	6	×	100	×	1	)	÷	(	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	=	(	1.98E+00	×	1E-06	×	350	×	6	×	100	×	1	)	÷	(	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	=	(	3.95E-01	×	1E-06	×	350	×	6	×	100	×	1	)	÷	(	15	×	2,190	×	NV	)
Fluoranthene	1.79E-04	=	(	1.12E+01	×	1E-06	×	350	×	6	×	100	×	1	)	÷	(	15	×	2,190	×	4.0E-01	)
Indeno(1,2,3-cd)pyrene	NA	=	(	1.54E+00	×	1E-06	×	350	×	6	×	100	×	1	)	÷	(	15	×	2,190	×	NV	)
Naphthalene	9.00E-04	=	(	2.82E+00	×	1E-06	×	350	×	6	×	100	×	1	)	÷	(	15	×	2,190	×	2.0E-02	)
Pyrene	4.07E-04	=	(	1.91E+01	×	1E-06	×	350	×	6	×	100	×	1	)	÷	(	15	×	2,190	×	3.0E-01	)
1,2,4-Trimethylbenzene	7.84E-05	=	(	6.13E-01	×	1E-06	×	350	×	6	×	100	×	1	)	÷	(	15	×	2,190	×	5.0E-02	)
1,3,5-Trimethylbenzene	2.98E-06	=	(	2.33E-01	×	1E-06	×	350	×	6	×	100	×	1	)	÷	(	15	×	2,190	×	5.0E-01	)
Benzene	1.43E-03	=	(	8.92E-01	×	1E-06	×	350	×	6	×	100	×	1	)	÷	(	15	×	2,190	×	4.0E-03	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
EDc – Exposure Duration, child
SIRc – Soil Ingestion Rate, child
FI – Fraction Ingested from Contaminated Source
BWc – Body Weight, child
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment F

Table 5a
Risk Calculations: Central Tendency Evaluation
Residential Adult and Child: Dermal Contact with Soil Pathway (0-3 feet) – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{EV} \times \text{SCRadj} \times \text{ABSd})}{\text{ATc}}$$

Equation / Units	Derm - Risk unitless	= (	Csoil mg/kg	×	SFabs kg-day/mg	×	CF kg/mg	×	EF days/year	×	EV events/day	×	SCRadj mg-yr/kg-event	×	ABSd unitless	) ÷ (	ATc days	)
Arsenic	1.00E-07	= (	2.97E+00	×	1.58E+00	×	1E-06	×	350	×	1	×	52	×	3.00E-02	) ÷ (	25,550	)
Lead	NA	= (	1.76E+02	×	a	×	1E-06	×	350	×	1	×	52	×	NA	) ÷ (	25,550	)
1-Methylnaphthalene	NA	= (	7.21E+00	×	NV	×	1E-06	×	350	×	1	×	52	×	1.30E-01	) ÷ (	25,550	)
Benzo(a)anthracene	3.91E-07	= (	5.77E+00	×	7.30E-01	×	1E-06	×	350	×	1	×	52	×	1.30E-01	) ÷ (	25,550	)
Benzo(a)pyrene	4.73E-06	= (	6.97E+00	×	7.30E+00	×	1E-06	×	350	×	1	×	52	×	1.30E-01	) ÷ (	25,550	)
Benzo(b)fluoranthene	4.15E-07	= (	6.12E+00	×	7.30E-01	×	1E-06	×	350	×	1	×	52	×	1.30E-01	) ÷ (	25,550	)
Benzo(k)fluoranthene	1.34E-08	= (	1.98E+00	×	7.30E-02	×	1E-06	×	350	×	1	×	52	×	1.30E-01	) ÷ (	25,550	)
Dibenzo(a,h)anthracene	2.67E-07	= (	3.95E-01	×	7.30E+00	×	1E-06	×	350	×	1	×	52	×	1.30E-01	) ÷ (	25,550	)
Fluoranthene	NA	= (	1.12E+01	×	NV	×	1E-06	×	350	×	1	×	52	×	1.30E-01	) ÷ (	25,550	)
Indeno(1,2,3-cd)pyrene	1.05E-07	= (	1.54E+00	×	7.30E-01	×	1E-06	×	350	×	1	×	52	×	1.30E-01	) ÷ (	25,550	)
Naphthalene	NA	= (	2.82E+00	×	NV	×	1E-06	×	350	×	1	×	52	×	1.30E-01	) ÷ (	25,550	)
Pyrene	NA	= (	1.91E+01	×	NV	×	1E-06	×	350	×	1	×	52	×	1.30E-01	) ÷ (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	6.13E-01	×	NV	×	1E-06	×	350	×	1	×	52	×	NA	) ÷ (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	2.33E-01	×	NV	×	1E-06	×	350	×	1	×	52	×	NA	) ÷ (	25,550	)
Benzene	NA	= (	8.92E-01	×	5.50E-02	×	1E-06	×	350	×	1	×	52	×	NA	) ÷ (	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csoil – Soil Concentration
SFabs – Absorbed slope factor (SFo + ABSgi)
CF – Unit Conversion Factor
EF – Exposure Frequency
EV – Event Frequency
SCRadj – Age-adjusted Soil Contact Rate
ABSd – Dermal Soil Absorption Factor
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment F

Table 5b

Risk Calculations: Central Tendency Evaluation
Residential Child: Dermal Contact with Soil Pathway (0-3 feet) – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{EDc} \times \text{EV} \times \text{SAc} \times \text{AFc} \times \text{ABSd})}{(\text{BWc} \times \text{ATn} \times \text{RfDabs})}$$

Equation / Units	Derm - HQ unitless	= (	Csoil mg/kg	×	CF kg/mg	×	EF days/year	×	EDc years	×	EV events/day	×	SAc cm²	×	AFc mg/cm²-event	×	ABSd unitless	) + (	BWc kg	×	ATn days	×	RfDabs [b] mg/kg-day	)
Arsenic	1.12E-02	= (	2.97E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	3.00E-02	) + (	15	×	2,190	×	2.85E-04	)
Lead	NA	= (	1.76E+02	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	NA	) + (	15	×	2,190	×	a	)
1-Methylnaphthalene	4.79E-04	= (	7.21E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) + (	15	×	2,190	×	7.00E-02	)
Benzo(a)anthracene	NA	= (	5.77E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) + (	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	= (	6.97E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) + (	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	= (	6.12E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) + (	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.98E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) + (	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	3.95E-01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) + (	15	×	2,190	×	NV	)
Fluoranthene	1.30E-04	= (	1.12E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) + (	15	×	2,190	×	4.00E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.54E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) + (	15	×	2,190	×	NV	)
Naphthalene	6.55E-04	= (	2.82E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) + (	15	×	2,190	×	2.00E-02	)
Pyrene	2.96E-04	= (	1.91E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) + (	15	×	2,190	×	3.00E-01	)
1,2,4-Trimethylbenzene	NA	= (	6.13E-01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	NA	) + (	15	×	2,190	×	5.00E-02	)
1,3,5-Trimethylbenzene	NA	= (	2.33E-01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	NA	) + (	15	×	2,190	×	5.00E-01	)
Benzene	NA	= (	8.92E-01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	NA	) + (	15	×	2,190	×	4.00E-03	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
EDc – Exposure Duration, child
EV – Event Frequency
SAc – Skin Surface Area, child
AFc – Soil-to-skin Adherence Factor, child
ABSd – Dermal Soil Absorption Factor
BWc – Body Weight, child
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo × ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment F

Table 6a
Risk Calculations: Central Tendency Evaluation
Residential Adult and Child: Inhalation of Soil-derived Chemicals Pathway (0-3 feet)– Carcinogenic Effects

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{EF} \times \text{SInhRadj} \times [(1/\text{VF}) + (1/\text{PEF})])}{\text{ATc}}$$

Equation Units	Inh - Risk unitless	= (	Csoil mg/kg	×	SFi kg-day/mg	×	EF days/year	×	SInhRadj m3-yr/kg-day	× [	1	/	VF_{adult} m³/kg	+	1	/	PEF m³/kg	]) ÷ (	ATc days	)
Arsenic	4.27E-10	= (	2.97E+00	×	1.51E+01	×	350	×	4.58	× [	1	/	NA	+	1	/	6.58E+09	]) ÷ (	25,550	)
Lead	NA	= (	1.76E+02	×	a	×	350	×	4.58	× [	1	/	NA	+	1	/	6.58E+09	]) ÷ (	25,550	)
1-Methylnaphthalene	NA	= (	7.21E+00	×	NV	×	350	×	4.58	× [	1	/	3.28E+04	+	1	/	6.58E+09	]) ÷ (	25,550	)
Benzo(a)anthracene	NA	= (	5.77E+00	×	NV	×	350	×	4.58	× [	1	/	NC	+	1	/	6.58E+09	]) ÷ (	25,550	)
Benzo(a)pyrene	2.05E-10	= (	6.97E+00	×	3.08E+00	×	350	×	4.58	× [	1	/	NC	+	1	/	6.58E+09	]) ÷ (	25,550	)
Benzo(b)fluoranthene	NA	= (	6.12E+00	×	NV	×	350	×	4.58	× [	1	/	NC	+	1	/	6.58E+09	]) ÷ (	25,550	)
Benzo(k)fluoranthene	NA	= (	1.98E+00	×	NV	×	350	×	4.58	× [	1	/	NC	+	1	/	6.58E+09	]) ÷ (	25,550	)
Dibenzo(a,h)anthracene	NA	= (	3.95E-01	×	NV	×	350	×	4.58	× [	1	/	NC	+	1	/	6.58E+09	]) ÷ (	25,550	)
Fluoranthene	NA	= (	1.12E+01	×	NV	×	350	×	4.58	× [	1	/	NC	+	1	/	6.58E+09	]) ÷ (	25,550	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.54E+00	×	NV	×	350	×	4.58	× [	1	/	NC	+	1	/	6.58E+09	]) ÷ (	25,550	)
Naphthalene	NA	= (	2.82E+00	×	NV	×	350	×	4.58	× [	1	/	2.87E+04	+	1	/	6.58E+09	]) ÷ (	25,550	)
Pyrene	NA	= (	1.91E+01	×	NV	×	350	×	4.58	× [	1	/	3.05E+05	+	1	/	6.58E+09	]) ÷ (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	6.13E-01	×	NV	×	350	×	4.58	× [	1	/	5.47E+03	+	1	/	6.58E+09	]) ÷ (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	2.33E-01	×	NV	×	350	×	4.58	× [	1	/	4.52E+03	+	1	/	6.58E+09	]) ÷ (	25,550	)
Benzene	4.78E-07	= (	8.92E-01	×	2.73E-02	×	350	×	4.58	× [	1	/	3.20E+03	+	1	/	6.58E+09	]) ÷ (	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Soil Concentration
SFi – Inhalation Slope Factor
EF – Exposure frequency
SInhRadj – Age-adjusted Soil Inhalation Rate
VF – Volatilization Factor
PEF – Particulate Emission Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment F

Table 6b
Risk Calculations: Central Tendency Evaluation
Residential Child: Inhalation of Soil-derived Pathway (0-3 feet) – Noncarcinogenic Effects

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{InhRc} \times \text{EF} \times \text{EDc} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BWc} \times \text{ATn} \times \text{RfDi})}$$

Equation / Units	Inh - HQ unitless	=	Csoil mg/kg	×	InhRc m³/day	×	EF days/year	×	EDc year	×	[	1	/	VF_{child} m³/kg	+	1	/	PEF m³/kg	]	÷	(	BWc kg	×	ATn days	×	RfDi (b) mg/kg-day	)
Arsenic	NA	=	2.97E+00	×	7.2	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Lead	NA	=	1.76E+02	×	7.2	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	a	)
1-Methylnaphthalene	NA	=	7.21E+00	×	7.2	×	350	×	6	×	[	1	/	1.47E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Benzo(a)anthracene	NA	=	5.77E+00	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	=	6.97E+00	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	=	6.12E+00	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	=	1.98E+00	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	=	3.95E-01	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Fluoranthene	NA	=	1.12E+01	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	=	1.54E+00	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Naphthalene	1.18E-01	=	2.82E+00	×	7.2	×	350	×	6	×	[	1	/	1.29E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	8.57E-04	)
Pyrene	NA	=	1.91E+01	×	7.2	×	350	×	6	×	[	1	/	1.36E+05	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
1,2,4-Trimethylbenzene	6.75E-02	=	6.13E-01	×	7.2	×	350	×	6	×	[	1	/	2.44E+03	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	1.71E-03	)
1,3,5-Trimethylbenzene	3.12E-03	=	2.33E-01	×	7.2	×	350	×	6	×	[	1	/	2.02E+03	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	1.70E-02	)
Benzene	3.35E-02	=	8.92E-01	×	7.2	×	350	×	6	×	[	1	/	1.43E+03	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	8.57E-03	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Csoil – Soil Concentration
InhRc – Inhalation Rate, child
EF – Exposure frequency
EDc – Exposure duration, child
VF – Volatilization Factor
PEF – Particulate Emission Factor
BWc – Body Weight, child
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment F

Table 6c
Residential Scenario: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} \times \frac{(3.14 \times D_A \times T)^{1/2}}{(2 \times \rho_b \times D_A)} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} $(g/m^2\text{-}s)/(kg/m^3)$	π	D_A (cm^2/s)	T_{adult} (s)	T_{child} (s)	2	ρb (g/cm^3)	10^{-4} (m^2/cm^2)	VF_{adult} (m^3/kg)	VF_{child} (m^3/kg)
1-Methylnaphthalene	73.32	3.14	1.95E-05	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.28E+04	1.47E+04
Benzo(a)anthracene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Benzo(a)pyrene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Benzo(b)fluoranthene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Benzo(k)fluoranthene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Dibenzo(a,h)anthracene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Fluoranthene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Indeno(1,2,3-cd)pyrene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Naphthalene	73.32	3.14	2.54E-05	9.46E+08	1.89E+08	2	1.38	1.00E-04	2.87E+04	1.29E+04
Pyrene	73.32	3.14	2.25E-07	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.05E+05	1.36E+05
1,2,4-Trimethylbenzene	73.32	3.14	7.01E-04	9.46E+08	1.89E+08	2	1.38	1.00E-04	5.47E+03	2.44E+03
1,3,5-Trimethylbenzene	73.32	3.14	1.02E-03	9.46E+08	1.89E+08	2	1.38	1.00E-04	4.52E+03	2.02E+03
Benzene	73.32	3.14	2.05E-03	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.20E+03	1.43E+03

Notes:

Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

VF_{adult} – Volatilization Factor (m^3/kg) for adults (calculated)

VF_{child} – Volatilization Factor (m^3/kg) for children (calculated)

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source $(g/m^2\text{-}s)/(kg/m^3)$(Value used is for Minneapolis, MN.)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T_{adult} – Exposure interval (s) for adults

T_{Child} – Exposure interval (s) for children

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated; PAHs are not considered volatile chemicals

Attachment F

Table 6d
Residential Scenario: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical Units	VOC?	θa (Lair /Lsoil)	Di (cm²/s)	H' unitless	θw (Lwater /Lsoil)	Dw (cm²/s)	η (Lpore /Lsoil)	ρb (g/cm³)	ρs (g/cm³)	Kd (cm³/g)	D_A (cm²/s)
1-Methylnaphthalene	Yes	3.29E-01	6.31E-02	1.64E-02	0.15	7.13E-06	4.79E-01	1.38	2.65	3.75E+01	1.95E-05
Benzo(a)anthracene	No	3.29E-01	5.10E-02	4.91E-04	0.15	9.00E-06	4.79E-01	1.38	2.65	1.39E+03	NC
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Benzo(b)fluoranthene	No	3.29E-01	2.26E-02	2.69E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.82E+03	NC
Benzo(k)fluoranthene	No	3.29E-01	2.26E-02	2.39E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Dibenzo(a,h)anthracene	No	3.29E-01	2.02E-02	5.03E-06	0.15	5.18E-06	4.79E-01	1.38	2.65	1.57E+04	NC
Fluoranthene	No	3.29E-01	3.02E-02	3.62E-04	0.15	6.35E-06	4.79E-01	1.38	2.65	4.25E+02	NC
Indeno(1,2,3-cd)pyrene	No	3.29E-01	1.90E-02	1.42E-05	0.15	5.66E-06	4.79E-01	1.38	2.65	1.61E+04	NC
Naphthalene	Yes	3.29E-01	5.90E-02	1.80E-02	0.15	7.50E-06	4.79E-01	1.38	2.65	1.10E+01	2.54E-05
Pyrene	Yes	3.29E-01	2.72E-02	4.87E-04	0.15	7.24E-06	4.79E-01	1.38	2.65	4.16E+02	2.25E-07
1,2,4-Trimethylbenzene	Yes	3.29E-01	6.44E-02	2.52E-01	0.15	7.92E-06	4.79E-01	1.38	2.65	4.31E+00	7.01E-04
1,3,5-Trimethylbenzene	Yes	3.29E-01	6.02E-02	3.59E-01	0.15	8.67E-06	4.79E-01	1.38	2.65	4.22E+00	1.02E-03
Benzene	Yes	3.29E-01	8.80E-02	2.27E-01	0.15	9.80E-06	4.79E-01	1.38	2.65	9.93E-01	2.05E-03

Notes:

D_A – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's Law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User'S Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density

Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm³ /g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)
VOC? – Volatile organic compounds; If no, an apparent diffusivity was not calculated.
NV – no value available
NC – not calculated

Attachment E

Table 7a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Ingestion of Soil Pathway – Carcinogenic Effects

$$\text{Ing-Risk} = \frac{(\text{Csoil} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	= (	Csoil	×	SFo	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		mg/day		unitless		kg		days	
Inorganics																				
Arsenic	8.29E-08	= (	4.51E+00	×	1.50E+00	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Lead	NA	= (	9.58E+01	×	a	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Manganese	NA	= (	3.08E+02	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Vanadium	NA	= (	3.15E+01	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
SVOCs																				
1-Methylnaphthalene	NA	= (	1.44E+03	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	1.60E+03	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25550	)
Acenaphthene	NA	= (	3.86E+02	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	4.12E+02	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Benzo(a)anthracene	1.52E-06	= (	1.71E+02	×	7.30E-01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	1.10E-05	= (	1.23E+02	×	7.30E+00	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	6.66E-07	= (	7.45E+01	×	7.30E-01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	8.25E-08	= (	9.23E+01	×	7.30E-02	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Chrysene	1.36E-08	= (	1.53E+02	×	7.30E-03	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	1.64E-06	= (	1.83E+01	×	7.30E+00	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	9.89E+01	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	2.82E+02	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	2.88E+02	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	6.01E-07	= (	6.72E+01	×	7.30E-01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	1.17E+03	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	3.95E+02	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
VOCs																) ÷ (				
1,2,3-Trimethylbenzene	NA	= (	1.96E+01	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
1,2,4-Trichlorobenzene	NA	= (	2.64E+02	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	4.21E+00	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	= (	1.97E+01	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Benzene	1.02E-08	= (	1.51E+01	×	5.50E-02	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)

Attachment E

Table 7a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Ingestion of Soil Pathway – Carcinogenic Effects

$$\text{Ing-Risk} = \frac{(\text{Csoil} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	= (	Csoil	×	SFo	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		mg/day		unitless		kg		days	
Ethylbenzene	NA	= (	5.04E+01	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
n-Butyl benzene	NA	= (	5.93E+01	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
p-Isopropyltoluene	NA	= (	2.30E+01	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
sec-Butyl benzene	NA	= (	5.02E+01	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Toluene	NA	= (	3.36E+01	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Xylenes (total)	NA	= (	2.35E+02	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – *Concentration in soil*
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
VOC – Volatile organic compound
SIR – Soil Ingestion Rate
FI – *Fraction Ingested from Contaminated Source*
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
SVOC – Semivolatile organic compound
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment E

Table 7b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Ingestion of Soil Pathway – Noncarcinogenic Effects

$$Ing\text{-}HQ = \frac{(Csoil \times CF \times EF \times ED \times SIR \times FI)}{(BW \times ATn \times RfDo)}$$

Equation	Ing - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATn	×	RfDo [B]	)
Units	unitless		mg/kg		kg/mg		days/year		years		mg/day		unitless		kg		days		mg/kg-day	
Inorganics																				
Arsenic	1.3E-02	= (	4.51E+00	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	3.0E-04	)
Lead	NA	= (	9.58E+01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	a	)
Manganese	1.9E-03	= (	3.08E+02	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	1.4E-01	
Vanadium	3.9E-03	= (	3.15E+01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	7.0E-03	
SVOCs																				
1-Methylnaphthalene	1.8E-02	= (	1.44E+03	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	7.0E-02	)
2-Methylnaphthalene	3.4E-01	= (	1.60E+03	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	4.0E-03	)
Acenaphthene	5.5E-04	= (	3.86E+02	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	6.0E-01	)
Acenaphthylene	NA	= (	4.12E+02	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	NV	
Benzo(a)anthracene	NA	= (	1.71E+02	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	NV	)
Benzo(a)pyrene	NA	= (	1.23E+02	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	NV	)
Benzo(b)fluoranthene	NA	= (	7.45E+01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	NV	)
Benzo(k)fluoranthene	NA	= (	9.23E+01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	NV	)
Chrysene	NA	= (	1.53E+02	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.83E+01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	NV	)
Dibenzofuran	4.2E-02	= (	9.89E+01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	2.0E-03	)
Fluoranthene	6.1E-04	= (	2.82E+02	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	4.0E-01	)
Fluorene	6.2E-04	= (	2.88E+02	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	4.0E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (	6.72E+01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	NV	)
Naphthalene	5.0E-02	= (	1.17E+03	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	2.0E-02	)
Pyrene	1.1E-03	= (	3.95E+02	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	3.0E-01	)
VOCs																				
1,2,3-Trimethylbenzene	NA	= (	1.96E+01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	NV	
1,2,4-Trichlorobenzene	2.3E-02	= (	2.64E+02	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	1.0E-02	)
1,2,4-Trimethylbenzene	7.2E-05	= (	4.21E+00	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	5.0E-02	)
1,3,5-Trimethylbenzene	3.4E-05	= (	1.97E+01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	5.0E-01	)
Benzene	3.2E-03	= (	1.51E+01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	4.0E-03	)

Attachment E

Table 7b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Ingestion of Soil Pathway – Noncarcinogenic Effects

$$\text{Ing - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation	Ing - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATn	×	RfDo [b]	)
Units	unitless		mg/kg		kg/mg		days/year		years		mg/day		unitless		kg		days		mg/kg-day	
Ethylbenzene	3.9E-04	= (	5.04E+01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	1.1E-01	)
n-Butyl benzene	1.3E-03	= (	5.93E+01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	4.0E-02	)
p-Isopropyltoluene	NA	= (	2.30E+01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	NV	
sec-Butyl benzene	1.1E-03	= (	5.02E+01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	4.0E-02	)
Toluene	1.4E-05	= (	3.36E+01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	2.0E+00	)
Xylenes (total)	5.6E-04	= (	2.35E+02	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	365	×	3.6E-01	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Concentration in Soil
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Soil Ingestion Rate
VOC – Volatile organic compound
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose
NV – No toxicity value available for this pathway.
NA – Not Applicable
SVOC – Semivolatile organic compound

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available. Toxicity criteria is presented in Attachment A, Table 1b.

Attachment E

Table 8a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Dermal Contact with Soil Pathway – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATc})}$$

Equation	Derm - Risk	= (	Csoil	×	SFabs	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless		kg		days	
Inorganics																								
Arsenic	5.05E-09	= (	4.51E+00	×	1.58E+00	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	3.00E-02	) ÷ (	70	×	25,550	)
Lead	NA	= (	9.58E+01	×	a	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	25,550	)
Manganese	NA	= (	3.08E+02	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	25,550	)
Vanadium	NA	= (	3.15E+01	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	25,550	)
SVOCs																								
1-Methylnaphthalene	NA	= (	1.44E+03	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	1.60E+03	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.00E-01	) ÷ (	70	×	25,550	)
Acenaphthene	NA	= (	3.86E+02	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	4.12E+02	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(a)anthracene	3.82E-07	= (	1.71E+02	×	7.30E-01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	2.75E-06	= (	1.23E+02	×	7.30E+00	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	1.67E-07	= (	7.45E+01	×	7.30E-01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	2.07E-08	= (	9.23E+01	×	7.30E-02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Chrysene	3.42E-09	= (	1.53E+02	×	7.30E-03	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	4.11E-07	= (	1.83E+01	×	7.30E+00	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	9.89E+01	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	2.82E+02	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	2.88E+02	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.51E-07	= (	6.72E+01	×	7.30E-01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	1.17E+03	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	3.95E+02	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
VOCs																								
1,2,3-Trimethylbenzene	NA	= (	1.96E+01	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	25,550	)
1,2,4-Trichlorobenzene	NA	= (	2.64E+02	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	4.21E+00	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	= (	1.97E+01	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	25,550	)

Attachment E

Table 8a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Dermal Contact with Soil Pathway – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATc})}$$

Equation	Derm - Risk	= (	Csoil	×	SFabs	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless		kg		days	
Benzene	NA	= (	1.51E+01	×	5.50E-02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	25,550	)
Ethylbenzene	NA	= (	5.04E+01	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	25,550	)
n-Butyl benzene	NA	= (	5.93E+01	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	25,550	)
p-Isopropyltoluene	NA	= (	2.30E+01	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NV	) ÷ (	70	×	25,550	)
sec-Butyl benzene	NA	= (	5.02E+01	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	25,550	)
Toluene	NA	= (	3.36E+01	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	25,550	)
Xylenes (total)	NA	= (	2.35E+02	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csoil – Concentration in Soil
SFabs – Absorbed slope factor (SFo + ABSgi)
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
VOC – Volatile organic compound
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment E

Table 8b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Dermal Contact with Soil Pathway – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATn} \times \text{RfDabs})}$$

Equation	Derm - HQ	=	Csoil	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	÷	BW	×	ATn	×	RfDabs [b]
Units	unitless		mg/kg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless		kg		days		mg/kg-day
Inorganics																							
Arsenic	7.86E-04	=	4.51E+00	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	3.00E-02	÷	70	×	365	×	2.85E-04
Lead	NA	=	9.58E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	÷	70	×	365	×	a
Manganese	NA	=	3.08E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	÷	70	×	365	×	5.60E-03
Vanadium	NA	=	3.15E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	÷	70	×	365	×	1.82E-04
SVOCs																							
1-Methylnaphthalene	4.41E-03	=	1.44E+03	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	÷	70	×	365	×	7.00E-02
2-Methylnaphthalene	6.60E-02	=	1.60E+03	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.00E-01	÷	70	×	365	×	4.00E-03
Acenaphthene	1.38E-04	=	3.86E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	÷	70	×	365	×	6.00E-01
Acenaphthylene	NA	=	4.12E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	÷	70	×	365	×	NV
Benzo(a)anthracene	NA	=	1.71E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	÷	70	×	365	×	NV
Benzo(a)pyrene	NA	=	1.23E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	÷	70	×	365	×	NV
Benzo(b)fluoranthene	NA	=	7.45E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	÷	70	×	365	×	NV
Benzo(k)fluoranthene	NA	=	9.23E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	÷	70	×	365	×	NV
Chrysene	NA	=	1.53E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	÷	70	×	365	×	NV
Dibenzo(a,h)anthracene	NA	=	1.83E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	÷	70	×	365	×	NV
Dibenzofuran	1.06E-02	=	9.89E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	÷	70	×	365	×	2.00E-03
Fluoranthene	1.52E-04	=	2.82E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	÷	70	×	365	×	4.00E-01
Fluorene	1.55E-04	=	2.88E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	÷	70	×	365	×	4.00E-01
Indeno(1,2,3-cd)pyrene	NA	=	6.72E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	÷	70	×	365	×	NV
Naphthalene	1.26E-02	=	1.17E+03	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	÷	70	×	365	×	2.00E-02
Pyrene	2.83E-04	=	3.95E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	÷	70	×	365	×	3.00E-01
VOCs																							
1,2,3-Trimethylbenzene	NA	=	1.96E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	÷	70	×	365	×	NV
1,2,4-Trichlorobenzene	NA	=	2.64E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NV	÷	70	×	365	×	NV
1,2,4-Trimethylbenzene	NA	=	4.21E+00	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	÷	70	×	365	×	5.00E-02
1,3,5-Trimethylbenzene	NA	=	1.97E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	÷	70	×	365	×	5.00E-01
Benzene	NA	=	1.51E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	÷	70	×	365	×	4.00E-03
Ethylbenzene	NA	=	5.04E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	÷	70	×	365	×	1.10E-01
n-Butyl benzene	NA	=	5.93E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	÷	70	×	365	×	4.00E-02

Attachment E

Table 8b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Dermal Contact with Soil Pathway – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATn} \times \text{RfDabs})}$$

Equation	Derm - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) ÷ (	BW	×	ATn	×	RfDabs [6]	)
Units	unitless		mg/kg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless		kg		days		mg/kg-day	
p-Isopropyltoluene	NA	= (	2.30E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NV	) ÷ (	70	×	365	×	NV	
sec-Butyl benzene	NA	= (	5.02E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	365	×	4.00E-02	)
Toluene	NA	= (	3.36E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	365	×	2.00E+00	)
Xylenes (total)	NA	= (	2.35E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	365	×	3.57E-01	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Concentration in Soil
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
SSAF – Soil-to-skin Adherence Factor
ABSd – Dermal Soil Absorption Factor
BW – Body Weight
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo ×ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.
VOC – Volatile organic compound
SVOC – Semivolatile organic compound

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available. Toxicity criteria is presented in Attachment A, Table 1b.

Attachment E

Table 9a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Inhalation of Soil (Fugitive Emissions and Volatile Compounds) Pathway– Carcinogenic Effects

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times [(1/\text{VF}) + (1/\text{PEF})])}{(\text{BW} \times \text{ATc})}$$

Equation	Inh - Risk	= (	Csoil	×	SFi	×	IR	×	ET	×	EF	×	ED	× [	1	/	VF	+	1	/	PEF	]) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		m³/hour		hours/day		days/year		year				m³/kg				m³/kg		kg		days	
Inorganics																										
Arsenic	6.31E-09	= (	4.51E+00	×	1.51E+01	×	1.3	×	8	×	219	×	1	× [	1	/	NA	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Lead	NA	= (	9.58E+01	×	a	×	1.3	×	8	×	219	×	1	× [	1	/	NA	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Manganese	NA	= (	3.08E+02	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	NA	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Vanadium	NA	= (	3.15E+01	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	NA	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
SVOCs																										
1-Methylnaphthalene	NA	= (	1.44E+03	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	6.00E+03	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	1.60E+03	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	5.68E+03	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Acenaphthene	NA	= (	3.86E+02	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	1.10E+04	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	4.12E+02	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	1.30E+04	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Benzo(a)anthracene	NA	= (	1.71E+02	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Benzo(a)pyrene	3.51E-08	= (	1.23E+02	×	3.08E+00	×	1.3	×	8	×	219	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	NA	= (	7.45E+01	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	NA	= (	9.23E+01	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Chrysene	NA	= (	1.53E+02	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	NA	= (	1.83E+01	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	9.89E+01	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	9.09E+03	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	2.82E+02	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Fluorene	NA	= (	2.88E+02	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	1.67E+04	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	NA	= (	6.72E+01	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	1.17E+03	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	5.25E+03	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Pyrene	NA	= (	3.95E+02	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	5.57E+04	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
VOCs																										
1,2,3-Trimethylbenzene	NA	= (	1.96E+01	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	1.35E+03	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
1,2,4-Trichlorobenzene	NA	= (	2.64E+02	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	2.62E+04	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	4.21E+00	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	9.98E+02	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	= (	1.97E+01	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	8.26E+02	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Benzene	9.00E-07	= (	1.51E+01	×	2.73E-02	×	1.3	×	8	×	219	×	1	× [	1	/	5.83E+02	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
Ethylbenzene	NA	= (	5.04E+01	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	7.41E+02	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
n-Butyl benzene	NA	= (	5.93E+01	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	7.70E+02	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
p-Isopropyltoluene	NA	= (	2.30E+01	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	NV	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)
sec-Butyl benzene	NA	= (	5.02E+01	×	NV	×	1.3	×	8	×	219	×	1	× [	1	/	7.70E+02	+	1	/	1.37E+07	]) ÷ (	70	×	25,550	)

Attachment E

Table 9a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Inhalation of Soil (Fugitive Emissions and Volatile Compounds) Pathway– Carcinogenic Effects

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times [(1/\text{VF}) + (1/\text{PEF})])}{(\text{BW} \times \text{ATc})}$$

Equation	Inh - Risk	=	(	Csoil	×	SFi	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	)	÷	(	BW	×	ATc	)
Units	unitless			mg/kg		kg-day/mg		m³/hour		hours/day		days/year		year					m³/kg				m³/kg					kg		days	
Toluene	NA	=	(	3.36E+01	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	6.32E+02	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Xylenes (total)	NA	=	(	2.35E+02	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	8.09E+02	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Concentration in Soil
SFi – Inhalation Slope Factor
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VOC – Volatile organic compound
VF – Volatilization Factor
PEF – Particulate Emission Factor (See Attachment G)
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
SVOC – Semivolatile organic compound
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment E

Table 9b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Inhalation of Soil (Fugitive Emissions and Volatile Compounds) Pathway – Carcinogenic Effects

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BW} \times \text{ATn} \times \text{RfDi})}$$

Equation	Inh - HQ	=	(	Csoil	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	÷	(	BW	×	ATn	×	RfDi [6]	)
Units	unitless			mg/kg		m³/hour		hours/day		days/year		year					m³/kg				m³/kg				kg		days		mg/kg-day	
Inorganics																														
Arsenic	NA	=	(	4.51E+00	×	1.3	×	8	×	219	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Lead	NA	=	(	9.58E+01	×	1.3	×	8	×	219	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	÷	(	70	×	365	×	a	)
Manganese	1.40E-01	=	(	3.08E+02	×	1.3	×	8	×	219	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	÷	(	70	×	365	×	1.43E-05	
Vanadium	NA	=	(	3.15E+01	×	1.3	×	8	×	219	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
SVOCs																														
1-Methylnaphthalene	NA	=	(	1.44E+03	×	1.3	×	8	×	219	×	1	×	[	1	/	6.00E+03	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
2-Methylnaphthalene	NA	=	(	1.60E+03	×	1.3	×	8	×	219	×	1	×	[	1	/	5.68E+03	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Acenaphthene	NA	=	(	3.86E+02	×	1.3	×	8	×	219	×	1	×	[	1	/	1.10E+04	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
Acenaphthylene	NA	=	(	4.12E+02	×	1.3	×	8	×	219	×	1	×	[	1	/	1.30E+04	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
Benzo(a)anthracene	NA	=	(	1.71E+02	×	1.3	×	8	×	219	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Benzo(a)pyrene	NA	=	(	1.23E+02	×	1.3	×	8	×	219	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Benzo(b)fluoranthene	NA	=	(	7.45E+01	×	1.3	×	8	×	219	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Benzo(k)fluoranthene	NA	=	(	9.23E+01	×	1.3	×	8	×	219	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
Chrysene	NA	=	(	1.53E+02	×	1.3	×	8	×	219	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
Dibenzo(a,h)anthracene	NA	=	(	1.83E+01	×	1.3	×	8	×	219	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Dibenzofuran	NA	=	(	9.89E+01	×	1.3	×	8	×	219	×	1	×	[	1	/	9.09E+03	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Fluoranthene	NA	=	(	2.82E+02	×	1.3	×	8	×	219	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
Fluorene	NA	=	(	2.88E+02	×	1.3	×	8	×	219	×	1	×	[	1	/	1.67E+04	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
Indeno(1,2,3-cd)pyrene	NA	=	(	6.72E+01	×	1.3	×	8	×	219	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Naphthalene	2.32E+01	=	(	1.17E+03	×	1.3	×	8	×	219	×	1	×	[	1	/	5.25E+03	+	1	/	1.37E+07	]	÷	(	70	×	365	×	8.57E-04	)
Pyrene	NA	=	(	3.95E+02	×	1.3	×	8	×	219	×	1	×	[	1	/	5.57E+04	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
VOCs																														
1,2,3-Trimethylbenzene	NA	=	(	1.96E+01	×	1.3	×	8	×	219	×	1	×	[	1	/	1.35E+03	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	
1,2,4-Trichlorobenzene	7.90E-01	=	(	2.64E+02	×	1.3	×	8	×	219	×	1	×	[	1	/	2.62E+04	+	1	/	1.37E+07	]	÷	(	70	×	365	×	1.14E-03	)
1,2,4-Trimethylbenzene	2.20E-01	=	(	4.21E+00	×	1.3	×	8	×	219	×	1	×	[	1	/	9.98E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	1.71E-03	)
1,3,5-Trimethylbenzene	1.25E-01	=	(	1.97E+01	×	1.3	×	8	×	219	×	1	×	[	1	/	8.26E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	1.70E-02	)
Benzene	2.69E-01	=	(	1.51E+01	×	1.3	×	8	×	219	×	1	×	[	1	/	5.83E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	8.57E-03	)
Ethylbenzene	2.09E-02	=	(	5.04E+01	×	1.3	×	8	×	219	×	1	×	[	1	/	7.41E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	2.90E-01	
n-Butyl benzene	NA	=	(	5.93E+01	×	1.3	×	8	×	219	×	1	×	[	1	/	7.70E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	

Attachment E

Table 9b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Inhalation of Soil (Fugitive Emissions and Volatile Compounds) Pathway – Carcinogenic Effects

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BW} \times \text{ATn} \times \text{RfDi})}$$

Equation	Inh - HQ	=	(	Csoil	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	÷	(	BW	×	ATn	×	RfDi [b]	)
Units	unitless			mg/kg		m³/hour		hours/day		days/year		year					m³/kg				m³/kg				kg		days		mg/kg-day	
p-Isopropyltoluene	NA	=	(	2.30E+01	×	1.3	×	8	×	219	×	1	×	[	1	/	NV	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
sec-Butyl benzene	NA	=	(	5.02E+01	×	1.3	×	8	×	219	×	1	×	[	1	/	7.70E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Toluene	1.83E-02	=	(	3.36E+01	×	1.3	×	8	×	219	×	1	×	[	1	/	6.32E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	2.60E-01	)
Xylenes (total)	9.05E-01	=	(	2.35E+02	×	1.3	×	8	×	219	×	1	×	[	1	/	8.09E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	2.86E-02	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Csoil – Concentration in Soil
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VF – Volatilization Factor
VOC – Volatile organic compound
PEF – Particulate Emission Factor (See Attachment G)
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
SVOC – Semivolatile organic compound

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available. Toxicity criteria is presented in Attachment A, Table 1b.

Attachment E

Table 9c
Construction Worker: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} x \frac{(3.14 \times D_A \times T)^{1/2}}{2 \times \rho_b \times D_A} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} (g/m^2-s)/(kg/m^3)	π	D_A (cm^2/s)	T (s)	2	ρb (g/cm^3)	10^{-4} (m^3/cm^3)	VF (m^3/kg)
1-Methylnaphthalene	73.32	3.14	1.94E-05	3.15E+07	2	1.38	1.00E-04	6.00E+03
2-Methylnaphthalene	73.32	3.14	2.17E-05	3.15E+07	2	1.38	1.00E-04	5.68E+03
Acenaphthene	73.32	3.14	5.82E-06	3.15E+07	2	1.38	1.00E-04	1.10E+04
Acenaphthylene	73.32	3.14	4.15E-06	3.15E+07	2	1.38	1.00E-04	1.30E+04
Benzo(a)anthracene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Benzo(a)pyrene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Benzo(b)fluoranthene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Benzo(k)fluoranthene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Chrysene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Dibenzo(a,h)anthracene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Dibenzofuran	73.32	3.14	8.46E-06	3.15E+07	2	1.38	1.00E-04	9.09E+03
Fluoranthene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Fluorene	73.32	3.14	2.50E-06	3.15E+07	2	1.38	1.00E-04	1.67E+04
Indeno(1,2,3-cd)pyrene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Naphthalene	73.32	3.14	2.54E-05	3.15E+07	2	1.38	1.00E-04	5.25E+03
Pyrene	73.32	3.14	2.25E-07	3.15E+07	2	1.38	1.00E-04	5.57E+04
1,2,4-Trichlorobenzene	73.32	3.14	1.02E-06	3.15E+07	2	1.38	1.00E-04	2.62E+04
1,2,3-Trimethylbenzene	73.32	3.14	3.85E-04	3.15E+07	2	1.38	1.00E-04	1.35E+03
1,2,4-Trimethylbenzene	73.32	3.14	7.01E-04	3.15E+07	2	1.38	1.00E-04	9.98E+02
1,3,5-Trimethylbenzene	73.32	3.14	1.02E-03	3.15E+07	2	1.38	1.00E-04	8.26E+02
Benzene	73.32	3.14	2.05E-03	3.15E+07	2	1.38	1.00E-04	5.83E+02
Ethylbenzene	73.32	3.14	1.27E-03	3.15E+07	2	1.38	1.00E-04	7.41E+02
sec-Butyl benzene	73.32	3.14	1.18E-03	3.15E+07	2	1.38	1.00E-04	7.70E+02
Toluene	73.32	3.14	1.75E-03	3.15E+07	2	1.38	1.00E-04	6.32E+02
Xylenes (total)	73.32	3.14	1.07E-03	3.15E+07	2	1.38	1.00E-04	8.09E+02

Notes:

Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

VF – Volatilization Factor (m^3/kg) (calculated)

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source (g/m^2-s)/(kg/m^3)(Value used is for Minneapolis, MN.)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T – Exposure interval (s)

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated

Attachment E

Table 9d
Construction Worker: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical	VOC?	θa	Di	H'	θw	Dw	η	ρb	ρs	Kd	D_A
Units		(Lair /Lsoil)	(cm^2/s)	unitless	(Lwater /Lsoil)	(cm^2/s)	(Lpore /Lsoil)	(g/cm^3)	(g/cm^3)	(cm^3/g)	(cm^2/s)
1-Methylnaphthalene	*Yes*	3.29E-01	6.31E-02	1.64E-02	0.15	7.13E-06	4.79E-01	1.38	2.65	3.75E+01	1.948E-05
2-Methylnaphthalene	*Yes*	3.29E-01	4.80E-02	2.12E-02	0.15	7.84E-06	4.79E-01	1.38	2.65	1.79E+01	2.166E-05
Acenaphthene	*Yes*	3.29E-01	4.21E-02	7.44E-03	0.15	7.69E-06	4.79E-01	1.38	2.65	3.67E+01	5.819E-06
Acenaphthylene	*Yes*	3.29E-01	4.39E-02	5.11E-03	0.15	7.53E-06	4.79E-01	1.38	2.65	3.67E+01	4.148E-06
Benzo(a)*anthracene*	No	3.29E-01	5.10E-02	4.91E-04	0.15	9.00E-06	4.79E-01	1.38	2.65	1.39E+03	NC
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Benzo(b)fluoranthene	No	3.29E-01	2.26E-02	2.69E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.82E+03	NC
Benzo(k)fluoranthene	No	3.29E-01	2.26E-02	2.39E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Chrysene	No	3.29E-01	2.48E-02	2.14E-04	0.15	6.21E-06	4.79E-01	1.38	2.65	1.42E+03	NC
Dibenzo(a,h)anthracene	No	3.29E-01	2.02E-02	5.03E-06	0.15	5.18E-06	4.79E-01	1.38	2.65	1.57E+04	NC
Dibenzofuran	*Yes*	3.29E-01	5.51E-02	8.71E-03	0.15	7.04E-06	4.79E-01	1.38	2.65	6.78E+01	8.463E-06
Fluoranthene	No	3.29E-01	3.02E-02	3.62E-04	0.15	6.35E-06	4.79E-01	1.38	2.65	4.25E+02	NC
Fluorene	*Yes*	3.29E-01	3.63E-02	3.93E-03	0.15	7.88E-06	4.79E-01	1.38	2.65	6.78E+01	2.499E-06
Indeno(1,2,3-cd)pyrene	No	3.29E-01	1.90E-02	1.42E-05	0.15	5.66E-06	4.79E-01	1.38	2.65	1.61E+04	NC
Naphthalene	*Yes*	3.29E-01	5.90E-02	1.80E-02	0.15	7.50E-06	4.79E-01	1.38	2.65	1.10E+01	2.537E-05
Pyrene	*Yes*	3.29E-01	2.72E-02	4.87E-04	0.15	7.24E-06	4.79E-01	1.38	2.65	4.16E+02	2.254E-07
1,2,4-Trichlorobenzene	NV	3.29E-01	3.00E-02	1.42E-03	0.15	8.23E-06	4.79E-01	1.38	2.65	1.07E+01	1.02E-06
1,2,3-Trimethylbenzene	NV	3.29E-01	6.77E-02	1.33E-01	0.15	7.41E-06	4.79E-01	1.38	2.65	3.53E+00	3.85E-04
1,2,4-Trimethylbenzene	*Yes*	3.29E-01	6.44E-02	2.52E-01	0.15	7.92E-06	4.79E-01	1.38	2.65	4.31E+00	7.01E-04
1,3,5-Trimethylbenzene	*Yes*	3.29E-01	6.02E-02	3.59E-01	0.15	8.67E-06	4.79E-01	1.38	2.65	4.22E+00	1.02E-03
Benzene	*Yes*	3.29E-01	8.80E-02	2.27E-01	0.15	9.80E-06	4.79E-01	1.38	2.65	9.93E-01	2.05E-03
Ethylbenzene	*Yes*	3.29E-01	7.50E-02	3.22E-01	0.15	7.80E-06	4.79E-01	1.38	2.65	3.11E+00	1.27E-03
sec-Butyl benzene	*Yes*	3.29E-01	5.76E-02	5.07E-01	0.15	6.75E-06	4.79E-01	1.38	2.65	1.25E+01	1.18E-03
Toluene	*Yes*	3.29E-01	8.70E-02	2.71E-01	0.15	8.60E-06	4.79E-01	1.38	2.65	1.61E+00	1.75E-03
Xylenes (total)	*Yes*	3.29E-01	7.14E-02	2.71E-01	0.15	9.34E-06	4.79E-01	1.38	2.65	2.66E+00	1.07E-03

Notes:

D_A – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's Law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User'S Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density
Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm^3/g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)
VOC? – Volatile organic compounds; if no an apparent diffusivity was not calculated.
NV – no value available
NC – not calculated

Attachment E

Table 9e
Calculation of Particulate Emission Factor for Unpaved Road Traffic

Equation E-18:

$$PEF_{sc} = Q \Big/ C_{sr} \times \frac{1}{F_D} \times \frac{T \times A_R}{\frac{2.6 \times (s/12)^{0.8} (W/3)^{0.4}}{(M_{dry}/0.2)^{0.3}} \times \frac{(365 \quad p)}{365}} \times 281.9 \times \sum VKT$$

PEF_{sc} =	Subchronic particulate emission factor for unpaved road traffic (m^3/kg)	
Q/c_{sr} =	*Inverse of 1-h. average air concentration along a straight road segment bisecting a square site* (g/m^2-s per kg/m^3)	Calculated *Calculated, see Equation E-19*
F_D =	Dispersion correction factor (unitless)	Calculated, see Equation E-16
T =	Total time over which construction occurs (s)	7.49E+06 Assumed time period over which traffic will occur is 1 year.
A_R =	Surface area of contaminated road segment (m^2) $A_R = L_R \times W_R \times 0.092903$ m^2/ft^2	1.06E+04
L_R =	Length of road segment (ft) L_R = square root of site surface contamination configured as a square	5.32E+02 Assumes construction is limited to half of Kreher Park; therefore, exposure area is limted to the 6.5 acre
W_R =	Width of road segment (ft)	2.00E+01 Default
s =	Road surface silt content (%)	8.50E+00
W =	Mean vehicle weight (tons)	8.00E+00 Value presented in Supplemental Soil Screening Guidance
M_{dry} =	Road surface material moisture content under dry, uncontrolled conditions (%)	2.00E-01 Default
p =	Number of days per year with at least 0.01 inches of precipitation	1.20E+02 From Exhibit E-1
ΣVKT=	Sum of fleet vehicle kilometers traveled during the exposure duration (km) ΣVKT= 30 vehicles × 0.162 km/day × (52 weeks/year ÷ 2) × 5 days/week	6.33E+02 Assumes area of surface contamination is limite to one half of Kreher Park of 6.5 acres or 0.1621862 km.

PEF_{sc} (m^3/kg)	=	Q/c_{sr} (g/m^2-s per kg/m^3)	×	(	1	+	F_D unitless	)	×	[	(	T s	×	A_R m^2/ft^2	)	+	[	2.6	×	(	s %	+	12	)	0.8	×	(	W tons	+	3	)	0.4	)	+	((	M_{dry} %	+	0.2	)	0.3	)	×	((	365	-	p days/year	)	+	365	)	×	281.9	×	ΣVKT km	]
1.37E+07	=	15.931	×	(	1	+	1.88E-01	)	×	[	(	7.49E+06	×	1.06E+04	)	+	[	2.6	×	(	8.50E+00	+	12	)	0.8	×	(	8	+	3	)	0.4	)	+	((	0.2	+	0.2	)	0.3	)	×	((	365	-	120	)	+	365	)	×	281.9	×	893.1	]

Attachment E

Table 10a
Risk Calculations: Central Tendency Evaluation
Industrial Worker: Inhalation of Chemicals in Indoor Air Pathway– Carcinogenic Effects

$$\text{Inh - Risk} = \frac{(\text{Cair} \times \text{SFi} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED})}{(\text{BW} \times \text{ATc})}$$

Equation	Inh - Risk	= (	Cair	×	SFi	×	IR	×	ET	×	EF	×	ED	) ÷ (	BW	×	ATc	)
Units	unitless		mg/m³		kg-day/mg		m³/hour		hours/day		days/year		year		kg		days	
1,2,4-Trimethylbenzene	NA	= (	3.88E-02	×	NV	×	1	×	8	×	219	×	6.6	) ÷ (	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	= (	9.32E-03	×	NV	×	1	×	8	×	219	×	6.6	) ÷ (	70	×	25,550	)
1,4-Dichlorobenzene	NA	= (	9.62E-01	×	NV	×	1	×	8	×	219	×	6.6	) ÷ (	70	×	25,550	)
Benzene	6.76E-06	= (	3.83E-02	×	2.73E-02	×	1	×	8	×	219	×	6.6	) ÷ (	70	×	25,550	)
Carbon tetrachloride	3.63E-06	= (	1.07E-02	×	5.25E-02	×	1	×	8	×	219	×	6.6	) ÷ (	70	×	25,550	)
Methylene chloride	5.18E-08	= (	4.86E-03	×	1.65E-03	×	1	×	8	×	219	×	6.6	) ÷ (	70	×	25,550	)
Trichloroethylene	8.17E-06	= (	3.16E-03	×	4.00E-01	×	1	×	8	×	219	×	6.6	) ÷ (	70	×	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Cair – Air Concentration
SFi – Inhalation Slope Factor
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable

Attachment E

Table 10b
Risk Calculations: Central Tendency Evaluation
Industrial Worker: Inhalation of Chemicals in Indoor Air Pathway – Carcinogenic Effects

$$\text{Inh - HQ} = \frac{(\text{Cair} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED})}{(\text{BW} \times \text{ATn} \times \text{RfDi})}$$

Equation / Units	Inh - HQ unitless	=	Cair mg/m³	×	IR m³/day	×	ET hours/day	×	EF days/year	×	ED year	) ÷ (	BW kg	×	ATn days	×	RfDi mg/kg-day	)
1,2,4-Trimethylbenzene	8.55E-01	= (	3.88E-02	×	0.55	×	8	×	219	×	6.6	) + (	70	×	2,409	×	1.71E-03	)
1,3,5-Trimethylbenzene	2.06E-01	= (	9.32E-03	×	0.55	×	8	×	219	×	6.6	) + (	70	×	2,409	×	1.71E-03	)
1,4-Dichlorobenzene	1.58E-01	= (	9.62E-01	×	0.55	×	8	×	219	×	6.6	) + (	70	×	2,409	×	2.29E-01	)
Benzene	1.69E-01	= (	3.83E-02	×	0.55	×	8	×	219	×	6.6	) + (	70	×	2,409	×	8.57E-03	)
Carbon tetrachloride	NA	= (	1.07E-02	×	0.55	×	8	×	219	×	6.6	) + (	70	×	2,409	×	NV	)
Methylene chloride	2.14E-04	= (	4.86E-03	×	0.55	×	8	×	219	×	6.6	) + (	70	×	2,409	×	8.57E-01	)
Trichloroethylene	1.05E-02	= (	3.16E-03	×	0.55	×	8	×	219	×	6.6	) + (	70	×	2,409	×	1.14E-02	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Cair – Air Concentration
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose
NV – No toxicity value available for this pathway.
NA – Not Applicable

Table 11a
Risk Calculations
Subsistence Fisher – Adult: Ingestion of Fish Pathway – Carcinogenic Effects
Central Tendency Evaluation

$$\text{Ing-Risk} = \frac{(\text{Cfish} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{FIR} \times \text{FI})}{(\text{BW} \times \text{ATc})}$$

Equation / Units	Ing - Risk unitless	=	Cfish mg/kg	×	SFo kg-day/mg	×	EF events/year	×	ED years	×	FIR kg/event	×	FI unitless	÷	BW kg	×	ATc days
Shorthead Redhorse and Walleye																	
1-Methylnaphthalene	NA	=	1.01E-01	×	NV	×	350	×	9	×	0.0172	×	1	÷	70	×	25,550
Smelt																	
Benzo(a)anthracene	1.64E-07	=	7.43E-03	×	7.30E-01	×	350	×	9	×	0.0172	×	1	÷	70	×	25,550
Benzo(a)pyrene	1.92E-06	=	8.70E-03	×	7.30E+00	×	350	×	9	×	0.0172	×	1	÷	70	×	25,550
Benzo(b)fluoranthene	2.48E-07	=	1.12E-02	×	7.30E-01	×	350	×	9	×	0.0172	×	1	÷	70	×	25,550
Benzo(e)pyrene	NA	=	9.80E-03	×	NV	×	350	×	9	×	0.0172	×	1	÷	70	×	25,550
Dibenzo(a,h)anthracene	5.75E-07	=	2.60E-03	×	7.30E+00	×	350	×	9	×	0.0172	×	1	÷	70	×	25,550
Indeno(1,2,3-cd)pyrene	1.68E-07	=	7.60E-03	×	7.30E-01	×	350	×	9	×	0.0172	×	1	÷	70	×	25,550

Notes:

Ing - Risk – Ingestion risk
Cfish – Concentration in fish
SFo – Oral Slope Factor
EF – Exposure Frequency
ED – *Exposure Duration*
FIR – Fish Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – *Not Applicable*

Table 11b
Risk Calculations
Subsistence Fisher – Adult: Ingestion of Fish Pathway – Noncarcinogenic Effects
Central Tendency Evaluation

$$Ing\text{-}HQ = \frac{(Cfish \times CF \times EF \times ED \times FIR \times FI)}{(BW \times ATn \times RfDo)}$$

Equation / Units	Ing - HQ unitless	= (	Cfish mg/kg	×	EF events/year	×	ED years	×	FIR kg/event	×	FI unitless	) ÷ (	BW kg	×	ATn days	×	RfDo mg/kg-day	)
Shorthead Redhorse & Walleye																		
1-Methylnaphthalene	3.40E-04	= (	1.01E-01	×	350	×	9	×	0.0172	×	1	) ÷ (	70	×	3,285	×	7.0E-02	)
Smelt																		
Benzo(a)anthracene	NA	= (	7.43E-03	×	350	×	9	×	0	×	1	) ÷ (	70	×	3,285	×	NV	)
Benzo(a)pyrene	NA	= (	8.70E-03	×	350	×	9	×	0.017	×	1	) ÷ (	70	×	3,285	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.12E-02	×	350	×	9	×	0.017	×	1	) ÷ (	70	×	3,285	×	NV	)
Benzo(e)pyrene	NA	= (	9.80E-03	×	350	×	9	×	0.017	×	1	) ÷ (	70	×	3,285	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.60E-03	×	350	×	9	×	0.017	×	1	) ÷ (	70	×	3,285	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	= (	7.60E-03	×	350	×	9	×	0.017	×	1	) ÷ (	70	×	3,285	×	NV	)

Notes:

Ing - HQ – Ingestion Hazard
Cfish – Concentration in fish
EF – Exposure Frequency
ED – Exposure Duration
FIR – Fish Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose
NV – No toxicity value available for this pathway.
NA – Not Applicable

ATTACHMENT F

Supporting Information for Uncertainty Analysis

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ATTACHMENT F1

Exposure Point Concentration Summary

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Attachment F1

Table 1
Exposure Point Concentration
Residential Receptor Exposed to Surface Soil (0-1 feet)

Analyte	Detection Range (mg/kg)	Frequency of Detection	Maximum Concentration (mg/kg)	Average Concentration (mg/kg)	95% UCL (mg/kg)	Distribution	Statistic used for 95% UCL	Rationale	Selected EPC (mg/kg)
Inorganics									
Arsenic	1.4 - 8.5	11 / 12	8.5	2.8	3.67	gamma	Standard Boostrap		3.67
Lead	22 - 440	11 / 12	440	83.4	-	-	-	Per EPA Guidance	83.40
SVOCs									
Benzo(a)pyrene	0.085 - 0.39	6 / 12	0.39	0.1	0.18	gamma	Standard Boostrap		0.18

All units are milligrams per kilogram (mg/kg).

EPC– Exposure Point Concentration
mg/kg – milligrams per kilogram
Sd– Standard Deviation
SVOC– Semi-volatile organic compound
UCL– Upper Confidence Limit
VOC– Volatile organic compound

Attachment F1

Table 2
Exposure Point Concentration
Residential Receptor Exposed to Surface and Subsurface Soil (0-3 feet)

Analyte	Detection Range (mg/kg)	Frequency of Detection	Maximum Concentration (mg/kg)	Average Concentration (mg/kg)	95% UCL (mg/kg)	Distribution	Statistic used for 95% UCL	Rationale	Selected EPC (mg/kg)
Inorganics									
Arsenic	0.87 - 13	29 / 40	13	2.97	3.74	gamma	Standard Boostrap		3.7
Lead	9.6 - 4000	26 / 40	4000	176.19	-	-	-	Per EPA Guidance	176.2
SVOCs									
1-Methylnaphthalene	0.051 - 230	8 / 40	230	7.21	16.61	non-parametric	Standard Boostrap		16.6
Benzo(a)anthracene	0.044 - 190	18 / 40	190	5.77	13.58	non-parametric	Standard Boostrap		13.6
Benzo(a)pyrene	0.060 - 220	18 / 40	220	6.97	16.13	non-parametric	Standard Boostrap		16.1
Benzo(b)fluoranthene	0.070 - 180	21 / 40	180	6.12	13.47	non-parametric	Standard Boostrap		13.5
Benzo(k)fluoranthene	0.069 - 56	13 / 40	56	1.98	4.23	non-parametric	Standard Boostrap		4.2
Dibenzo(a,h)anthracene	0.12 - 3.8	3 / 40	3.8	0.39	0.76	non-parametric	Standard Boostrap		0.8
Fluoranthene	0.047 - 390	21 / 40	390	11.18	26.47	non-parametric	Standard Boostrap		26.5
Indeno(1,2,3-cd)pyrene	0.037 - 45	12 / 40	45	1.54	3.39	non-parametric	Standard Boostrap		3.4
Naphthalene	0.051 - 91	7 / 40	91	2.82	6.46	non-parametric	Standard Boostrap		6.5
Pyrene	0.046 - 670	24 / 40	670	19.10	46.98	non-parametric	Standard Boostrap		47.0
VOCs									
1,2,4-Trimethylbenzene	0.02 - 15	13 / 40	15	0.61	1.31	non-parametric	Standard Boostrap		1.3
1,3,5-Trimethylbenzene	0.041 - 5.4	4 / 40	5.4	0.23	0.48	non-parametric	Standard Boostrap		0.5
Benzene	0.018 - 25	7 / 40	25	0.89	1.93	non-parametric	Standard Boostrap		1.9

All units are milligrams per kilogram (mg/kg).

EPC– Exposure Point Concentration
mg/kg – milligrams per kilogram
Sd– Standard Deviation
SVOC– Semi-volatile organic compound
UCL– Upper Confidence Limit
VOC– Volatile organic compound

Attachment F1

Table 3
Exposure Point Concentration
Construction Worker Receptor Exposed to Surface and Subsurface Soil (0-4 feet)

Analyte	Detection Range (mg/kg)	Frequency of Detection	Maximum Concentration (mg/kg)	Average Concentration (mg/kg)	95% UCL (mg/kg)	Distribution	Statistic used for 95% UCL	Rationale	Selected EPC (mg/kg)
Inorganics									
Arsenic	0.83 - 27	87 / 127	27	3.74	4.40	non-parametric	Standard Bootstrap		4.40
Lead	3.32 - 4000	104 / 131	4000	100.18	-	-	-	Per EPA Guidance	100.18
Vanadium	8.8 - 110	90 / 90	110	28.69	31.24	gamma	Standard Bootstrap		31.24
SVOCs									
2-Methylnaphthalene	0.066 - 30000	39 / 119	30000	1,141.94	1,875.53	non-parametric	Standard Bootstrap		1,875.53
Acenaphthene	0.074 - 7400	32 / 121	7400	205.28	337.87	non-parametric	Standard Bootstrap		337.87
Acenaphthylene	0.045 - 9700	49 / 122	9700	324.90	549.86	non-parametric	Standard Bootstrap		549.86
Benzo(a)anthracene	0.0173 - 2400	72 / 132	2400	130.01	200.02	non-parametric	Standard Bootstrap		200.02
Benzo(a)pyrene	0.0219 - 2600	75 / 145	2600	95.89	147.36	non-parametric	Standard Bootstrap		147.36
Benzo(b)fluoranthene	0.0149 - 1200	79 / 128	1200	61.33	91.47	non-parametric	Standard Bootstrap		91.47
Benzo(k)fluoranthene	0.00669 - 1500	55 / 129	1500	72.78	112.03	non-parametric	Standard Bootstrap		112.03
Chrysene	0.0118 - 2300	67 / 127	2300	115.48	175.37	non-parametric	Standard Bootstrap		175.37
Dibenzo(a,h)anthracene	0.12 - 290	21 / 116	290	14.15	21.43	non-parametric	Standard Bootstrap		21.43
Dibenzofuran	0.042 - 1400	22 / 108	1400	69.47	111.12	non-parametric	Standard Bootstrap		111.12
Fluoranthene	0.047 - 5400	77 / 132	5400	207.20	317.80	non-parametric	Standard Bootstrap		317.80
Fluorene	0.00195 - 4600	37 / 125	4600	198.10	306.26	non-parametric	Standard Bootstrap		306.26
Indeno(1,2,3-cd)pyrene	0.0113 - 1200	58 / 132	1200	52.58	81.40	non-parametric	Standard Bootstrap		81.40
Naphthalene	0.031 - 37000	64 / 158	37000	766.19	1,324.29	non-parametric	Standard Bootstrap		1,324.29
Pyrene	0.046 - 8400	83 / 145	8400	284.58	442.29	non-parametric	Standard Bootstrap		442.29
VOCs									
1,2,4-Trimethylbenzene	0.019 - 54	25 / 94	54	1.06	2.04	non-parametric	Standard Bootstrap		2.04
1,3,5-Trimethylbenzene	0.03 - 21	21 / 108	21	0.50	0.88	non-parametric	Standard Bootstrap		0.88
Benzene	0.018 - 52	29 / 127	52	0.99	1.78	non-parametric	Standard Bootstrap		1.78

All units are milligrams per kilogram (mg/kg).

EPC– Exposure Point Concentration
mg/kg – milligrams per kilogram
SVOC– Semi-volatile organic compound
UCL– Upper Confidence Limit
VOC– Volatile organic compound

ATTACHMENT F2

ProUCL Output Tables

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Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
1,2,4-Trimethylbenzene

Raw Statistics	
Number of Valid Samples	94
Number of Unique Samples	27
Minimum	7.5
Maximum	54000
Mean	1057.04255
Median	7.5
Standard Deviation	5942.02949
Variance	35307714.5
Coefficient of Variation	5.62137208
Skewness	8.00283819

Gamma Statistics	
k hat	0.18339203
k star (bias corrected)	0.18463129
Theta hat	5763.84144
Theta star	5725.15402
nu hat	34.4777007
nu star	34.7106819
Approx.Chi Square Value (.05)	22.230945
Adjusted Level of Significance	0.04744681
Adjusted Chi Square Value	22.0754263

Log-transformed Statistics	
Minimum of log data	2.01490302
Maximum of log data	10.8967393
Mean of log data	2.89626482
Standard Deviation of log data	1.91492888
Variance of log data	3.66695261

RECOMMENDATION

Data are Non-parametric (0.05)

Use 97.5% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.47356435
Lilliefors 5% Critical Value	0.09138392
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	2075.27269

Gamma Distribution Test	
A-D Test Statistic	26.7252893
A-D 5% Critical Value	0.92876172
K-S Test Statistic	0.41920667
K-S 5% Critical Value	0.10289104
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	1650.43222
Adjusted Gamma UCL	1662.05931

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.36882391
Lilliefors 5% Critical Value	0.09138392
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	214.395105
95% Chebyshev (MVUE) UCL	249.729044
97.5% Chebyshev (MVUE) UCL	311.284433
99% Chebyshev (MVUE) UCL	432.198077

95% Non-parametric UCLs	
CLT UCL	2065.12983
Adj-CLT UCL (Adjusted for skewness)	2605.67426
Mod-t UCL (Adjusted for skewness)	2159.5867
Jackknife UCL	2075.27269
Standard Bootstrap UCL	2041.35143
Bootstrap-t UCL	4904.74242
Hall's Bootstrap UCL	5032.36566
Percentile Bootstrap UCL	2191.99468
BCA Bootstrap UCL	2843.90957
95% Chebyshev (Mean, Sd) UCL	3728.49641
97.5% Chebyshev (Mean, Sd) UCL	4884.43662
99% Chebyshev (Mean, Sd) UCL	7155.05734

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
1,3,5-Trimethylbenzene

Raw Statistics	
Number of Valid Samples	108
Number of Unique Samples	26
Minimum	8
Maximum	21000
Mean	502.736111
Median	8
Standard Deviation	2436.62655
Variance	5937148.96
Coefficient of Variation	4.84673072
Skewness	6.91905779

Gamma Statistics	
k hat	0.22165551
k star (bias corrected)	0.22167125
Theta hat	2268.0966
Theta star	2267.93553
nu hat	47.8775905
nu star	47.8809907
Approx.Chi Square Value (.05)	32.9964793
Adjusted Level of Significance	0.04777778
Adjusted Chi Square Value	32.8296736

Log-transformed Statistics	
Minimum of log data	2.07944154
Maximum of log data	9.95227772
Mean of log data	2.95325565
Standard Deviation of log data	1.81496228
Variance of log data	3.29408806

RECOMMENDATION

Data are Non-parametric (0.05)

Use 97.5% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.4457922
Lilliefors 5% Critical Value	0.08525539
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	891.764051

Gamma Distribution Test	
A-D Test Statistic	28.0127715
A-D 5% Critical Value	0.90277809
K-S Test Statistic	0.4140183
K-S 5% Critical Value	0.0963714
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	729.517317
Adjusted Gamma UCL	733.223954

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.40712397
Lilliefors 5% Critical Value	0.08525539
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	170.205099
95% Chebyshev (MVUE) UCL	206.168468
97.5% Chebyshev (MVUE) UCL	253.95539
99% Chebyshev (MVUE) UCL	347.823545

95% Non-parametric UCLs	
CLT UCL	888.395894
Adj-CLT UCL (Adjusted for skewness)	1055.19457
Mod-t UCL (Adjusted for skewness)	917.781273
Jackknife UCL	891.764051
Standard Bootstrap UCL	884.603038
Bootstrap-t UCL	1717.63566
Hall's Bootstrap UCL	2308.15391
Percentile Bootstrap UCL	945.138889
BCA Bootstrap UCL	1129.96759
95% Chebyshev (Mean, Sd) UCL	1524.74317
97.5% Chebyshev (Mean, Sd) UCL	1966.96644
99% Chebyshev (Mean, Sd) UCL	2835.62843

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Dibenzofuran

Raw Statistics	
Number of Valid Samples	108
Number of Unique Samples	33
Minimum	16
Maximum	1400000
Mean	69471.4676
Median	80
Standard Deviation	264707.474
Variance	7.01E+10
Coefficient of Variation	3.81030491
Skewness	4.07464934

Gamma Statistics	
k hat	0.12964901
k star (bias corrected)	0.13222049
Theta hat	535842.628
Theta star	525421.342
nu hat	28.0041867
nu star	28.559626
Approx.Chi Square Value (.05)	17.3624012
Adjusted Level of Significance	0.04777778
Adjusted Chi Square Value	17.2442629

Log-transformed Statistics	
Minimum of log data	2.77258872
Maximum of log data	14.1519828
Mean of log data	5.09640529
Standard Deviation of log data	3.08253181
Variance of log data	9.50200238

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.4876173
Lilliefors 5% Critical Value	0.08525539
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	111734.244

Gamma Distribution Test	
A-D Test Statistic	22.5922559
A-D 5% Critical Value	0.99241055
K-S Test Statistic	0.37583454
K-S 5% Critical Value	0.09964028
Data do not follow gamma distribution at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	114274.466
Adjusted Gamma UCL	115057.346

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.23564258
Lilliefors 5% Critical Value	0.08525539
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	75620.6893
95% Chebyshev (MVUE) UCL	52042.0044
97.5% Chebyshev (MVUE) UCL	68042.2609
99% Chebyshev (MVUE) UCL	99471.6665

95% Non-parametric UCLs	
CLT UCL	111368.338
Adj-CLT UCL (Adjusted for skewness)	122039.534
Mod-t UCL (Adjusted for skewness)	113398.735
Jackknife UCL	111734.244
Standard Bootstrap UCL	111118.865
Bootstrap-t UCL	133541.317
Hall's Bootstrap UCL	111148.732
Percentile Bootstrap UCL	113869.296
BCA Bootstrap UCL	125220.833
95% Chebyshev (Mean, Sd) UCL	180499.112
97.5% Chebyshev (Mean, Sd) UCL	228540.863
99% Chebyshev (Mean, Sd) UCL	322909.579

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Dibenzo(a,h)anthracene

Raw Statistics	
Number of Valid Samples	116
Number of Unique Samples	40
Minimum	17
Maximum	290000
Mean	14152.01724
Median	85
Standard Deviation	49139.86648
Variance	2414726477
Coefficient of Variation	3.47228707
Skewness	3.981484095

Gamma Statistics	
k hat	0.17349028
k star (bias corrected)	0.174750589
Theta hat	81572.39278
Theta star	80984.08913
nu hat	40.2497449
nu star	40.54213655
Approx.Chi Square Value (.05)	26.94916502
Adjusted Level of Significance	0.047931034
Adjusted Chi Square Value	26.80992256

Log-transformed Statistics	
Minimum of log data	2.833213344
Maximum of log data	12.5776362
Mean of log data	5.222067114
Standard Deviation of log data	2.678888018
Variance of log data	7.17644101

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.46273571
Lilliefors 5% Critical Value	0.08226303
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	21717.6436

Gamma Distribution Test	
A-D Test Statistic	19.0862675
A-D 5% Critical Value	0.94447465
K-S Test Statistic	0.33030487
K-S 5% Critical Value	0.09559749
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	21290.1964
Adjusted Gamma UCL	21400.7711

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.1862679
Lilliefors 5% Critical Value	0.08226303
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	18673.425
95% Chebyshev (MVUE) UCL	17510.0692
97.5% Chebyshev (MVUE) UCL	22543.266
99% Chebyshev (MVUE) UCL	32430.0066

95% Non-parametric UCLs	
CLT UCL	21656.6982
Adj-CLT UCL (Adjusted for skewness)	23458.8916
Mod-t UCL (Adjusted for skewness)	21998.7494
Jackknife UCL	21717.6436
Standard Bootstrap UCL	21430.3552
Bootstrap-t UCL	24514.2449
Hall's Bootstrap UCL	22189.6452
Percentile Bootstrap UCL	22093.6552
BCA Bootstrap UCL	23514.4741
95% Chebyshev (Mean, Sd) UCL	34039.5898
97.5% Chebyshev (Mean, Sd) UCL	42644.9584
99% Chebyshev (Mean, Sd) UCL	59548.5386

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
2-Methylnaphthalene

Raw Statistics	
Number of Valid Samples	119
Number of Unique Samples	48
Minimum	15.5
Maximum	*30000000*
Mean	1141938.09
Median	80
Standard Deviation	4953956.8
Variance	2.45E+13
Coefficient of Variation	4.33820084
Skewness	4.77585526

Gamma Statistics	
k hat	0.09887446
k star (bias corrected)	0.10198406
Theta hat	11549374.2
Theta star	11197221
nu hat	23.5321205
nu star	24.2722071
Approx.Chi Square Value (.05)	14.0541221
Adjusted Level of Significance	0.04798319
Adjusted Chi Square Value	13.9587132

Log-transformed Statistics	
Minimum of log data	2.74084002
Maximum of log data	17.2167079
Mean of log data	5.72293678
Standard Deviation of log data	3.79445961
Variance of log data	14.3979238

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.48615076
Lilliefors 5% Critical Value	0.08121949
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	1894823.72

Gamma Distribution Test	
A-D Test Statistic	25.6900887
A-D 5% Critical Value	1.06600965
K-S Test Statistic	0.39076651
K-S 5% Critical Value	0.09851127
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	1972187.08
Adjusted Gamma UCL	1985667.13

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.21596058
Lilliefors 5% Critical Value	0.08121949
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	2839058.99
95% Chebyshev (MVUE) UCL	1082217.53
97.5% Chebyshev (MVUE) UCL	1435362.79
99% Chebyshev (MVUE) UCL	2129048.25

95% Non-parametric UCLs	
CLT UCL	1888912.96
Adj-CLT UCL (Adjusted for skewness)	2101353.22
Mod-t UCL (Adjusted for skewness)	1927960.11
Jackknife UCL	1894823.72
Standard Bootstrap UCL	1875527.18
Bootstrap-t UCL	2355803.85
Hall's Bootstrap UCL	1871617.67
Percentile Bootstrap UCL	1938119.56
BCA Bootstrap UCL	2131075.35
95% Chebyshev (Mean, Sd) UCL	3121438.22
97.5% Chebyshev (Mean, Sd) UCL	3977969.51
99% Chebyshev (Mean, Sd) UCL	5660459.37

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Acenaphthene

Raw Statistics	
Number of Valid Samples	121
Number of Unique Samples	47
Minimum	16
Maximum	7400000
Mean	205284.669
Median	80
Standard Deviation	886419.23
Variance	7.86E+11
Coefficient of Variation	4.31800013
Skewness	5.99499991

Gamma Statistics	
k hat	0.11859909
k star (bias corrected)	0.12116826
Theta hat	1730912.64
Theta star	1694211.55
nu hat	28.7009806
nu star	29.3227194
Approx.Chi Square Value (.05)	17.9592468
Adjusted Level of Significance	0.04801653
Adjusted Chi Square Value	17.8520337

Log-transformed Statistics	
Minimum of log data	2.77258872
Maximum of log data	15.8169906
Mean of log data	5.53497763
Standard Deviation of log data	3.4336752
Variance of log data	11.7901254

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.47684906
Lilliefors 5% Critical Value	0.08054545
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	338864.068

Gamma Distribution Test	
A-D Test Statistic	23.6839422
A-D 5% Critical Value	1.013869
K-S Test Statistic	0.35788045
K-S 5% Critical Value	0.09645984
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	335175.792
Adjusted Gamma UCL	337188.741

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.22168962
Lilliefors 5% Critical Value	0.08054545
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	449668.542
95% Chebyshev (MVUE) UCL	253892.671
97.5% Chebyshev (MVUE) UCL	334210.447
99% Chebyshev (MVUE) UCL	491979.165

95% Non-parametric UCLs	
CLT UCL	337832.841
Adj-CLT UCL (Adjusted for skewness)	384759.906
Mod-t UCL (Adjusted for skewness)	346183.742
Jackknife UCL	338864.068
Standard Bootstrap UCL	337871.862
Bootstrap-t UCL	468069.817
Hall's Bootstrap UCL	416608.445
Percentile Bootstrap UCL	354282.083
BCA Bootstrap UCL	394828.302
95% Chebyshev (Mean, Sd) UCL	556540.292
97.5% Chebyshev (Mean, Sd) UCL	708528.88
99% Chebyshev (Mean, Sd) UCL	1007081.03

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Fluorene

Raw Statistics	
Number of Valid Samples	125
Number of Unique Samples	50
Minimum	1.95
Maximum	4600000
Mean	198104.337
Median	80
Standard Deviation	749871.794
Variance	5.62E+11
Coefficient of Variation	3.78523663
Skewness	4.11977253

Gamma Statistics	
k hat	0.11840144
k star (bias corrected)	0.12089314
Theta hat	1673158.11
Theta star	1638673.06
nu hat	29.6003612
nu star	30.2232859
Approx.Chi Square Value (.05)	18.6664118
Adjusted Level of Significance	0.04808
Adjusted Chi Square Value	18.5604833

Log-transformed Statistics	
Minimum of log data	0.66782937
Maximum of log data	15.3415669
Mean of log data	5.48668989
Standard Deviation of log data	3.47379961
Variance of log data	12.0672837

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.47980039
Lilliefors 5% Critical Value	0.07924625
Data not normal at 5% significance level	
95% UCL (Assuming Normal Distribution)	
Student's-t UCL	309256.016
Gamma Distribution Test	
A-D Test Statistic	24.3112576
A-D 5% Critical Value	1.01685988
K-S Test Statistic	0.35393406
K-S 5% Critical Value	0.09535194
Data do not follow gamma distribution	
at 5% significance level	
95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	320756.023
Adjusted Gamma UCL	322586.645
Lognormal Distribution Test	
Lilliefors Test Statisitic	0.20962278
Lilliefors 5% Critical Value	0.07924625
Data not lognormal at 5% significance level	
95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	494799.306
95% Chebyshev (MVUE) UCL	277916.594
97.5% Chebyshev (MVUE) UCL	365950.389
99% Chebyshev (MVUE) UCL	538875.732
95% Non-parametric UCLs	
CLT UCL	308425.611
Adj-CLT UCL (Adjusted for skewness)	334833.316
Mod-t UCL (Adjusted for skewness)	313375.084
Jackknife UCL	309256.016
Standard Bootstrap UCL	306256.768
Bootstrap-t UCL	369518.515
Hall's Bootstrap UCL	319264.174
Percentile Bootstrap UCL	315075.62
BCA Bootstrap UCL	343095.386
95% Chebyshev (Mean, Sd) UCL	490458.184
97.5% Chebyshev (Mean, Sd) UCL	616959.927
99% Chebyshev (Mean, Sd) UCL	865448.105

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Benzene

Raw Statistics	
Number of Valid Samples	127
Number of Unique Samples	33
Minimum	2.5
Maximum	52000
Mean	990.590551
Median	7.5
Standard Deviation	5311.90064
Variance	28216288.4
Coefficient of Variation	5.36235747
Skewness	8.04217502

Gamma Statistics	
k hat	0.18419738
k star (bias corrected)	0.18509561
Theta hat	5377.87525
Theta star	5351.77772
nu hat	46.7861354
nu star	47.0142845
Approx.Chi Square Value (.05)	32.276833
Adjusted Level of Significance	0.04811024
Adjusted Chi Square Value	32.1369846

Log-transformed Statistics	
Minimum of log data	0.91629073
Maximum of log data	10.858999
Mean of log data	2.85183539
Standard Deviation of log data	2.19427219
Variance of log data	4.81483044

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.44267853
Lilliefors 5% Critical Value	0.07861979
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	1771.64302

Gamma Distribution Test	
A-D Test Statistic	28.5351817
A-D 5% Critical Value	0.93323691
K-S Test Statistic	0.40947438
K-S 5% Critical Value	0.09202776
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	1442.88958
Adjusted Gamma UCL	1449.16851

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.38083643
Lilliefors 5% Critical Value	0.07861979
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	379.215232
95% Chebyshev (MVUE) UCL	438.851877
97.5% Chebyshev (MVUE) UCL	550.481332
99% Chebyshev (MVUE) UCL	769.755781

95% Non-parametric UCLs	
CLT UCL	1765.90047
Adj-CLT UCL (Adjusted for skewness)	2125.31874
Mod-t UCL (Adjusted for skewness)	1827.70501
Jackknife UCL	1771.64302
Standard Bootstrap UCL	1781.74088
Bootstrap-t UCL	3226.91369
Hall's Bootstrap UCL	4318.63965
Percentile Bootstrap UCL	1858.31496
BCA Bootstrap UCL	2266.1063
95% Chebyshev (Mean, Sd) UCL	3045.17919
97.5% Chebyshev (Mean, Sd) UCL	3934.20134
99% Chebyshev (Mean, Sd) UCL	5680.5132

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Chrysene

Raw Statistics	
Number of Valid Samples	127
Number of Unique Samples	73
Minimum	11.8
Maximum	2300000
Mean	115482.006
Median	210
Standard Deviation	416724.349
Variance	1.74E+11
Coefficient of Variation	3.6085652
Skewness	4.01626009

Gamma Statistics	
k hat	0.14222963
k star (bias corrected)	0.14411922
Theta hat	811940.588
Theta star	801294.999
nu hat	36.1263251
nu star	36.6062806
Approx.Chi Square Value (.05)	23.7549591
Adjusted Level of Significance	0.04811024
Adjusted Chi Square Value	23.636251

Log-transformed Statistics	
Minimum of log data	2.46809953
Maximum of log data	14.6484197
Mean of log data	6.21146606
Standard Deviation of log data	3.30826043
Variance of log data	10.9445871

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.46915215
Lilliefors 5% Critical Value	0.07861979
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	176756.417

Gamma Distribution Test	
A-D Test Statistic	18.2235834
A-D 5% Critical Value	0.98745112
K-S Test Statistic	0.29476853
K-S 5% Critical Value	0.09379212
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	177957.23
Adjusted Gamma UCL	178850.983

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.14984438
Lilliefors 5% Critical Value	0.07861979
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	499777.294
95% Chebyshev (MVUE) UCL	328296.26
97.5% Chebyshev (MVUE) UCL	430417.173
99% Chebyshev (MVUE) UCL	631013.933

95% Non-parametric UCLs	
CLT UCL	176305.908
Adj-CLT UCL (Adjusted for skewness)	190387.358
Mod-t UCL (Adjusted for skewness)	178952.839
Jackknife UCL	176756.417
Standard Bootstrap UCL	175374.202
Bootstrap-t UCL	207459.249
Hall's Bootstrap UCL	180609.96
Percentile Bootstrap UCL	178544.825
BCA Bootstrap UCL	197575.575
95% Chebyshev (Mean, Sd) UCL	276666.707
97.5% Chebyshev (Mean, Sd) UCL	346411.456
99% Chebyshev (Mean, Sd) UCL	483411.509

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Arsenic

Raw Statistics	
Number of Valid Samples	127
Number of Unique Samples	85
Minimum	0.325
Maximum	27
Mean	3.74129921
Median	2.165
Standard Deviation	4.53906829
Variance	20.603141
Coefficient of Variation	1.21323317
Skewness	2.38243287

Gamma Statistics	
k hat	0.92678322
k star (bias corrected)	0.91014005
Theta hat	4.03686551
Theta star	4.1106852
nu hat	235.402938
nu star	231.175572
Approx.Chi Square Value (.05)	196.973414
Adjusted Level of Significance	0.04811024
Adjusted Chi Square Value	196.614116

Log-transformed Statistics	
Minimum of log data	-1.1239301
Maximum of log data	3.29583687
Mean of log data	0.69091531
Standard Deviation of log data	1.15929275
Variance of log data	1.34395968

RECOMMENDATION

Data are Non-parametric (0.05)

Use 97.5% Chebyshev (Mean, Sd) UCL

All units are in milligrams/kilogram (mg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.22583208
Lilliefors 5% Critical Value	0.07861979
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	4.40871578

Gamma Distribution Test	
A-D Test Statistic	2.64953541
A-D 5% Critical Value	0.78677016
K-S Test Statistic	0.13549311
K-S 5% Critical Value	0.08517572
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	4.39093259
Adjusted Gamma UCL	4.39895672

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.15932906
Lilliefors 5% Critical Value	0.07861979
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	4.96942263
95% Chebyshev (MVUE) UCL	6.06849418
97.5% Chebyshev (MVUE) UCL	7.01823701
99% Chebyshev (MVUE) UCL	8.8838229

95% Non-parametric UCLs	
CLT UCL	4.40380872
Adj-CLT UCL (Adjusted for skewness)	4.49479252
Mod-t UCL (Adjusted for skewness)	4.42290741
Jackknife UCL	4.40871578
Standard Bootstrap UCL	4.40436271
Bootstrap-t UCL	4.51598096
Hall's Bootstrap UCL	4.55697929
Percentile Bootstrap UCL	4.41472441
BCA Bootstrap UCL	4.50527559
95% Chebyshev (Mean, Sd) UCL	5.49696424
97.5% Chebyshev (Mean, Sd) UCL	6.25664189
99% Chebyshev (Mean, Sd) UCL	7.74888155

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Benzo(b)fluoranthene

Raw Statistics	
Number of Valid Samples	128
Number of Unique Samples	73
Minimum	14.9
Maximum	1200000
Mean	61328.65
Median	375
Standard Deviation	209200.819
Variance	4.38E+10
Coefficient of Variation	3.41114339
Skewness	3.99192713

Gamma Statistics	
k hat	0.16351415
k star (bias corrected)	0.16489012
Theta hat	375066.312
Theta star	371936.47
nu hat	41.8596229
nu star	42.2118714
Approx.Chi Square Value (.05)	28.3153035
Adjusted Level of Significance	0.048125
Adjusted Chi Square Value	28.1859197

Log-transformed Statistics	
Minimum of log data	2.70136121
Maximum of log data	13.9978321
Mean of log data	6.38288746
Standard Deviation of log data	3.14491271
Variance of log data	9.89047597

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.44700603
Lilliefors 5% Critical Value	0.07831208
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	91966.9858

Gamma Distribution Test	
A-D Test Statistic	15.1002466
A-D 5% Critical Value	0.96027302
K-S Test Statistic	0.26706973
K-S 5% Critical Value	0.09261453
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	91427.4883
Adjusted Gamma UCL	91847.1744

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.12931054
Lilliefors 5% Critical Value	0.07831208
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	305607.044
95% Chebyshev (MVUE) UCL	228475.887
97.5% Chebyshev (MVUE) UCL	298147.941
99% Chebyshev (MVUE) UCL	435005.199

95% Non-parametric UCLs	
CLT UCL	91743.4981
Adj-CLT UCL (Adjusted for skewness)	98714.8408
Mod-t UCL (Adjusted for skewness)	93054.3744
Jackknife UCL	91966.9858
Standard Bootstrap UCL	91472.7651
Bootstrap-t UCL	105630.447
Hall's Bootstrap UCL	95308.6733
Percentile Bootstrap UCL	93811.6531
BCA Bootstrap UCL	101137.446
95% Chebyshev (Mean, Sd) UCL	141928.679
97.5% Chebyshev (Mean, Sd) UCL	176804.375
99% Chebyshev (Mean, Sd) UCL	245310.928

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Benzo(k)fluoranthene

Raw Statistics	
Number of Valid Samples	129
Number of Unique Samples	63
Minimum	6.69
Maximum	1500000
Mean	72775.6278
Median	165
Standard Deviation	268566.496
Variance	7.21E+10
Coefficient of Variation	3.69033569
Skewness	4.03764476

Gamma Statistics	
k hat	0.143497
k star (bias corrected)	0.14532782
Theta hat	507157.831
Theta star	500768.729
nu hat	37.0222263
nu star	37.4945776
Approx.Chi Square Value (.05)	24.4724793
Adjusted Level of Significance	0.04813953
Adjusted Chi Square Value	24.353755

Log-transformed Statistics	
Minimum of log data	1.90061387
Maximum of log data	14.2209757
Mean of log data	5.8046788
Standard Deviation of log data	3.09896184
Variance of log data	9.6035645

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.46888634
Lilliefors 5% Critical Value	0.07800795
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	111953.32

Gamma Distribution Test	
A-D Test Statistic	21.2803171
A-D 5% Critical Value	0.98677608
K-S Test Statistic	0.30704642
K-S 5% Critical Value	0.09317662
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	111500.408
Adjusted Gamma UCL	112043.972

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.17026021
Lilliefors 5% Critical Value	0.07800795
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	142548.337
95% Chebyshev (MVUE) UCL	110600.617
97.5% Chebyshev (MVUE) UCL	144103.805
99% Chebyshev (MVUE) UCL	209914.33

95% Non-parametric UCLs	
CLT UCL	111669.773
Adj-CLT UCL (Adjusted for skewness)	120651.724
Mod-t UCL (Adjusted for skewness)	113354.322
Jackknife UCL	111953.32
Standard Bootstrap UCL	112025.089
Bootstrap-t UCL	130356.128
Hall's Bootstrap UCL	115090.333
Percentile Bootstrap UCL	113146.012
BCA Bootstrap UCL	123071.923
95% Chebyshev (Mean, Sd) UCL	175845.985
97.5% Chebyshev (Mean, Sd) UCL	220444.61
99% Chebyshev (Mean, Sd) UCL	308049.974

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Lead

Raw Statistics	
Number of Valid Samples	131
Number of Unique Samples	105
Minimum	0.5
Maximum	4000
Mean	100.177557
Median	22
Standard Deviation	367.22057
Variance	134850.947
Coefficient of Variation	3.66569699
Skewness	9.50071397

Gamma Statistics	
k hat	0.43255584
k star (bias corrected)	0.42773904
Theta hat	231.594509
Theta star	234.202512
nu hat	113.32963
nu star	112.067628
Approx.Chi Square Value (.05)	88.6259968
Adjusted Level of Significance	0.04816794
Adjusted Chi Square Value	88.3955372

Log-transformed Statistics	
Minimum of log data	-0.69314718
Maximum of log data	8.29404964
Mean of log data	3.10463065
Standard Deviation of log data	1.68303451
Variance of log data	2.83260517

RECOMMENDATION

Data are Non-parametric (0.05)

Use 97.5% Chebyshev (Mean, Sd) UCL

All units are in milligrams/kilogram (mg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.39302721
Lilliefors 5% Critical Value	0.07741018
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	153.330157

Gamma Distribution Test	
A-D Test Statistic	5.44619201
A-D 5% Critical Value	0.83568695
K-S Test Statistic	0.1392773
K-S 5% Critical Value	0.08691404
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	126.674584
Adjusted Gamma UCL	127.004842

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.10099354
Lilliefors 5% Critical Value	0.07741018
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	140.403942
95% Chebyshev (MVUE) UCL	174.530309
97.5% Chebyshev (MVUE) UCL	211.271801
99% Chebyshev (MVUE) UCL	283.443348

95% Non-parametric UCLs	
CLT UCL	152.951387
Adj-CLT UCL (Adjusted for skewness)	181.4086
Mod-t UCL (Adjusted for skewness)	157.768907
Jackknife UCL	153.330157
Standard Bootstrap UCL	152.550077
Bootstrap-t UCL	251.954659
Hall's Bootstrap UCL	348.184777
Percentile Bootstrap UCL	157.989542
BCA Bootstrap UCL	201.490458
95% Chebyshev (Mean, Sd) UCL	240.029387
97.5% Chebyshev (Mean, Sd) UCL	300.543385
99% Chebyshev (Mean, Sd) UCL	419.411418

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Indeno(1,2,3-c,d)pyrene

Raw Statistics	
Number of Valid Samples	132
Number of Unique Samples	71
Minimum	11.3
Maximum	1200000
Mean	52584.2455
Median	155
Standard Deviation	198707.752
Variance	3.95E+10
Coefficient of Variation	3.77884575
Skewness	4.41134159

Gamma Statistics	
k hat	0.15080988
k star (bias corrected)	0.15243289
Theta hat	348679.043
Theta star	344966.532
nu hat	39.8138089
nu star	40.2422829
Approx.Chi Square Value (.05)	26.7044963
Adjusted Level of Significance	0.04818182
Adjusted Chi Square Value	26.5829523

Log-transformed Statistics	
Minimum of log data	2.42480273
Maximum of log data	13.9978321
Mean of log data	5.77780445
Standard Deviation of log data	3.10517331
Variance of log data	9.64210131

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.46267707
Lilliefors 5% Critical Value	0.0771164
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	81235.0741

Gamma Distribution Test	
A-D Test Statistic	19.4096657
A-D 5% Critical Value	0.97847347
K-S Test Statistic	0.28066171
K-S 5% Critical Value	0.09202282
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	79241.7149
Adjusted Gamma UCL	79604.0282

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.15984382
Lilliefors 5% Critical Value	0.0771164
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	139793.698
95% Chebyshev (MVUE) UCL	109685.427
97.5% Chebyshev (MVUE) UCL	142862.062
99% Chebyshev (MVUE) UCL	208031.138

95% Non-parametric UCLs	
CLT UCL	81032.4657
Adj-CLT UCL (Adjusted for skewness)	88128.1124
Mod-t UCL (Adjusted for skewness)	82341.8516
Jackknife UCL	81235.0741
Standard Bootstrap UCL	81396.229
Bootstrap-t UCL	94435.0416
Hall's Bootstrap UCL	86898.0564
Percentile Bootstrap UCL	83489.2417
BCA Bootstrap UCL	89383.6652
95% Chebyshev (Mean, Sd) UCL	127972.666
97.5% Chebyshev (Mean, Sd) UCL	160593.296
99% Chebyshev (Mean, Sd) UCL	224670.207

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Fluoranthene

Raw Statistics	
Number of Valid Samples	132
Number of Unique Samples	85
Minimum	18.5
Maximum	5400000
Mean	207198.737
Median	357.5
Standard Deviation	772954.894
Variance	5.97E+11
Coefficient of Variation	3.73050002
Skewness	4.58304162

Gamma Statistics	
k hat	0.13455152
k star (bias corrected)	0.13654404
Theta hat	1539921.15
Theta star	1517449.89
nu hat	35.5216022
nu star	36.0476264
Approx.Chi Square Value (.05)	23.3047823
Adjusted Level of Significance	0.04818182
Adjusted Chi Square Value	23.1917977

Log-transformed Statistics	
Minimum of log data	2.91777073
Maximum of log data	15.5019095
Mean of log data	6.43983132
Standard Deviation of log data	3.42012687
Variance of log data	11.6972678

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.47956674
Lilliefors 5% Critical Value	0.0771164
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	318647.827

Gamma Distribution Test	
A-D Test Statistic	19.6293356
A-D 5% Critical Value	1.00014092
K-S Test Statistic	0.30934369
K-S 5% Critical Value	0.09271308
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	320493.132
Adjusted Gamma UCL	322054.493

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.15155101
Lilliefors 5% Critical Value	0.0771164
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	970962.981
95% Chebyshev (MVUE) UCL	601494.749
97.5% Chebyshev (MVUE) UCL	790203.052
99% Chebyshev (MVUE) UCL	1160883.97

95% Non-parametric UCLs	
CLT UCL	317859.699
Adj-CLT UCL (Adjusted for skewness)	346535.426
Mod-t UCL (Adjusted for skewness)	323120.661
Jackknife UCL	318647.827
Standard Bootstrap UCL	317804.378
Bootstrap-t UCL	376139.183
Hall's Bootstrap UCL	348268.668
Percentile Bootstrap UCL	323457.071
BCA Bootstrap UCL	351450.56
95% Chebyshev (Mean, Sd) UCL	500452.765
97.5% Chebyshev (Mean, Sd) UCL	627344.017
99% Chebyshev (Mean, Sd) UCL	876597.311

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Benzo(a)anthracene

Raw Statistics	
Number of Valid Samples	132
Number of Unique Samples	80
Minimum	17
Maximum	2400000
Mean	130008.924
Median	236.5
Standard Deviation	481834.429
Variance	2.32E+11
Coefficient of Variation	3.70616429
Skewness	3.97987394

Gamma Statistics	
k hat	0.13761233
k star (bias corrected)	0.13953528
Theta hat	944747.616
Theta star	931727.939
nu hat	36.3296559
nu star	36.8373152
Approx.Chi Square Value (.05)	23.9413771
Adjusted Level of Significance	0.04818182
Adjusted Chi Square Value	23.826745

Log-transformed Statistics	
Minimum of log data	2.83321334
Maximum of log data	14.6909793
Mean of log data	6.12075941
Standard Deviation of log data	3.29822293
Variance of log data	10.8782745

RECOMMENDATION
Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.47777252
Lilliefors 5% Critical Value	0.0771164
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	199482.588

Gamma Distribution Test	
A-D Test Statistic	20.3204602
A-D 5% Critical Value	0.99606179
K-S Test Statistic	0.30371775
K-S 5% Critical Value	0.09258313
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	200037.77
Adjusted Gamma UCL	201000.166

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.15943982
Lilliefors 5% Critical Value	0.0771164
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	424388.089
95% Chebyshev (MVUE) UCL	289987.691
97.5% Chebyshev (MVUE) UCL	379786.897
99% Chebyshev (MVUE) UCL	556180.05

95% Non-parametric UCLs	
CLT UCL	198991.295
Adj-CLT UCL (Adjusted for skewness)	214514.222
Mod-t UCL (Adjusted for skewness)	201903.851
Jackknife UCL	199482.588
Standard Bootstrap UCL	200015.861
Bootstrap-t UCL	224642.826
Hall's Bootstrap UCL	201269.415
Percentile Bootstrap UCL	202977.55
BCA Bootstrap UCL	223214.641
95% Chebyshev (Mean, Sd) UCL	312813.752
97.5% Chebyshev (Mean, Sd) UCL	391913.548
99% Chebyshev (Mean, Sd) UCL	547289.78

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Pyrene

Raw Statistics	
Number of Valid Samples	145
Number of Unique Samples	90
Minimum	10
Maximum	8400000
Mean	284577.952
Median	330
Standard Deviation	1160613.97
Variance	1.35E+12
Coefficient of Variation	4.07836925
Skewness	5.15915181

Gamma Statistics	
k hat	0.12588668
k star (bias corrected)	0.12787983
Theta hat	2260588.21
Theta star	2225354.44
nu hat	36.5071382
nu star	37.0851514
Approx.Chi Square Value (.05)	24.141509
Adjusted Level of Significance	0.04834483
Adjusted Chi Square Value	24.0368114

Log-transformed Statistics	
Minimum of log data	2.30258509
Maximum of log data	15.9437423
Mean of log data	6.30022112
Standard Deviation of log data	3.61525157
Variance of log data	13.0700439

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.47915194
Lilliefors 5% Critical Value	0.0735783
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	444141.616

Gamma Distribution Test	
A-D Test Statistic	21.1727346
A-D 5% Critical Value	1.0198148
K-S Test Statistic	0.29220598
K-S 5% Critical Value	0.08944552
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	437156.453
Adjusted Gamma UCL	439060.584

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.13755158
Lilliefors 5% Critical Value	0.0735783
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	1812311.11
95% Chebyshev (MVUE) UCL	1037657.49
97.5% Chebyshev (MVUE) UCL	1366910.65
99% Chebyshev (MVUE) UCL	2013664.74

95% Non-parametric UCLs	
CLT UCL	443115.104
Adj-CLT UCL (Adjusted for skewness)	487239.473
Mod-t UCL (Adjusted for skewness)	451024.126
Jackknife UCL	444141.616
Standard Bootstrap UCL	442286.05
Bootstrap-t UCL	529251.633
Hall's Bootstrap UCL	499425.752
Percentile Bootstrap UCL	452073.608
BCA Bootstrap UCL	501099.588
95% Chebyshev (Mean, Sd) UCL	704704.953
97.5% Chebyshev (Mean, Sd) UCL	886494.242
99% Chebyshev (Mean, Sd) UCL	1243584.1

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Benzo(a)pyrene

Raw Statistics	
Number of Valid Samples	145
Number of Unique Samples	80
Minimum	10
Maximum	2600000
Mean	95887.04
Median	176
Standard Deviation	373311.873
Variance	1.39E+11
Coefficient of Variation	3.8932464
Skewness	4.58688256

Gamma Statistics	
k hat	0.14054303
k star (bias corrected)	0.14223295
Theta hat	682261.061
Theta star	674154.903
nu hat	40.7574801
nu star	41.2475552
Approx.Chi Square Value (.05)	27.5255663
Adjusted Level of Significance	0.04834483
Adjusted Chi Square Value	27.4132471

Log-transformed Statistics	
Minimum of log data	2.30258509
Maximum of log data	14.771022
Mean of log data	5.95078323
Standard Deviation of log data	3.35896669
Variance of log data	11.2826572

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.46133175
Lilliefors 5% Critical Value	0.0735783
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	147210.746

Gamma Distribution Test	
A-D Test Statistic	20.0424633
A-D 5% Critical Value	0.99872417
K-S Test Statistic	0.27809661
K-S 5% Critical Value	0.08880746
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	143688.451
Adjusted Gamma UCL	144277.18

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.14057227
Lilliefors 5% Critical Value	0.0735783
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	426172.974
95% Chebyshev (MVUE) UCL	299779.414
97.5% Chebyshev (MVUE) UCL	392459.937
99% Chebyshev (MVUE) UCL	574512.877

95% Non-parametric UCLs	
CLT UCL	146880.568
Adj-CLT UCL (Adjusted for skewness)	159498.897
Mod-t UCL (Adjusted for skewness)	149178.95
Jackknife UCL	147210.746
Standard Bootstrap UCL	147364.03
Bootstrap-t UCL	169187.077
Hall's Bootstrap UCL	155284.979
Percentile Bootstrap UCL	151220.809
BCA Bootstrap UCL	162485.761
95% Chebyshev (Mean, Sd) UCL	231021.031
97.5% Chebyshev (Mean, Sd) UCL	289493.616
99% Chebyshev (Mean, Sd) UCL	404351.689

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Naphthalene

Raw Statistics	
Number of Valid Samples	158
Number of Unique Samples	74
Minimum	10
Maximum	37000000
Mean	766186.864
Median	76
Standard Deviation	4307590.13
Variance	1.86E+13
Coefficient of Variation	5.62211431
Skewness	6.57611487

Gamma Statistics	
k hat	0.10168495
k star (bias corrected)	0.10397363
Theta hat	7534909.07
Theta star	7369049.58
nu hat	32.1324447
nu star	32.8556683
Approx.Chi Square Value (.05)	20.7496377
Adjusted Level of Significance	0.04848101
Adjusted Chi Square Value	20.6611582

Log-transformed Statistics	
Minimum of log data	2.30258509
Maximum of log data	17.4264285
Mean of log data	5.57941793
Standard Deviation of log data	3.56820331
Variance of log data	12.7320748

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.47734366
Lilliefors 5% Critical Value	0.07048638
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	1333213.19

Gamma Distribution Test	
A-D Test Statistic	33.3152317
A-D 5% Critical Value	1.0653406
K-S Test Statistic	0.36726697
K-S 5% Critical Value	0.08688983
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	1213205.83
Adjusted Gamma UCL	1218401.28

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.17921976
Lilliefors 5% Critical Value	0.07048638
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	663827.137
95% Chebyshev (MVUE) UCL	428274.082
97.5% Chebyshev (MVUE) UCL	562624.942
99% Chebyshev (MVUE) UCL	826531.191

95% Non-parametric UCLs	
CLT UCL	1329867.46
Adj-CLT UCL (Adjusted for skewness)	1521437.28
Mod-t UCL (Adjusted for skewness)	1363094.21
Jackknife UCL	1333213.19
Standard Bootstrap UCL	1324292.2
Bootstrap-t UCL	1961367.47
Hall's Bootstrap UCL	1285995.47
Percentile Bootstrap UCL	1391431.15
BCA Bootstrap UCL	1541112.4
95% Chebyshev (Mean, Sd) UCL	2259953.07
97.5% Chebyshev (Mean, Sd) UCL	2906306.9
99% Chebyshev (Mean, Sd) UCL	4175943.85

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Acenaphthylene

Raw Statistics	
Number of Valid Samples	122
Number of Unique Samples	60
Minimum	15.5
Maximum	9700000
Mean	324904.373
Median	155
Standard Deviation	1499858.85
Variance	2.25E+12
Coefficient of Variation	4.61630859
Skewness	5.18736351

Gamma Statistics	
k hat	0.11573805
k star (bias corrected)	0.11835652
Theta hat	2807238.94
Theta star	2745132.93
nu hat	28.2400852
nu star	28.8789902
Approx.Chi Square Value (.05)	17.6119179
Adjusted Level of Significance	0.04803279
Adjusted Chi Square Value	17.5067164

Log-transformed Statistics	
Minimum of log data	2.74084002
Maximum of log data	16.0876364
Mean of log data	5.80608619
Standard Deviation of log data	3.44957604
Variance of log data	11.8995749

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.48097967
Lilliefors 5% Critical Value	0.08021467
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	549983.659

Gamma Distribution Test	
A-D Test Statistic	22.9007769
A-D 5% Critical Value	1.01813262
K-S Test Statistic	0.32749624
K-S 5% Critical Value	0.09629989
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	532759.138
Adjusted Gamma UCL	535960.6

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.18711268
Lilliefors 5% Critical Value	0.08021467
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	626885.922
95% Chebyshev (MVUE) UCL	351608.849
97.5% Chebyshev (MVUE) UCL	462937.508
99% Chebyshev (MVUE) UCL	681621.101

95% Non-parametric UCLs	
CLT UCL	548260.429
Adj-CLT UCL (Adjusted for skewness)	616402.865
Mod-t UCL (Adjusted for skewness)	560612.502
Jackknife UCL	549983.659
Standard Bootstrap UCL	549859.297
Bootstrap-t UCL	694332.939
Hall's Bootstrap UCL	533141.051
Percentile Bootstrap UCL	555338.271
BCA Bootstrap UCL	616758.586
95% Chebyshev (Mean, Sd) UCL	916802.921
97.5% Chebyshev (Mean, Sd) UCL	1172917.9
99% Chebyshev (Mean, Sd) UCL	1676006.17

Attachment F2
ProUCL Summary Tables
Construction Worker Receptor Exposed to Surface and Subsurface Soils (0-4 feet)
Vanadium

Raw Statistics	
Number of Valid Samples	90
Number of Unique Samples	38
Minimum	8.8
Maximum	110
Mean	28.6877778
Median	29
Standard Deviation	14.7523819
Variance	217.63277
Coefficient of Variation	0.51423927
Skewness	2.1911587

Gamma Statistics	
k hat	4.62136899
k star (bias corrected)	4.47473077
Theta hat	6.20763627
Theta star	6.41106231
nu hat	831.846419
nu star	805.451538
Approx.Chi Square Value (.05)	740.576449
Adjusted Level of Significance	0.04733333
Adjusted Chi Square Value	739.573844

Log-transformed Statistics	
Minimum of log data	2.17475172
Maximum of log data	4.70048037
Mean of log data	3.24439409
Standard Deviation of log data	0.47587483
Variance of log data	0.22645685

RECOMMENDATION

Assuming gamma distribution (0.05)

Use Approximate Gamma UCL

All units are in milligrams/kilogram (mg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.13100882
Lilliefors 5% Critical Value	0.0933926
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	31.2724912

Gamma Distribution Test	
A-D Test Statistic	0.91871705
A-D 5% Critical Value	0.75500854
K-S Test Statistic	0.09323588
K-S 5% Critical Value	0.09446272
Data follow approximate gamma distibution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	31.20085
Adjusted Gamma UCL	31.2431476

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.12412091
Lilliefors 5% Critical Value	0.0933926
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	31.4867895
95% Chebyshev (MVUE) UCL	35.2641285
97.5% Chebyshev (MVUE) UCL	38.1127502
99% Chebyshev (MVUE) UCL	43.7083159

95% Non-parametric UCLs	
CLT UCL	31.245587
Adj-CLT UCL (Adjusted for skewness)	31.6293595
Mod-t UCL (Adjusted for skewness)	31.332352
Jackknife UCL	31.2724912
Standard Bootstrap UCL	31.2362163
Bootstrap-t UCL	31.8040909
Hall's Bootstrap UCL	32.2314217
Percentile Bootstrap UCL	*31.2755556*
BCA Bootstrap UCL	31.7977778
95% Chebyshev (Mean, Sd) UCL	35.4660295
97.5% Chebyshev (Mean, Sd) UCL	38.3989844
99% Chebyshev (Mean, Sd) UCL	44.1602064

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface and Subsurface Soils (0-3 feet)
1,2,4-Trimethylbenzene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	14
Minimum	7.5
Maximum	15000
Mean	613.3375
Median	7.5
Standard Deviation	2706.6269
Variance	7325829
Coefficient of Variation	4.4129486
Skewness	4.7623151

Gamma Statistics	
k hat	0.2060006
k star (bias corrected)	0.2072172
Theta hat	2977.358
Theta star	2959.8772
nu hat	16.480047
nu star	16.577377
Approx.Chi Square Value (.05)	8.3697549
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	8.1506601

Log-transformed Statistics	
Minimum of log data	2.014903
Maximum of log data	9.6158055
Mean of log data	2.8629751
Standard Deviation of log data	1.7393527
Variance of log data	3.0253479

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.2484836
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	1334.3886

Gamma Distribution Test	
A-D Test Statistic	11.399515
A-D 5% Critical Value	0.9001207
K-S Test Statistic	0.4161673
K-S 5% Critical Value	0.1542412
Data do not follow gamma distribution at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	1214.7939
Adjusted Gamma UCL	1247.4483

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.5566592
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	200.1478
95% Chebyshev (MVUE) UCL	191.69961
97.5% Chebyshev (MVUE) UCL	243.10381
99% Chebyshev (MVUE) UCL	344.07742

95% Non-parametric UCLs	
CLT UCL	1317.2613
Adj-CLT UCL (Adjusted for skewness)	1661.585
Mod-t UCL (Adjusted for skewness)	1388.0961
Jackknife UCL	1334.3886
Standard Bootstrap UCL	1309.5471
Bootstrap-t UCL	52671.997
Hall's Bootstrap UCL	45047.972
Percentile Bootstrap UCL	1365.9375
BCA Bootstrap UCL	1739.2
95% Chebyshev (Mean, Sd) UCL	2478.7513
97.5% Chebyshev (Mean, Sd) UCL	3285.9174
99% Chebyshev (Mean, Sd) UCL	4871.4388

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface and Subsurface Soils (0-3 feet)
1,3,5-Trimethylbenzene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	5
Minimum	8
Maximum	5400
Mean	232.8
Median	8
Standard Deviation	971.549732
Variance	943908.882
Coefficient of Variation	4.17332359
Skewness	4.74240511

Gamma Statistics	
k hat	0.24544169
k star (bias corrected)	0.24370023
Theta hat	948.494111
Theta star	955.271966
nu hat	19.6353354
nu star	19.4960186
Approx.Chi Square Value (.05)	10.4790035
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	10.2305484

Log-transformed Statistics	
Minimum of log data	2.07944154
Maximum of log data	8.59415423
Mean of log data	2.547663
Standard Deviation of log data	1.52230197
Variance of log data	2.31740328

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.26142057
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	
95% UCL (Assuming Normal Distribution)	
Student's-t UCL	491.622884
Gamma Distribution Test	
A-D Test Statistic	13.7192926
A-D 5% Critical Value	0.88231308
K-S Test Statistic	0.55922326
K-S 5% Critical Value	0.15306584
Data do not follow gamma distribution	
at 5% significance level	
95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	433.120681
Adjusted Gamma UCL	443.639278
Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.35128409
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	
95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	84.9584884
95% Chebyshev (MVUE) UCL	91.0735805
97.5% Chebyshev (MVUE) UCL	113.862084
99% Chebyshev (MVUE) UCL	158.625685
95% Non-parametric UCLs	
CLT UCL	485.475014
Adj-CLT UCL (Adjusted for skewness)	608.554056
Mod-t UCL (Adjusted for skewness)	510.820727
Jackknife UCL	491.622884
Standard Bootstrap UCL	479.499899
Bootstrap-t UCL	3204.32156
Hall's Bootstrap UCL	3886.93638
Percentile Bootstrap UCL	505.7
BCA Bootstrap UCL	657.65
95% Chebyshev (Mean, Sd) UCL	902.394444
97.5% Chebyshev (Mean, Sd) UCL	1192.12849
99% Chebyshev (Mean, Sd) UCL	1761.25493

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface and Subsurface Soils (0-3 feet)
1-Methylnaphthalene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	14
Minimum	16
Maximum	230000
Mean	7205.6875
Median	31.5
Standard Deviation	37158.42846
Variance	1380748806
Coefficient of Variation	5.156819313
Skewness	5.8679174

Gamma Statistics	
k hat	0.160733875
k star (bias corrected)	0.165345501
Theta hat	44829.92468
Theta star	43579.58011
nu hat	12.85870998
nu star	13.22764007
Approx.Chi Square Value (.05)	6.045016867
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	5.862857342

Log-transformed Statistics	
Minimum of log data	2.772588722
Maximum of log data	12.34583459
Mean of log data	4.149189138
Standard Deviation of log data	2.029651026
Variance of log data	4.119483289

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.21120548
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	17104.7707

Gamma Distribution Test	
A-D Test Statistic	10.8857694
A-D 5% Critical Value	0.9262601
K-S Test Statistic	0.46537446
K-S 5% Critical Value	0.15586107
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	15767.4069
Adjusted Gamma UCL	16257.3017

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.6632246
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	1670.64634
95% Chebyshev (MVUE) UCL	1290.22717
97.5% Chebyshev (MVUE) UCL	1661.36575
99% Chebyshev (MVUE) UCL	2390.39563

95% Non-parametric UCLs	
CLT UCL	16869.6358
Adj-CLT UCL (Adjusted for skewness)	22694.1775
Mod-t UCL (Adjusted for skewness)	18013.2815
Jackknife UCL	17104.7707
Standard Bootstrap UCL	16608.9212
Bootstrap-t UCL	2118790.42
Hall's Bootstrap UCL	1480369.76
Percentile Bootstrap UCL	17378.5875
BCA Bootstrap UCL	25814.6375
95% Chebyshev (Mean, Sd) UCL	32815.367
97.5% Chebyshev (Mean, Sd) UCL	43896.6957
99% Chebyshev (Mean, Sd) UCL	65663.8203

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface and Subsurface Soils (0-3 feet)
Arsenic (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	37
Minimum	0.325
Maximum	13
Mean	2.970375
Median	2.1
Standard Deviation	2.99074414
Variance	8.9445505
Coefficient of Variation	1.00685743
Skewness	1.60788608

Gamma Statistics	
k hat	1.10376882
k star (bias corrected)	1.03765282
Theta hat	2.6911206
Theta star	2.86259039
nu hat	88.3015055
nu star	83.0122259
Approx.Chi Square Value (.05)	63.0107351
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	62.3577453

Log-transformed Statistics	
Minimum of log data	-1.1239301
Maximum of log data	2.56494936
Mean of log data	0.57159141
Standard Deviation of log data	1.09451021
Variance of log data	1.19795261

RECOMMENDATION

Data follow gamma distribution (0.05)

Use Approximate Gamma UCL

All units are in milligrams/kilogram (mg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.81332856
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	3.7671155

Gamma Distribution Test	
A-D Test Statistic	0.62439236
A-D 5% Critical Value	0.77605069
K-S Test Statistic	0.12623353
K-S 5% Critical Value	0.14336926
Data follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	3.91326081
Adjusted Gamma UCL	3.9542392

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.92921742
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	4.97678314
95% Chebyshev (MVUE) UCL	5.98186692
97.5% Chebyshev (MVUE) UCL	7.20700042
99% Chebyshev (MVUE) UCL	9.61353794

95% Non-parametric UCLs	
CLT UCL	3.74819037
Adj-CLT UCL (Adjusted for skewness)	3.87664654
Mod-t UCL (Adjusted for skewness)	3.78715207
Jackknife UCL	3.7671155
Standard Bootstrap UCL	3.73815095
Bootstrap-t UCL	3.94941982
Hall's Bootstrap UCL	3.90765963
Percentile Bootstrap UCL	3.78175
BCA Bootstrap UCL	3.88475
95% Chebyshev (Mean, Sd) UCL	5.03160315
97.5% Chebyshev (Mean, Sd) UCL	5.92349822
99% Chebyshev (Mean, Sd) UCL	7.67545337

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface and Subsurface Soils (0-3 feet)
Benzo(a)anthracene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	21
Minimum	17
Maximum	190000
Mean	5771.725
Median	83.5
Standard Deviation	30200.5775
Variance	912074884
Coefficient of Variation	5.23250459
Skewness	6.13139117

Gamma Statistics	
k hat	0.19046437
k star (bias corrected)	0.19284621
Theta hat	30303.4366
Theta star	29929.1596
nu hat	15.2371497
nu star	15.4276968
Approx.Chi Square Value (.05)	7.55877209
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	7.35191691

Log-transformed Statistics	
Minimum of log data	2.83321334
Maximum of log data	12.1547794
Mean of log data	4.76749781
Standard Deviation of log data	2.21636618
Variance of log data	4.91227906

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.20334941
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	
95% UCL (Assuming Normal Distribution)	
Student's-t UCL	13817.2221

Gamma Distribution Test	
A-D Test Statistic	7.23125163
A-D 5% Critical Value	0.90851991
K-S Test Statistic	0.32068251
K-S 5% Critical Value	0.15476996
Data do not follow gamma distribution	
at 5% significance level	
95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	11780.2762
Adjusted Gamma UCL	12111.7287

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.82720329
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	
95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	5675.75084
95% Chebyshev (MVUE) UCL	3662.7293
97.5% Chebyshev (MVUE) UCL	4753.84894
99% Chebyshev (MVUE) UCL	6897.14221

95% Non-parametric UCLs	
CLT UCL	13626.1159
Adj-CLT UCL (Adjusted for skewness)	18572.5781
Mod-t UCL (Adjusted for skewness)	14588.7703
Jackknife UCL	13817.2221
Standard Bootstrap UCL	13584.3592
Bootstrap-t UCL	291895.378
Hall's Bootstrap UCL	178375.321
Percentile Bootstrap UCL	15220.35
BCA Bootstrap UCL	20703
95% Chebyshev (Mean, Sd) UCL	26586.0367
97.5% Chebyshev (Mean, Sd) UCL	35592.4059
99% Chebyshev (Mean, Sd) UCL	53283.6744

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface and Subsurface Soils (0-3 feet)
Pyrene (0-3)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	24
Minimum	18
Maximum	670000
Mean	19099.1625
Median	175
Standard Deviation	1.06E+05
Variance	1.12E+10
Coefficient of Variation	5.55125485
Skewness	6.2416462

Gamma Statistics	
k hat	0.16719782
k star (bias corrected)	0.17132465
Theta hat	114230.932
Theta star	111479.362
nu hat	13.3758254
nu star	13.7059719
Approx.Chi Square Value (.05)	6.36942889
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	6.18174448

Log-transformed Statistics	
Minimum of log data	2.89037176
Maximum of log data	13.415033
Mean of log data	5.3336107
Standard Deviation of log data	2.52880785
Variance of log data	6.39486916

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.18923659
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	47344.263

Gamma Distribution Test	
A-D Test Statistic	6.80227362
A-D 5% Critical Value	0.92240306
K-S Test Statistic	0.32210455
K-S 5% Critical Value	0.15562384
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	41098.2819
Adjusted Gamma UCL	42346.0699

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.86358359
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	30971.7382
95% Chebyshev (MVUE) UCL	13701.8073
97.5% Chebyshev (MVUE) UCL	17973.3281
99% Chebyshev (MVUE) UCL	26363.9036

95% Non-parametric UCLs	
CLT UCL	46673.3517
Adj-CLT UCL (Adjusted for skewness)	64351.0232
Mod-t UCL (Adjusted for skewness)	50101.6225
Jackknife UCL	47344.263
Standard Bootstrap UCL	46978.1257
Bootstrap-t UCL	1459311.23
Hall's Bootstrap UCL	809303.404
Percentile Bootstrap UCL	52417.55
BCA Bootstrap UCL	75499.525
95% Chebyshev (Mean, Sd) UCL	92171.3813
97.5% Chebyshev (Mean, Sd) UCL	123789.789
99% Chebyshev (Mean, Sd) UCL	185898.028

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface and Subsurface Soils (0-3 feet)
Dibenz(a,h)anthracene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	10
Minimum	17
Maximum	8500
Mean	394.725
Median	34
Standard Deviation	1450.06194
Variance	2102679.64
Coefficient of Variation	3.67360047
Skewness	5.05090365

Gamma Statistics	
k hat	0.33476519
k star (bias corrected)	0.32632447
Theta hat	1179.11004
Theta star	1209.60895
nu hat	26.7812156
nu star	26.1059577
Approx.Chi Square Value (.05)	15.459147
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	15.1512206

Log-transformed Statistics	
Minimum of log data	2.83321334
Maximum of log data	9.04782144
Mean of log data	3.95488067
Standard Deviation of log data	1.5278663
Variance of log data	2.33437543

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.29347434
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	781.024539

Gamma Distribution Test	
A-D Test Statistic	7.0848659
A-D 5% Critical Value	0.84993431
K-S Test Statistic	0.33464504
K-S 5% Critical Value	0.15076556
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	666.574562
Adjusted Gamma UCL	680.121715

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.74994656
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	351.557859
95% Chebyshev (MVUE) UCL	375.960787
97.5% Chebyshev (MVUE) UCL	470.22173
99% Chebyshev (MVUE) UCL	655.3791

95% Non-parametric UCLs	
CLT UCL	771.848691
Adj-CLT UCL (Adjusted for skewness)	967.496984
Mod-t UCL (Adjusted for skewness)	811.541719
Jackknife UCL	781.024539
Standard Bootstrap UCL	761.302133
Bootstrap-t UCL	3817.9069
Hall's Bootstrap UCL	2497.25376
Percentile Bootstrap UCL	814.275
BCA Bootstrap UCL	1123.75
95% Chebyshev (Mean, Sd) UCL	1394.11123
97.5% Chebyshev (Mean, Sd) UCL	1826.54645
99% Chebyshev (Mean, Sd) UCL	2675.9817

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface and Subsurface Soils (0-3 feet)
Indeno(1,2,3-c,d)pyrene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	17
Minimum	15.5
Maximum	45000
Mean	1544.4875
Median	31
Standard Deviation	7169.99555
Variance	51408836.1
Coefficient of Variation	4.64231374
Skewness	6.01783026

Gamma Statistics	
k hat	0.23381413
k star (bias corrected)	0.23294474
Theta hat	6605.62085
Theta star	6630.27425
nu hat	18.7051305
nu star	18.6355791
Approx.Chi Square Value (.05)	9.8503372
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	9.61030395

Log-transformed Statistics	
Minimum of log data	2.74084002
Maximum of log data	10.7144178
Mean of log data	4.27176549
Standard Deviation of log data	1.9441683
Variance of log data	3.77979036

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.23214832
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	3454.58933

Gamma Distribution Test	
A-D Test Statistic	7.15727483
A-D 5% Critical Value	0.88756292
K-S Test Statistic	0.34493939
K-S 5% Critical Value	0.15341234
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	2921.97296
Adjusted Gamma UCL	2994.95407

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.78609693
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	1457.03825
95% Chebyshev (MVUE) UCL	1208.55308
97.5% Chebyshev (MVUE) UCL	1549.84016
99% Chebyshev (MVUE) UCL	2220.23253

95% Non-parametric UCLs	
CLT UCL	3409.21831
Adj-CLT UCL (Adjusted for skewness)	4561.81998
Mod-t UCL (Adjusted for skewness)	3634.3719
Jackknife UCL	3454.58933
Standard Bootstrap UCL	3391.97213
Bootstrap-t UCL	18244.9302
Hall's Bootstrap UCL	13934.6091
Percentile Bootstrap UCL	3727.1625
BCA Bootstrap UCL	5099
95% Chebyshev (Mean, Sd) UCL	6486.06591
97.5% Chebyshev (Mean, Sd) UCL	8624.29083
99% Chebyshev (Mean, Sd) UCL	12824.4197

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface and Subsurface Soils (0-3 feet)
Fluoranthene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	25
Minimum	18.5
Maximum	390000
Mean	11182.175
Median	110
Standard Deviation	61754.2489
Variance	3813587257
Coefficient of Variation	5.522561478
Skewness	6.227491779

Gamma Statistics	
k hat	0.176212171
k star (bias corrected)	0.179662925
Theta hat	63458.58485
Theta star	62239.74709
nu hat	14.09697367
nu star	14.37303398
Approx.Chi Square Value (.05)	6.82637106
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	6.631131136

Log-transformed Statistics	
Minimum of log data	2.917770732
Maximum of log data	12.87390202
Mean of log data	5.063552213
Standard Deviation of log data	2.33542629
Variance of log data	5.454215957

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.19030753
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	27633.6363

Gamma Distribution Test	
A-D Test Statistic	7.2713734
A-D 5% Critical Value	0.9170242
K-S Test Statistic	0.33085177
K-S 5% Critical Value	0.15529301
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	23544.2492
Adjusted Gamma UCL	24237.4608

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.84336088
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	11536.869
95% Chebyshev (MVUE) UCL	6522.68582
97.5% Chebyshev (MVUE) UCL	8503.12406
99% Chebyshev (MVUE) UCL	12393.3115

95% Non-parametric UCLs	
CLT UCL	27242.8615
Adj-CLT UCL (Adjusted for skewness)	37515.9358
Mod-t UCL (Adjusted for skewness)	29236.0282
Jackknife UCL	27633.6363
Standard Bootstrap UCL	26466.06
Bootstrap-t UCL	980684.875
Hall's Bootstrap UCL	532416.418
Percentile Bootstrap UCL	30577.875
BCA Bootstrap UCL	50014.65
95% Chebyshev (Mean, Sd) UCL	53743.3539
97.5% Chebyshev (Mean, Sd) UCL	72159.61
99% Chebyshev (Mean, Sd) UCL	108334.779

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface and Subsurface Soils (0-3 feet)
Benzo(a)pyrene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	20
Minimum	17
Maximum	220000
Mean	6972.45
Median	85
Standard Deviation	35002.38071
Variance	1225166655
Coefficient of Variation	5.020097772
Skewness	6.09152635

Gamma Statistics	
k hat	0.188487277
k star (bias corrected)	0.191017398
Theta hat	36991.62141
Theta star	36501.6489
nu hat	15.07898218
nu star	15.28139185
Approx.Chi Square Value (.05)	7.456482833
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	7.251215935

Log-transformed Statistics	
Minimum of log data	2.833213344
Maximum of log data	12.30138283
Mean of log data	4.9093192
Standard Deviation of log data	2.372489203
Variance of log data	5.628705016

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.21406814
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	16297.1575

Gamma Distribution Test	
A-D Test Statistic	6.57786724
A-D 5% Critical Value	0.90969964
K-S Test Statistic	0.32345987
K-S 5% Critical Value	0.15484252
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	14289.41
Adjusted Gamma UCL	14693.9136

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.83328497
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	11295.4279
95% Chebyshev (MVUE) UCL	6110.83974
97.5% Chebyshev (MVUE) UCL	7976.40727
99% Chebyshev (MVUE) UCL	11640.9534

95% Non-parametric UCLs	
CLT UCL	16075.666
Adj-CLT UCL (Adjusted for skewness)	21771.327
Mod-t UCL (Adjusted for skewness)	17185.5656
Jackknife UCL	16297.1575
Standard Bootstrap UCL	16129.8489
Bootstrap-t UCL	177252.329
Hall's Bootstrap UCL	117575.428
Percentile Bootstrap UCL	17827.025
BCA Bootstrap UCL	25992.225
95% Chebyshev (Mean, Sd) UCL	31096.1761
97.5% Chebyshev (Mean, Sd) UCL	41534.5317
99% Chebyshev (Mean, Sd) UCL	62038.6599

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface and Subsurface Soils (0-3 feet)
Benzene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	8
Minimum	7.5
Maximum	25000
Mean	891.7375
Median	7.5
Standard Deviation	4070.682
Variance	16570452
Coefficient of Variation	4.56488821
Skewness	5.65837552

Gamma Statistics	
k hat	0.18213946
k star (bias corrected)	0.18514566
Theta hat	4895.90512
Theta star	4816.41038
nu hat	14.5711566
nu star	14.8116532
Approx.Chi Square Value (.05)	7.12954248
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	6.92942447

Log-transformed Statistics	
Minimum of log data	2.01490302
Maximum of log data	10.1266311
Mean of log data	2.69394106
Standard Deviation of log data	1.89640789
Variance of log data	3.59636288

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.24375089
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	1976.17571

Gamma Distribution Test	
A-D Test Statistic	13.0322635
A-D 5% Critical Value	0.91348739
K-S Test Statistic	0.47631005
K-S 5% Critical Value	0.15507548
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	1852.58824
Adjusted Gamma UCL	1906.08998

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.41304453
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	261.448187
95% Chebyshev (MVUE) UCL	225.02581
97.5% Chebyshev (MVUE) UCL	287.872169
99% Chebyshev (MVUE) UCL	411.321671

95% Non-parametric UCLs	
CLT UCL	1950.41684
Adj-CLT UCL (Adjusted for skewness)	2565.70615
Mod-t UCL (Adjusted for skewness)	2072.14841
Jackknife UCL	1976.17571
Standard Bootstrap UCL	1930.08035
Bootstrap-t UCL	4712.02531
Hall's Bootstrap UCL	4979.98777
Percentile Bootstrap UCL	2139.8875
BCA Bootstrap UCL	3025.825
95% Chebyshev (Mean, Sd) UCL	3697.26146
97.5% Chebyshev (Mean, Sd) UCL	4911.21392
99% Chebyshev (Mean, Sd) UCL	7295.78845

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface and Subsurface Soils (0-3 feet)
Napthalene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	13
Minimum	15.5
Maximum	91000
Mean	2815.7375
Median	30.5
Standard Deviation	14579.2552
Variance	212554682
Coefficient of Variation	5.17777499
Skewness	5.99655251

Gamma Statistics	
k hat	0.19003325
k star (bias corrected)	0.19244742
Theta hat	14817.0781
Theta star	14631.204
nu hat	15.20266
nu star	15.3957938
Approx.Chi Square Value (.05)	7.53644883
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	7.32993938

Log-transformed Statistics	
Minimum of log data	2.74084002
Maximum of log data	11.4186148
Mean of log data	4.03955324
Standard Deviation of log data	1.89585897
Variance of log data	3.59428124

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.20809109
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	6699.68162

Gamma Distribution Test	
A-D Test Statistic	9.8423071
A-D 5% Critical Value	0.90877716
K-S Test Statistic	0.41924945
K-S 5% Critical Value	0.15478578
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	5752.11416
Adjusted Gamma UCL	5914.17089

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.70231267
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	1002.50625
95% Chebyshev (MVUE) UCL	863.202966
97.5% Chebyshev (MVUE) UCL	1104.25124
99% Chebyshev (MVUE) UCL	1577.7439

95% Non-parametric UCLs	
CLT UCL	6607.42555
Adj-CLT UCL (Adjusted for skewness)	8942.80472
Mod-t UCL (Adjusted for skewness)	7063.95358
Jackknife UCL	6699.68162
Standard Bootstrap UCL	6460.36684
Bootstrap-t UCL	249593.143
Hall's Bootstrap UCL	168401.293
Percentile Bootstrap UCL	7353.5375
BCA Bootstrap UCL	9693.875
95% Chebyshev (Mean, Sd) UCL	12863.7957
97.5% Chebyshev (Mean, Sd) UCL	17211.5986
99% Chebyshev (Mean, Sd) UCL	25752.0153

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface and Subsurface Soils (0-3 feet)
Benzo(k)fluoranthene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	18
Minimum	19
Maximum	56000
Mean	1979.1
Median	38
Standard Deviation	9075.52846
Variance	82365216.8
Coefficient of Variation	4.58568463
Skewness	5.76349365

Gamma Statistics	
k hat	0.23312662
k star (bias corrected)	0.23230879
Theta hat	8489.37818
Theta star	8519.26454
nu hat	18.6501292
nu star	18.5847029
Approx.Chi Square Value (.05)	9.81333454
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	9.57380506

Log-transformed Statistics	
Minimum of log data	2.94443898
Maximum of log data	10.933107
Mean of log data	4.50920872
Standard Deviation of log data	1.94712275
Variance of log data	3.79128701

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.23682221
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	4396.83979

Gamma Distribution Test	
A-D Test Statistic	7.01815248
A-D 5% Critical Value	0.88787333
K-S Test Statistic	0.29027076
K-S 5% Critical Value	0.15343283
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	3748.06191
Adjusted Gamma UCL	3841.83563

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.79864498
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	1863.82421
95% Chebyshev (MVUE) UCL	1542.32655
97.5% Chebyshev (MVUE) UCL	1978.15923
99% Chebyshev (MVUE) UCL	2834.26814

95% Non-parametric UCLs	
CLT UCL	4339.41075
Adj-CLT UCL (Adjusted for skewness)	5736.67377
Mod-t UCL (Adjusted for skewness)	4614.78459
Jackknife UCL	4396.83979
Standard Bootstrap UCL	4225.49691
Bootstrap-t UCL	46376.9584
Hall's Bootstrap UCL	29436.7261
Percentile Bootstrap UCL	4666.7
BCA Bootstrap UCL	6536.625
95% Chebyshev (Mean, Sd) UCL	8233.97634
97.5% Chebyshev (Mean, Sd) UCL	10940.4663
99% Chebyshev (Mean, Sd) UCL	16256.8418

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface and Subsurface Soils (0-3 feet)
Lead (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	34
Minimum	1.95
Maximum	4000
Mean	176.19375
Median	28.5
Standard Deviation	632.19336
Variance	399668.44
Coefficient of Variation	3.5880578
Skewness	5.966169

Gamma Statistics	
k hat	0.3313524
k star (bias corrected)	0.3231677
Theta hat	531.74122
Theta star	545.20846
nu hat	26.508195
nu star	25.853414
Approx.Chi Square Value (.05)	15.264718
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	14.958919

Log-transformed Statistics	
Minimum of log data	0.6678294
Maximum of log data	8.2940496
Mean of log data	3.1240161
Standard Deviation of log data	2.0258913
Variance of log data	4.1042356

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in milligrams/kilogram (mg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.2812852
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	
95% UCL (Assuming Normal Distribution)	
Student's-t UCL	344.61139

Gamma Distribution Test	
A-D Test Statistic	2.5061583
A-D 5% Critical Value	0.8506947
K-S Test Statistic	0.1744151
K-S 5% Critical Value	0.1508318
Data do not follow gamma distribution	
at 5% significance level	
95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	298.41428
Adjusted Gamma UCL	304.51465

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.9033405
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	
95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	592.3865
95% Chebyshev (MVUE) UCL	458.99696
97.5% Chebyshev (MVUE) UCL	590.92655
99% Chebyshev (MVUE) UCL	850.07667

95% Non-parametric UCLs	
CLT UCL	340.61093
Adj-CLT UCL (Adjusted for skewness)	441.36577
Mod-t UCL (Adjusted for skewness)	360.3271
Jackknife UCL	344.61139
Standard Bootstrap UCL	340.58096
Bootstrap-t UCL	964.21134
Hall's Bootstrap UCL	880.1414
Percentile Bootstrap UCL	372.825
BCA Bootstrap UCL	473.495
95% Chebyshev (Mean, Sd) UCL	611.90295
97.5% Chebyshev (Mean, Sd) UCL	800.43467
99% Chebyshev (Mean, Sd) UCL	1170.7687

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface and Subsurface Soils (0-3 feet)
Benzo(b)fluoranthene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	22
Minimum	19
Maximum	180000
Mean	6121.8875
Median	107.5
Standard Deviation	28821.7591
Variance	830693797
Coefficient of Variation	4.70798575
Skewness	5.95156846

Gamma Statistics	
k hat	0.2037546
k star (bias corrected)	0.20513967
Theta hat	30045.3959
Theta star	29842.534
nu hat	16.3003677
nu star	16.4111734
Approx.Chi Square Value (.05)	8.2517554
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	8.03440445

Log-transformed Statistics	
Minimum of log data	2.94443898
Maximum of log data	12.1007121
Mean of log data	5.11830816
Standard Deviation of log data	2.35271263
Variance of log data	5.53525673

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in micrograms/kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.23055716
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	13800.0645

Gamma Distribution Test	
A-D Test Statistic	5.79391633
A-D 5% Critical Value	0.9011348
K-S Test Statistic	0.2930231
K-S 5% Critical Value	0.15430811
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	12175.2709
Adjusted Gamma UCL	12504.6428

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.85262189
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	12963.1721
95% Chebyshev (MVUE) UCL	7181.21229
97.5% Chebyshev (MVUE) UCL	9367.21935
99% Chebyshev (MVUE) UCL	13661.2069

95% Non-parametric UCLs	
CLT UCL	13617.6833
Adj-CLT UCL (Adjusted for skewness)	18199.8653
Mod-t UCL (Adjusted for skewness)	14514.7923
Jackknife UCL	13800.0645
Standard Bootstrap UCL	13467.0236
Bootstrap-t UCL	114615.385
Hall's Bootstrap UCL	77530.7422
Percentile Bootstrap UCL	14544.8125
BCA Bootstrap UCL	20389.975
95% Chebyshev (Mean, Sd) UCL	25985.9141
97.5% Chebyshev (Mean, Sd) UCL	34581.0943
99% Cheb	51464.6614

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface Soils (0-1 foot)
Lead (0-1)

Raw Statistics	
Number of Valid Samples	12
Number of Unique Samples	12
Minimum	2.8
Maximum	440
Mean	83.4
Median	37
Standard Deviation	119.61344
Variance	14307.375
Coefficient of Variation	1.4342139
Skewness	2.811318

Gamma Statistics	
k hat	0.8915822
k star (bias corrected)	0.7242422
Theta hat	93.541575
Theta star	115.15485
nu hat	21.397972
nu star	17.381812
Approx.Chi Square Value (.05)	8.9442971
Adjusted Level of Significance	0.02896
Adjusted Chi Square Value	8.0359767

Log-transformed Statistics	
Minimum of log data	1.0296194
Maximum of log data	6.0867747
Mean of log data	3.767181
Standard Deviation of log data	1.2340628
Variance of log data	1.5229111

RECOMMENDATION

Data follow gamma distribution (0.05)

Use Approximate Gamma UCL

All units are in milligrams/kilogram (mg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.611513
Shapiro-Wilk 5% Critical Value	0.859
Data not normal at 5% significance level	
95% UCL (Assuming Normal Distribution)	
Student's-t UCL	145.41087

Gamma Distribution Test	
A-D Test Statistic	0.6366391
A-D 5% Critical Value	0.7605823
K-S Test Statistic	0.2294362
K-S 5% Critical Value	0.2534168
Data follow gamma distribution	
at 5% significance level	
95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	162.07457
Adjusted Gamma UCL	180.39415

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.9332538
Shapiro-Wilk 5% Critical Value	0.859
Data are lognormal at 5% significance level	
95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	323.07554
95% Chebyshev (MVUE) UCL	225.83094
97.5% Chebyshev (MVUE) UCL	287.16819
99% Chebyshev (MVUE) UCL	407.65335

95% Non-parametric UCLs	
CLT UCL	140.19585
Adj-CLT UCL (Adjusted for skewness)	170.13842
Mod-t UCL (Adjusted for skewness)	150.0813
Jackknife UCL	145.41087
Standard Bootstrap UCL	138.48303
Bootstrap-t UCL	269.8494
Hall's Bootstrap UCL	350.05716
Percentile Bootstrap UCL	137.15
BCA Bootstrap UCL	180.16667
95% Chebyshev (Mean, Sd) UCL	233.91028
97.5% Chebyshev (Mean, Sd) UCL	299.03619
99% Chebyshev (Mean, Sd) UCL	426.96344

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface Soils (0-1 foot)
Benzo(a)pyrene (0-1)

Raw Statistics	
Number of Valid Samples	12
Number of Unique Samples	7
Minimum	17
Maximum	390
Mean	138
Median	140
Standard Deviation	96.432737
Variance	9299.2727
Coefficient of Variation	0.6987879
Skewness	1.5566246

Gamma Statistics	
k hat	2.1074941
k star (bias corrected)	1.6361761
Theta hat	65.480611
Theta star	84.342999
nu hat	50.579858
nu star	39.268227
Approx.Chi Square Value (.05)	25.911153
Adjusted Level of Significance	0.02896
Adjusted Chi Square Value	24.265208

Log-transformed Statistics	
Minimum of log data	2.8332133
Maximum of log data	5.9661467
Mean of log data	4.6716278
Standard Deviation of log data	0.8291598
Variance of log data	0.687506

RECOMMENDATION

Data follow gamma distribution (0.05)

Use Approximate Gamma UCL

All units are in micrograms/kilogram (mg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.8330616
Shapiro-Wilk 5% Critical Value	0.859
Data not normal at 5% significance level	
95% UCL (Assuming Normal Distribution)	
Student's-t UCL	187.99336

Gamma Distribution Test	
A-D Test Statistic	0.5371884
A-D 5% Critical Value	0.7412502
K-S Test Statistic	0.2107995
K-S 5% Critical Value	0.2484275
Data follow gamma distribution	
at 5% significance level	
95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	209.13833
Adjusted Gamma UCL	223.32449

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.890894
Shapiro-Wilk 5% Critical Value	0.859
Data are lognormal at 5% significance level	
95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	289.98261
95% Chebyshev (MVUE) UCL	305.32254
97.5% Chebyshev (MVUE) UCL	374.52066
99% Chebyshev (MVUE) UCL	510.44696

95% Non-parametric UCLs	
CLT UCL	183.789
Adj-CLT UCL (Adjusted for skewness)	197.15518
Mod-t UCL (Adjusted for skewness)	190.07821
Jackknife UCL	187.99336
Standard Bootstrap UCL	182.12898
Bootstrap-t UCL	207.05152
Hall's Bootstrap UCL	410.54355
Percentile Bootstrap UCL	184.5
BCA Bootstrap UCL	197.08333
95% Chebyshev (Mean, Sd) UCL	259.34187
97.5% Chebyshev (Mean, Sd) UCL	311.84659
99% Chebyshev (Mean, Sd) UCL	414.98195

Attachment F2
ProUCL Summary Tables
Residential Receptor Exposed to Surface Soils (0-1 foot)
Arsenic (0-1)

Raw Statistics	
Number of Valid Samples	12
Number of Unique Samples	12
Minimum	0.55
Maximum	8.5
Mean	2.7541667
Median	2.35
Standard Deviation	2.0074247
Variance	4.0297538
Coefficient of Variation	0.7288683
Skewness	2.3513053

Gamma Statistics	
k hat	2.7451198
k star (bias corrected)	2.1143954
Theta hat	1.0032956
Theta star	1.3025788
nu hat	65.882874
nu star	50.745489
Approx.Chi Square Value (.05)	35.384255
Adjusted Level of Significance	0.02896
Adjusted Chi Square Value	33.435119

Log-transformed Statistics	
Minimum of log data	-0.597837
Maximum of log data	2.1400662
Mean of log data	0.8200535
Standard Deviation of log data	0.6519918
Variance of log data	0.4250933

RECOMMENDATION

Data follow gamma distribution (0.05)

Use Approximate Gamma UCL

All units are in milligrams/kilogram (mg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.7516129
Shapiro-Wilk 5% Critical Value	0.859
Data not normal at 5% significance level	
95% UCL (Assuming Normal Distribution)	
Student's-t UCL	3.7948703

Gamma Distribution Test	
A-D Test Statistic	0.4334293
A-D 5% Critical Value	0.7396497
K-S Test Statistic	0.1704712
K-S 5% Critical Value	0.2477006
Data follow gamma distribution	
at 5% significance level	
95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	3.9498227
Adjusted Gamma UCL	4.1800819

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.9454435
Shapiro-Wilk 5% Critical Value	0.859
Data are lognormal at 5% significance level	
95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	4.4519252
95% Chebyshev (MVUE) UCL	5.0928155
97.5% Chebyshev (MVUE) UCL	6.1060015
99% Chebyshev (MVUE) UCL	8.0962093

95% Non-parametric UCLs	
CLT UCL	3.7073488
Adj-CLT UCL (Adjusted for skewness)	4.1276372
Mod-t UCL (Adjusted for skewness)	3.8604268
Jackknife UCL	3.7948703
Standard Bootstrap UCL	3.6681243
Bootstrap-t UCL	4.6753064
Hall's Bootstrap UCL	8.0444328
Percentile Bootstrap UCL	3.7541667
BCA Bootstrap UCL	4.2666667
95% Chebyshev (Mean, Sd) UCL	5.2801206
97.5% Chebyshev (Mean, Sd) UCL	6.3731029
99% Chebyshev (Mean, Sd) UCL	8.520055

ATTACHMENT F3

Risk Calculations

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Attachment F

Table 1a
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Incidental Ingestion of Soil Pathway (0-1 feet) – Carcinogenic Effects

$$\text{Ing-Risk} = \frac{(\text{Csoil} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{SIRadj} \times \text{FI})}{\text{ATc}}$$

Equation Units	Ing - Risk unitless	= (	Csoil mg/kg	×	SFo kg-day/mg	×	CF kg/mg	×	EF days/year	×	SIRadj mg-yr/kg-day	×	FI unitless	) + (	ATc days	)
Arsenic	3.50E-06	= (	3.67E+00	×	1.50E+00	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Lead	NA	= (	8.34E+01	×	a	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Benzo(a)pyrene	8.46E-07	= (	1.82E-01	×	7.30E+00	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – Soil Concentration
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
SIRadj – Age-adjusted Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment F

Table 1b
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Incidental Ingestion of Soil Pathway (0-1 feet) – Noncarcinogenic Effects

$$\text{Ing - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{EDc} \times \text{SIRc} \times \text{FI})}{(\text{BWc} \times \text{ATn} \times \text{RfDo})}$$

Equation		Ing - HQ	= (	Csoil	×	CF	×	EF	×	EDc	×	SIRc	×	FI	) + (	BWc	×	ATn	×	RfDo [b]	)
Units		unitless		mg/kg		kg/mg		days/year		years		mg/day		unitless		kg		days		mg/kg-day	
Arsenic		7.82E-02	= (	3.67E+00	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	3.0E-04	)
Lead		NA	= (	8.34E+01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	a	)
Benzo(a)pyrene		NA	= (	1.82E-01	×	1E-06	×	350	×	6	×	100	×	1	) + (	15	×	2,190	×	NV	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
EDc – Exposure Duration, child
SIRc – Soil Ingestion Rate, child
FI – Fraction Ingested from Contaminated Source
BWc – Body Weight, child
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment F

Table 2a
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Dermal Contact with Soil Pathway (0-1 feet) – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{EV} \times \text{SCRadj} \times \text{ABSd})}{\text{ATc}}$$

Equation / Units	Derm - Risk unitless	= (	Csoil mg/kg	×	SFabs kg-day/mg	×	CF kg/mg	×	EF days/year	×	EV events/day	×	SCRadj mg-yr/kg-event	×	ABSd unitless	) ÷ (	ATc days	)
Arsenic	1.24E-07	= (	3.67E+00	×	1.58E+00	×	1E-06	×	350	×	1	×	52	×	3.00E-02	) ÷ (	25,550	)
Lead	NA	= (	8.34E+01	×	a	×	1E-06	×	350	×	1	×	52	×	NA	) ÷ (	25,550	)
Benzo(a)pyrene	1.23E-07	= (	1.82E-01	×	7.30E+00	×	1E-06	×	350	×	1	×	52	×	1.30E-01	) ÷ (	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csoil – Soil Concentration
SFabs – Absorbed slope factor (SFo ÷ ABSgi)
CF – Unit Conversion Factor
EF – Exposure Frequency
EV – Event Frequency
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.
SCRadj – Age-adjusted Soil Contact Rate
ABSd – Dermal Soil Absorption Factor
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment F

Table 2b
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Dermal Contact with Soil Pathway (0-1 feet) – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{EDc} \times \text{EV} \times \text{SAc} \times \text{AFc} \times \text{ABSd})}{(\text{BWc} \times \text{ATn} \times \text{RfDabs})}$$

Equation / Units	Derm - HQ unitless	=	Csoil mg/kg	×	CF kg/mg	×	EF days/year	×	EDc years	×	EV events/day	×	SAc cm^2	×	AFc mg/cm^2-event	×	ABSd unitless	÷	BWc kg	×	ATn days	×	RfDabs [b] mg/kg-day
Arsenic	2.76E-03	=	3.67E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	3.00E-02	÷	15	×	2,190	×	2.85E-04
Lead	NA	=	8.34E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	NA	÷	15	×	2,190	×	a
Benzo(a)pyrene	NA	=	1.82E-01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	÷	15	×	2,190	×	NV

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
EDc – Exposure Duration, child
EV – Event Frequency
SAc – Skin Surface Area, child
AFc – Soil-to-skin Adherence Factor, child
ABSd – Dermal Soil Absorption Factor
BWc – Body Weight, child
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo × ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment F

Table 3a
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Inhalation of Soil-derived Chemicals Pathway (0-1 feet) – Carcinogenic Effects

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{EF} \times \text{SInhRadj} \times [(1/\text{VF}) + (1/\text{PEF})])}{\text{ATc}}$$

Equation	Inh - Risk	= (	Csoil	×	SFi	×	EF	×	SInhRadj	× [1 /	VF_{adult}	+ 1 /	PEF	]) ÷ (	ATc	)
Units	unitless		mg/kg		kg-day/mg		days/year		m3-yr/kg-day		m^3/kg		m^3/kg		days	
Arsenic	5.27E-10	= (	3.67E+00	×	1.51E+01	×	350	×	4.58	× [1 /	NA	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Lead	NA	= (	8.34E+01	×	a	×	350	×	4.58	× [1 /	NA	+ 1 /	6.58E+09	]) ÷ (	25,550	)
Benzo(a)pyrene	5.35E-12	= (	1.82E-01	×	3.08E+00	×	350	×	4.58	× [1 /	NC	+ 1 /	6.58E+09	]) ÷ (	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Soil Concentration
SFi – Inhalation Slope Factor
EF – Exposure frequency
SInhRadj – Age-adjusted Soil Inhalation Rate
VF – Volatilization Factor
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.
PEF – Particulate Emission Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated

Attachment F

Table 3b
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Inhalation of Soil-derived Chemicals Pathway (0-1 feet) – Noncarcinogenic Effects

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{InhRc} \times \text{EF} \times \text{EDc} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BWc} \times \text{ATn} \times \text{RfDi})}$$

Equation	Inh - HQ	=	(	Csoil	×	InhRc	×	EF	×	EDc	×	[	1	/	VF_{child}	+	1	/	PEF	]	÷	(	BWc	×	ATn	×	*RfDi (b)*	)
Units	**unitless**			**mg/kg**		**m³/day**		**days/year**		**year**					**m³/kg**				**m³/kg**				**kg**		**days**		**mg/kg-day**	
Arsenic	NA	=	(	3.67E+00	×	7.2	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Lead	NA	=	(	8.34E+01	×	7.2	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	a	)
Benzo(a)pyrene	NA	=	(	1.82E-01	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Csoil – Soil Concentration
InhRc – Inhalation Rate, child
EF – Exposure frequency
EDc – Exposure duration, child
VF – Volatilization Factor
PEF – Particulate Emission Factor
BWc – Body Weight, child
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – *Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.*

Attachment F

Table 3c
Residential Scenario: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} \times \frac{(3.14 \times D_A \times T)^{1/2}}{2 \times \rho_b \times D_A} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} $(g/m^2\text{-}s)/(kg/m^3)$	π	D_A (cm^2/s)	T_{adult} (s)	T_{child} (s)	2	ρb (g/cm^3)	10^{-4} (m^2/cm^2)	VF_{adult} (m^3/kg)	VF_{child} (m^3/kg)
Benzo(a)pyrene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC	NC

Notes:

Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

VF_{adult} – Volatilization Factor (m^3/kg) for adults (calculated)

VF_{child} – Volatilization Factor (m^3/kg) for children (calculated)

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source $(g/m^2\text{-}s)/(kg/m^3)$(Value used is for Minneapolis, MN.)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T_{adult} – Exposure interval (s) for adults

T_{Child} – Exposure interval (s) for children

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated; PAHs are not considered volatile chemicals

Attachment F

Table 3d
Residential Scenario: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)},$$

Chemical Units	VOC?	θa (Lair /Lsoil)	Di (cm^2/s)	H' unitless	θw (Lwater /Lsoil)	Dw (cm^2/s)	η (Lpore /Lsoil)	ρb (g/cm^3)	ρs (g/cm^3)	Kd (cm^3/g)	D_A (cm^2/s)
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC

Notes:

D_A – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's Law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User'S Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density

Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm^3 /g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)
VOC? – Volatile organic compounds; If no, an apparent diffusivity was not calculated.
NV – no value available
NC – not calculated

Attachment F

Table 3e
Residential Scenario: Particulation Emission Factor Calculations

$$PEF = Q/C \times \frac{3600\ s/h}{0.036 \times (1\ \ V) \times (U_m/U_t)^3 \times F(x)}$$

PEF – Particulate emission factor
Q/C – Inverse of mean concentration at center of a 0.5-acre-square source (see calculation presented below)
V – Fraction of vegetative cover. It is assumed that 10% of the surface cover at residential properties are bare (garden beds)
Um – Mean annual windspeed
Ut – Equivalent threshold value of windspeed at 7 m
F(x) – Function dependent on UmUt derived using Cowherd

Equation	PEF	=	Q/C	× [	3600	÷ (	0.036	×	(	1	-	V	)	× (	Um	/	Ut	) ³	×	F(x)	)
Units	m^3/kg		g/m^2-s per kg/m^3		s/h		unitless					unitless			m/s		m/s			unitless	
All Chemicals	6.58E+09	=	90.8	× [	3600	÷	0.036	×	(	1	-	0.9	)	× [	4.69	/	11.32	) ³	×	0.194	)

Default values are as presented in Soil Screening Technical Background Document (USEPA 1996).

Attachment F

Table 4a
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Incidental Ingestion of Soil Pathway (0-3 feet) – Carcinogenic Effects

$$\text{Ing-Risk} = \frac{(\text{Csoil} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{SIRadj} \times \text{FI})}{\text{ATc}}$$

Equation Units	Ing - Risk unitless	= (	Csoil mg/kg	×	SFo kg-day/mg	×	CF kg/mg	×	EF days/year	×	SIRadj mg-yr/kg-day	×	FI unitless	) + (	ATc days	)
Arsenic	8.78E-06	= (	3.74E+00	×	1.50E+00	×	1E-06	×	350	×	114.28	×	1	) + (	25,550	)
Lead	NA	= (	1.76E+02	×	a	×	1E-06	×	350	×	114.28	×	1	) + (	25,550	)
1-Methylnaphthalene	NA	= (	1.66E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) + (	25,550	)
Benzo(a)anthracene	1.55E-05	= (	1.36E+01	×	7.30E-01	×	1E-06	×	350	×	114.28	×	1	) + (	25,550	)
Benzo(a)pyrene	1.84E-04	= (	1.61E+01	×	7.30E+00	×	1E-06	×	350	×	114.28	×	1	) + (	25,550	)
Benzo(b)fluoranthene	1.54E-05	= (	1.35E+01	×	7.30E-01	×	1E-06	×	350	×	114.28	×	1	) + (	25,550	)
Benzo(k)fluoranthene	4.83E-07	= (	4.23E+00	×	7.30E-02	×	1E-06	×	350	×	114.28	×	1	) + (	25,550	)
Dibenzo(a,h)anthracene	8.70E-06	= (	7.61E-01	×	7.30E+00	×	1E-06	×	350	×	114.28	×	1	) + (	25,550	)
Fluoranthene	NA	= (	2.65E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) + (	25,550	)
Indeno(1,2,3-cd)pyrene	3.88E-06	= (	3.39E+00	×	7.30E-01	×	1E-06	×	350	×	114.28	×	1	) + (	25,550	)
Naphthalene	NA	= (	6.46E+00	×	NV	×	1E-06	×	350	×	114.28	×	1	) + (	25,550	)
Pyrene	NA	= (	4.70E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) + (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	1.31E+00	×	NV	×	1E-06	×	350	×	114.28	×	1	) + (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	4.79E-01	×	NV	×	1E-06	×	350	×	114.28	×	1	) + (	25,550	)
Benzene	1.66E-07	= (	1.93E+00	×	5.50E-02	×	1E-06	×	350	×	114.28	×	1	) + (	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – Soil Concentration
SFo – *Oral Slope Factor*
CF – Unit Conversion Factor
EF – Exposure Frequency
SIRadj – Age-adjusted Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
ATc – *Averaging Time for Carcinogens*
NV – No toxicity value available for this pathway.
NA – Not Applicable
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. *Toxicity criteria for lead have not been derived by USEPA.*

Attachment F

Table 4b
Risk Calculations: Reasonable Maximum Exposure
Residential Child: Incidental Ingestion of Soil Pathway (0-3 feet) – Noncarcinogenic Effects

$$Ing\text{-}HQ = \frac{(Csoil \times CF \times EF \times EDc \times SIRc \times FI)}{(BWc \times ATn \times RfDo)}$$

Equation / Units	Ing - HQ unitless	= (	Csoil mg/kg	×	CF kg/mg	×	EF days/year	×	EDc years	×	SIRc mg/day	×	FI unitless	) + (	BWc kg	×	ATn days	×	RfDo [b] mg/kg-day	)
Arsenic	1.59E-01	= (	3.74E+00	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	3.0E-04	)
Lead	NA	= (	1.76E+02	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	a	)
1-Methylnaphthalene	3.03E-03	= (	1.66E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	7.0E-02	)
Benzo(a)anthracene	NA	= (	1.36E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	= (	1.61E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.35E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	= (	4.23E+00	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	7.61E-01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	NV	)
Fluoranthene	8.46E-04	= (	2.65E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	4.0E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (	3.39E+00	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	NV	)
Naphthalene	4.13E-03	= (	6.46E+00	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	2.0E-02	)
Pyrene	2.00E-03	= (	4.70E+01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	3.0E-01	)
1,2,4-Trimethylbenzene	3.35E-04	= (	1.31E+00	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	5.0E-02	)
1,3,5-Trimethylbenzene	1.23E-05	= (	4.79E-01	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	5.0E-01	)
Benzene	6.17E-03	= (	1.93E+00	×	1E-06	×	350	×	6	×	200	×	1	) + (	15	×	2,190	×	4.0E-03	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
EDc – Exposure Duration, child
SIRc – Soil Ingestion Rate, child
FI – Fraction Ingested from Contaminated Source
BWc – Body Weight, child
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment F

Table 5a
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Dermal Contact with Soil Pathway (0-3 feet) – Carcinogenic Effects

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{EV} \times \text{SCRadj} \times \text{ABSd})}{\text{ATc}}$$

Equation / Units	Derm - Risk unitless	= (	Csoil mg/kg	×	SFabs kg-day/mg	×	CF kg/mg	×	EF days/year	×	EV events/day	×	SCRadj mg-yr/kg-event	×	ABSd unitless	) ÷ (	ATc days	)
Arsenic	8.74E-07	= (	3.74E+00	×	1.58E+00	×	1E-06	×	350	×	1	×	360	×	3.00E-02	) ÷ (	25,550	)
Lead	NA	= (	1.76E+02	×	a	×	1E-06	×	350	×	1	×	360	×	NA	) ÷ (	25,550	)
1-Methylnaphthalene	NA	= (	1.66E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Benzo(a)anthracene	6.36E-06	= (	1.36E+01	×	7.30E-01	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Benzo(a)pyrene	7.55E-05	= (	1.61E+01	×	7.30E+00	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Benzo(b)fluoranthene	6.31E-06	= (	1.35E+01	×	7.30E-01	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Benzo(k)fluoranthene	1.98E-07	= (	4.23E+00	×	7.30E-02	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Dibenzo(a,h)anthracene	3.57E-06	= (	7.61E-01	×	7.30E+00	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Fluoranthene	NA	= (	2.65E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Indeno(1,2,3-cd)pyrene	1.59E-06	= (	3.39E+00	×	7.30E-01	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Naphthalene	NA	= (	6.46E+00	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Pyrene	NA	= (	4.70E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	1.31E+00	×	NV	×	1E-06	×	350	×	1	×	360	×	NA	) ÷ (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	4.79E-01	×	NV	×	1E-06	×	350	×	1	×	360	×	NA	) ÷ (	25,550	)
Benzene	NA	= (	1.93E+00	×	5.50E-02	×	1E-06	×	350	×	1	×	360	×	NA	) ÷ (	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csoil – Soil Concentration
SFabs – Absorbed slope factor (SFo + ABSgi)
CF – Unit Conversion Factor
EF – Exposure Frequency
EV – Event Frequency
SCRadj – Age-adjusted Soil Contact Rate
ABSd – Dermal Soil Absorption Factor
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment F

Table 5b
Risk Calculations: Reasonable Maximum Exposure
Residential Child: Dermal Contact with Soil Pathway (0-3 feet) – Noncarcinogenic Effects

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{EDc} \times \text{EV} \times \text{SAc} \times \text{AFc} \times \text{ABSd})}{(\text{BWc} \times \text{ATn} \times \text{RfDabs})}$$

Equation / Units	Derm - HQ unitless	= (Csoil mg/kg	× CF kg/mg	× EF days/year	× EDc years	× EV events/day	× SAc cm²	× AFc mg/cm²-event	× ABSd unitless	) ÷ (BWc kg	× ATn days	× RfDabs [b] mg/kg-day	)
Arsenic	1.41E-02	= (3.74E+00	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 3.00E-02	) ÷ (15	× 2,190	× 2.85E-04	)
Lead	NA	= (1.76E+02	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× NA	) ÷ (15	× 2,190	× a	)
1-Methylnaphthalene	1.10E-03	= (1.66E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× 7.00E-02	)
Benzo(a)anthracene	NA	= (1.36E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× NV	)
Benzo(a)pyrene	NA	= (1.61E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× NV	)
Benzo(b)fluoranthene	NA	= (1.35E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× NV	)
Benzo(k)fluoranthene	NA	= (4.23E+00	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× NV	)
Dibenzo(a,h)anthracene	NA	= (7.61E-01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× NV	)
Fluoranthene	3.08E-04	= (2.65E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× 4.00E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (3.39E+00	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× NV	)
Naphthalene	1.50E-03	= (6.46E+00	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× 2.00E-02	)
Pyrene	7.29E-04	= (4.70E+01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× 1.30E-01	) ÷ (15	× 2,190	× 3.00E-01	)
1,2,4-Trimethylbenzene	NA	= (1.31E+00	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× NA	) ÷ (15	× 2,190	× 5.00E-02	)
1,3,5-Trimethylbenzene	NA	= (4.79E-01	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× NA	) ÷ (15	× 2,190	× 5.00E-01	)
Benzene	NA	= (1.93E+00	× 1E-06	× 350	× 6	× 1	× 2,800	× 0.2	× NA	) ÷ (15	× 2,190	× 4.00E-03	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
EDc – Exposure Duration, child
EV – Event Frequency
SAc – Skin Surface Area, child
AFc – Soil-to-skin Adherence Factor, child
ABSd – Dermal Soil Absorption Factor
BWc – Body Weight, child
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo × ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment F

Table 6a
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Inhalation of Soil-derived Chemicals Pathway (0-3 feet)– Carcinogenic Effects

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{EF} \times \text{SInhRadj} \times [(1/\text{VF}) + (1/\text{PEF})])}{\text{ATc}}$$

Equation Units	Inh - Risk unitless	= (	Csoil mg/kg	×	SFi kg-day/mg	×	EF days/year	×	SInhRadj m3-yr/kg-day	× [	1	/	VF_{adult} m^3/kg	+	1	/	PEF m^3/kg	]	)	÷ (	ATc days	)
Arsenic	1.27E-09	= (	3.74E+00	×	1.51E+01	×	350	×	10.86	× [	1	/	NA	+	1	/	6.58E+09	]	)	÷ (	25,550	)
Lead	NA	= (	1.76E+02	×	a	×	350	×	10.86	× [	1	/	NA	+	1	/	6.58E+09	]	)	÷ (	25,550	)
1-Methylnaphthalene	NA	= (	1.66E+01	×	NV	×	350	×	10.86	× [	1	/	3.28E+04	+	1	/	6.58E+09	]	)	÷ (	25,550	)
Benzo(a)anthracene	NA	= (	1.36E+01	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]	)	÷ (	25,550	)
Benzo(a)pyrene	1.12E-09	= (	1.61E+01	×	3.08E+00	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]	)	÷ (	25,550	)
Benzo(b)fluoranthene	NA	= (	1.35E+01	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]	)	÷ (	25,550	)
Benzo(k)fluoranthene	NA	= (	4.23E+00	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]	)	÷ (	25,550	)
Dibenzo(a,h)anthracene	NA	= (	7.61E-01	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]	)	÷ (	25,550	)
Fluoranthene	NA	= (	2.65E+01	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]	)	÷ (	25,550	)
Indeno(1,2,3-cd)pyrene	NA	= (	3.39E+00	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]	)	÷ (	25,550	)
Naphthalene	NA	= (	6.46E+00	×	NV	×	350	×	10.86	× [	1	/	2.87E+04	+	1	/	6.58E+09	]	)	÷ (	25,550	)
Pyrene	NA	= (	4.70E+01	×	NV	×	350	×	10.86	× [	1	/	3.05E+05	+	1	/	6.58E+09	]	)	÷ (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	1.31E+00	×	NV	×	350	×	10.86	× [	1	/	5.47E+03	+	1	/	6.58E+09	]	)	÷ (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	4.79E-01	×	NV	×	350	×	10.86	× [	1	/	4.52E+03	+	1	/	6.58E+09	]	)	÷ (	25,550	)
Benzene	2.45E-06	= (	1.93E+00	×	2.73E-02	×	350	×	10.86	× [	1	/	3.20E+03	+	1	/	6.58E+09	]	)	÷ (	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Soil Concentration
SFi – Inhalation Slope Factor
EF – Exposure frequency
SInhRadj – Age-adjusted Soil Inhalation Rate
VF – Volatilization Factor
PEF – Particulate Emission Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment F

Table 6b
Risk Calculations: Reasonable Maximum Exposure
Residential Child: Inhalation of Soil-derived Pathway (0-3 feet) – Noncarcinogenic Effects

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{InhRc} \times \text{EF} \times \text{EDc} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BWc} \times \text{ATn} \times \text{RfDi})}$$

Equation	Inh - HQ	= (	Csoil	×	InhRc	×	EF	×	EDc	× [	1	/	VF_{child}	+	1	/	PEF	] ÷ (	BWc	×	ATn	×	RfDi (b)	)
Units	unitless		mg/kg		m^3/day		days/year		year				m^3/kg				m^3/kg		kg		days		mg/kg-day	
Arsenic	NA	= (	3.74E+00	×	10	×	350	×	6	× [	1	/	NA	+	1	/	6.58E+09	] ÷ (	15	×	2,190	×	NV	)
Lead	NA	= (	1.76E+02	×	10	×	350	×	6	× [	1	/	NA	+	1	/	6.58E+09	] ÷ (	15	×	2,190	×	a	)
1-Methylnaphthalene	NA	= (	1.66E+01	×	10	×	350	×	6	× [	1	/	1.47E+04	+	1	/	6.58E+09	] ÷ (	15	×	2,190	×	NV	)
Benzo(a)anthracene	NA	= (	1.36E+01	×	10	×	350	×	6	× [	1	/	NC	+	1	/	6.58E+09	] ÷ (	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	= (	1.61E+01	×	10	×	350	×	6	× [	1	/	NC	+	1	/	6.58E+09	] ÷ (	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.35E+01	×	10	×	350	×	6	× [	1	/	NC	+	1	/	6.58E+09	] ÷ (	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	= (	4.23E+00	×	10	×	350	×	6	× [	1	/	NC	+	1	/	6.58E+09	] ÷ (	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	7.61E-01	×	10	×	350	×	6	× [	1	/	NC	+	1	/	6.58E+09	] ÷ (	15	×	2,190	×	NV	)
Fluoranthene	NA	= (	2.65E+01	×	10	×	350	×	6	× [	1	/	NC	+	1	/	6.58E+09	] ÷ (	15	×	2,190	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	= (	3.39E+00	×	10	×	350	×	6	× [	1	/	NC	+	1	/	6.58E+09	] ÷ (	15	×	2,190	×	NV	)
Naphthalene	3.75E-01	= (	6.46E+00	×	10	×	350	×	6	× [	1	/	1.29E+04	+	1	/	6.58E+09	] ÷ (	15	×	2,190	×	8.57E-04	)
Pyrene	NA	= (	4.70E+01	×	10	×	350	×	6	× [	1	/	1.36E+05	+	1	/	6.58E+09	] ÷ (	15	×	2,190	×	NV	)
1,2,4-Trimethylbenzene	2.00E-01	= (	1.31E+00	×	10	×	350	×	6	× [	1	/	2.44E+03	+	1	/	6.58E+09	] ÷ (	15	×	2,190	×	1.71E-03	)
1,3,5-Trimethylbenzene	8.91E-03	= (	4.79E-01	×	10	×	350	×	6	× [	1	/	2.02E+03	+	1	/	6.58E+09	] ÷ (	15	×	2,190	×	1.70E-02	)
Benzene	1.01E-01	= (	1.93E+00	×	10	×	350	×	6	× [	1	/	1.43E+03	+	1	/	6.58E+09	] ÷ (	15	×	2,190	×	8.57E-03	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Csoil – Soil Concentration
InhRc – Inhalation Rate, child
EF – Exposure frequency
EDc – Exposure duration, child
VF – Volatilization Factor
PEF – Particulate Emission Factor
BWc – Body Weight, child
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment F

Table 6c
Residential Scenario: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} \times \frac{(3.14 \times D_A \times T)^{1/2}}{(2 \times \rho_b \times D_A)} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} $(g/m^2\text{-}s)/(kg/m^3)$	π	D_A (cm^2/s)	T_{adult} (s)	T_{child} (s)	2	ρb (g/cm^3)	10^{-4} (m^2/cm^2)	VF_{adult} (m^3/kg)	VF_{child} (m^3/kg)
1-Methylnaphthalene	73.32	3.14	1.95E-05	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.28E+04	1.47E+04
Benzo(a)anthracene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Benzo(a)pyrene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Benzo(b)fluoranthene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Benzo(k)fluoranthene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Dibenzo(a,h)anthracene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Fluoranthene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Indeno(1,2,3-cd)pyrene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Naphthalene	73.32	3.14	2.54E-05	9.46E+08	1.89E+08	2	1.38	1.00E-04	2.87E+04	1.29E+04
Pyrene	73.32	3.14	2.25E-07	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.05E+05	1.36E+05
1,2,4-Trimethylbenzene	73.32	3.14	7.01E-04	9.46E+08	1.89E+08	2	1.38	1.00E-04	5.47E+03	2.44E+03
1,3,5-Trimethylbenzene	73.32	3.14	1.02E-03	9.46E+08	1.89E+08	2	1.38	1.00E-04	4.52E+03	2.02E+03
Benzene	73.32	3.14	2.05E-03	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.20E+03	1.43E+03

Notes: Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

VF_{adult} – Volatilization Factor (m^3/kg) for adults (calculated)

VF_{child} – Volatilization Factor (m^3/kg) for children (calculated)

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source $(g/m^2\text{-}s)/(kg/m^3)$(Value used is for Minneapolis, MN.)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T_{adult} – Exposure interval (s) for adults

T_{Child} – Exposure interval (s) for children

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated; PAHs are not considered volatile chemicals

Attachment F

Table 6d
Residential Scenario: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical Units	VOC?	θa (Lair /Lsoil)	Di (cm^2/s)	H' unitless	θw (Lwater /Lsoil)	Dw (cm^2/s)	η (Lpore /Lsoil)	ρb (g/cm^3)	ρs (g/cm^3)	Kd (cm^3/g)	D_A (cm^2/s)
1-Methylnaphthalene	Yes	3.29E-01	6.31E-02	1.64E-02	0.15	7.13E-06	4.79E-01	1.38	2.65	3.75E+01	1.95E-05
Benzo(a)anthracene	No	3.29E-01	5.10E-02	4.91E-04	0.15	9.00E-06	4.79E-01	1.38	2.65	1.39E+03	NC
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Benzo(b)fluoranthene	No	3.29E-01	2.26E-02	2.69E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.82E+03	NC
Benzo(k)fluoranthene	No	3.29E-01	2.26E-02	2.39E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Dibenzo(a,h)anthracene	No	3.29E-01	2.02E-02	5.03E-06	0.15	5.18E-06	4.79E-01	1.38	2.65	1.57E+04	NC
Fluoranthene	No	3.29E-01	3.02E-02	3.62E-04	0.15	6.35E-06	4.79E-01	1.38	2.65	4.25E+02	NC
Indeno(1,2,3-cd)pyrene	No	3.29E-01	1.90E-02	1.42E-05	0.15	5.66E-06	4.79E-01	1.38	2.65	1.61E+04	NC
Naphthalene	Yes	3.29E-01	5.90E-02	1.80E-02	0.15	7.50E-06	4.79E-01	1.38	2.65	1.10E+01	2.54E-05
Pyrene	Yes	3.29E-01	2.72E-02	4.87E-04	0.15	7.24E-06	4.79E-01	1.38	2.65	4.16E+02	2.25E-07
1,2,4-Trimethylbenzene	Yes	3.29E-01	6.44E-02	2.52E-01	0.15	7.92E-06	4.79E-01	1.38	2.65	4.31E+00	7.01E-04
1,3,5-Trimethylbenzene	Yes	3.29E-01	6.02E-02	3.59E-01	0.15	8.67E-06	4.79E-01	1.38	2.65	4.22E+00	1.02E-03
Benzene	Yes	3.29E-01	8.80E-02	2.27E-01	0.15	9.80E-06	4.79E-01	1.38	2.65	9.93E-01	2.05E-03

Notes:

D_A – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's Law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User'S Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density
Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm^3/g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)
VOC? – Volatile organic compounds; If no, an apparent diffusivity was not calculated.
NV – no value available
NC – not calculated

Attachment F

Table 7a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Ingestion of Soil Pathway – Carcinogenic Effects (0-4 feet)

$$\text{Ing-Risk} = \frac{(\text{Csoil} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	= (	Csoil	×	SFo	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		mg/day		unitless		kg		days	
Inorganics																				
Arsenic	3.05E-07	= (	4.40E+00	×	1.50E+00	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Lead	NA	= (	1.00E+02	×	a	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Vanadium	NA	= (	3.12E+01	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
SVOCs																				
2-Methylnaphthalene	NA	= (	1.88E+03	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Acenaphthene	NA	= (	3.38E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	5.50E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Benzo(a)anthracene	6.74E-06	= (	2.00E+02	×	7.30E-01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	4.96E-05	= (	1.47E+02	×	7.30E+00	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	3.08E-06	= (	9.15E+01	×	7.30E-01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	3.77E-07	= (	1.12E+02	×	7.30E-02	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Chrysene	5.91E-08	= (	1.75E+02	×	7.30E-03	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	7.22E-06	= (	2.14E+01	×	7.30E+00	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	1.11E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	3.18E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	3.06E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	2.74E-06	= (	8.14E+01	×	7.30E-01	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	1.32E+03	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	4.42E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
VOCs																				
1,2,4-Trimethylbenzene	NA	= (	2.04E+00	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	= (	8.85E-01	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)
Benzene	4.52E-09	= (	1.78E+00	×	5.50E-02	×	1E-06	×	250	×	1	×	330	×	1	) ÷ (	70	×	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – Concentration in soil
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
VOC – Volatile organic compound
SIR – Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
SVOC – Semivolatile organic compound
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment F

Table 7b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Ingestion of Soil Pathway – Noncarcinogenic Effects (0-4 feet)

$$Ing\text{-}HQ = \frac{(Csoil \times CF \times EF \times ED \times SIR \times FI)}{(BW \times ATn \times RfDo)}$$

Equation	Ing - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	SIR	×	FI	) + (	BW	×	ATn	×	RfDo [b]	)
Units	unitless		mg/kg		kg/mg		days/year		years		mg/day		unitless		kg		days		mg/kg-day	
Inorganics																				
Arsenic	4.7E-02	= (	4.40E+00	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	3.0E-04	)
Lead	NA	= (	1.00E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	a	)
Vanadium	1.4E-02	= (	3.12E+01	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	7.0E-03	)
SVOCs																				
2-Methylnaphthalene	1.5E+00	= (	1.88E+03	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	4.0E-03	)
Acenaphthene	1.8E-03	= (	3.38E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	6.0E-01	)
Acenaphthylene	NA	= (	5.50E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	NV	)
Benzo(a)anthracene	NA	= (	2.00E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	NV	)
Benzo(a)pyrene	NA	= (	1.47E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	NV	)
Benzo(b)fluoranthene	NA	= (	9.15E+01	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.12E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	NV	)
Chrysene	NA	= (	1.75E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.14E+01	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	NV	)
Dibenzofuran	1.8E-01	= (	1.11E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	2.0E-03	)
Fluoranthene	2.6E-03	= (	3.18E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	4.0E-01	)
Fluorene	2.5E-03	= (	3.06E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	4.0E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (	8.14E+01	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	NV	)
Naphthalene	2.1E-01	= (	1.32E+03	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	2.0E-02	)
Pyrene	4.8E-03	= (	4.42E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	3.0E-01	)
VOCs																				
1,2,4-Trimethylbenzene	1.3E-04	= (	2.04E+00	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	5.0E-02	)
1,3,5-Trimethylbenzene	5.7E-06	= (	8.85E-01	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	5.0E-01	)
Benzene	1.4E-03	= (	1.78E+00	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	4.0E-03	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Concentration in Soil
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Soil Ingestion Rate
VOC – Volatile organic compound
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose
NV – No toxicity value available for this pathway.
NA – Not Applicable
SVOC – Semivolatile organic compound

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available. Toxicity criteria is presented in Attachment A, Table 1b.

Attachment F

Table 8a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Dermal Contact with Soil Pathway – Carcinogenic Effects (0-4 feet)

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATc})}$$

Equation	Derm - Risk	= (	Csoil	×	SFabs	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless		kg		days	
Inorganics																								
Arsenic	1.69E-08	= (	4.40E+00	×	1.58E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	3.00E-02	) ÷ (	70	×	25,550	)
Lead	NA	= (	1.00E+02	×	a	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
Vanadium	NA	= (	3.12E+01	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
SVOCs																								
2-Methylnaphthalene	NA	= (	1.88E+03	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.00E-01	) ÷ (	70	×	25,550	)
Acenaphthene	NA	= (	3.38E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	5.50E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(a)anthracene	1.54E-06	= (	2.00E+02	×	7.30E-01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	1.13E-05	= (	1.47E+02	×	7.30E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	7.03E-07	= (	9.15E+01	×	7.30E-01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	8.60E-08	= (	1.12E+02	×	7.30E-02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Chrysene	1.35E-08	= (	1.75E+02	×	7.30E-03	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	1.65E-06	= (	2.14E+01	×	7.30E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	1.11E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	3.18E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	3.06E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	6.25E-07	= (	8.14E+01	×	7.30E-01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	1.32E+03	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	4.42E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
VOCs																								
1,2,4-Trimethylbenzene	NA	= (	2.04E+00	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	= (	8.85E-01	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
Benzene	NA	= (	1.78E+00	×	5.50E-02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csoil – Concentration in Soil
SFabs – Absorbed slope factor (SFo ÷ ABSgi)
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
VOC – Volatile organic compound
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment F

Table 8b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Dermal Contact with Soil Pathway – Noncarcinogenic Effects (0-4 feet)

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATn} \times \text{RfDabs})}$$

Equation	Derm - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) + (	BW	×	ATn	×	RfDabs [b]	)
Units	unitless		mg/kg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless		kg		days		mg/kg-day	
Inorganics																								
Arsenic	2.63E-03	= (	4.40E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	3.00E-02	) + (	70	×	365	×	2.85E-04	)
Lead	NA	= (	1.00E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	a	)
Vanadium	NA	= (	3.12E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	1.82E-04	)
SVOCs																								
2-Methylnaphthalene	2.66E-01	= (	1.88E+03	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.00E-01	) + (	70	×	365	×	4.00E-03	)
Acenaphthene	4.15E-04	= (	3.38E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0	×	1.30E-01	) + (	70	×	365	×	6.00E-01	)
Acenaphthylene	NA	= (	5.50E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0	×	1.30E-01	) + (	70	×	365	×	NV	)
Benzo(a)anthracene	NA	= (	2.00E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Benzo(a)pyrene	NA	= (	1.47E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Benzo(b)fluoranthene	NA	= (	9.15E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.12E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Chrysene	NA	= (	1.75E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.14E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Dibenzofuran	4.09E-02	= (	1.11E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	2.00E-03	)
Fluoranthene	5.85E-04	= (	3.18E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	4.00E-01	)
Fluorene	5.64E-04	= (	3.06E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	4.00E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (	8.14E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Naphthalene	4.88E-02	= (	1.32E+03	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	2.00E-02	)
Pyrene	1.09E-03	= (	4.42E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	3.00E-01	)
VOCs																								
1,2,4-Trimethylbenzene	NA	= (	2.04E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	5.00E-02	)
1,3,5-Trimethylbenzene	NA	= (	8.85E-01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	5.00E-01	)
Benzene	NA	= (	1.78E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	4.00E-03	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Concentration in Soil
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
SSAF – Soil-to-skin Adherence Factor
ABSd – Dermal Soil Absorption Factor
BW – Body Weight
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo ×ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.
VOC – Volatile organic compound
SVOC – Semivolatile organic compound

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available. Toxicity criteria is presented in Attachment A, Table 1b.

Attachment F

Table 9a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Inhalation of Soil (Fugitive Emissions and Volatile Compounds) Pathway– Carcinogenic Effects (0-4 feet)

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times [(1/\text{VF}) + (1/\text{PEF})])}{(\text{BW} \times \text{ATc})}$$

Equation	Inh - Risk	= (	Csoil	×	SFi	×	IR	×	ET	×	EF	×	ED	× [	1	/	VF	+	1	/	PEF	]) + (	BW	×	ATc	)
Units	*unitless*		*mg/kg*		*kg-day/mg*		*m³/hour*		*hours/day*		*days/year*		*year*				*m³/kg*				*m³/kg*		*kg*		*days*	
Inorganics																										
Arsenic	8.12E-09	= (	4.40E+00	×	1.51E+01	×	1.5	×	8	×	250	×	1	× [	1	/	NA	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Lead	NA	= (	1.00E+02	×	a	×	1.5	×	8	×	250	×	1	× [	1	/	NA	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Vanadium	NA	= (	3.12E+01	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	NA	+	1	/	1.37E+07	]) + (	70	×	25,550	
SVOCs																										
2-Methylnaphthalene	NA	= (	1.88E+03	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	5.68E+03	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Acenaphthene	NA	= (	3.38E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	1.10E+04	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Acenaphthylene	NA	= (	5.50E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	1.30E+04	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Benzo(a)anthracene	NA	= (	2.00E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Benzo(a)pyrene	5.56E-08	= (	1.47E+02	×	3.08E+00	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Benzo(b)fluoranthene	NA	= (	9.15E+01	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Benzo(k)fluoranthene	NA	= (	1.12E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Chrysene	NA	= (	1.75E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Dibenzo(a,h)anthracene	NA	= (	2.14E+01	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Dibenzofuran	NA	= (	1.11E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	9.09E+03	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Fluoranthene	NA	= (	3.18E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Fluorene	NA	= (	3.06E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	1.67E+04	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	NA	= (	8.14E+01	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Naphthalene	NA	= (	1.32E+03	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	5.25E+03	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Pyrene	NA	= (	4.42E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	5.57E+04	+	1	/	1.37E+07	]) + (	70	×	25,550	)
VOCs																										
1,2,4-Trimethylbenzene	NA	= (	2.04E+00	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	9.98E+02	+	1	/	1.37E+07	]) + (	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	= (	8.85E-01	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	8.26E+02	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Benzene	1.40E-07	= (	1.78E+00	×	2.73E-02	×	1.5	×	8	×	250	×	1	× [	1	/	5.83E+02	+	1	/	1.37E+07	]) + (	70	×	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Concentration in Soil
SFi – Inhalation Slope Factor
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VOC – Volatile organic compound
VF – Volatilization Factor
PEF – Particulate Emission Factor (See Attachment G)
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
SVOC – Semivolatile organic compound
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment F

Table 9b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Inhalation of Soil (Fugitive Emissions and Volatile Compounds) Pathway – Carcinogenic Effects

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BW} \times \text{ATn} \times \text{RfDI})}$$

Equation	Inh - HQ	=	(	Csoil	×	IR	×	ET	×	EF	×	ED	×	[	1	/	VF	+	1	/	PEF	]	÷	(	BW	×	ATn	×	RfDI [6]	)
Units	unitless			mg/kg		m³/hour		hours/day		days/year		year					m³/kg				m³/kg				kg		days		mg/kg-day	
Inorganics																														
Arsenic	NA	=	(	4.40E+00	×	1.5	×	8	×	250	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Lead	NA	=	(	1.00E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	÷	(	70	×	365	×	a	)
Vanadium	NA	=	(	3.12E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
SVOCs																														
2-Methylnaphthalene	NA	=	(	1.88E+03	×	1.5	×	8	×	250	×	1	×	[	1	/	5.68E+03	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Acenaphthene	NA	=	(	3.38E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	1.10E+04	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Acenaphthylene	NA	=	(	5.50E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	1.30E+04	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Benzo(a)anthracene	NA	=	(	2.00E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Benzo(a)pyrene	NA	=	(	1.47E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Benzo(b)fluoranthene	NA	=	(	9.15E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Benzo(k)fluoranthene	NA	=	(	1.12E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Chrysene	NA	=	(	1.75E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Dibenzo(a,h)anthracene	NA	=	(	2.14E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Dibenzofuran	NA	=	(	1.11E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	9.09E+03	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Fluoranthene	NA	=	(	3.18E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Fluorene	NA	=	(	3.06E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	1.67E+04	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	=	(	8.14E+01	×	1.5	×	8	×	250	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
Naphthalene	3.46E+01	=	(	1.32E+03	×	1.5	×	8	×	250	×	1	×	[	1	/	5.25E+03	+	1	/	1.37E+07	]	÷	(	70	×	365	×	8.57E-04	)
Pyrene	NA	=	(	4.42E+02	×	1.5	×	8	×	250	×	1	×	[	1	/	5.57E+04	+	1	/	1.37E+07	]	÷	(	70	×	365	×	NV	)
VOCs																														
1,2,4-Trimethylbenzene	1.40E-01	=	(	2.04E+00	×	1.5	×	8	×	250	×	1	×	[	1	/	9.98E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	1.71E-03	)
1,3,5-Trimethylbenzene	7.40E-03	=	(	8.85E-01	×	1.5	×	8	×	250	×	1	×	[	1	/	8.26E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	1.70E-02	)
Benzene	4.19E-02	=	(	1.78E+00	×	1.5	×	8	×	250	×	1	×	[	1	/	5.83E+02	+	1	/	1.37E+07	]	÷	(	70	×	365	×	8.57E-03	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Csoil – Concentration in Soil
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VF – Volatilization Factor
VOC – Volatile organic compound
PEF – Particulate Emission Factor (See Attachment G)
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
SVOC – Semivolatile organic compound

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available. Toxicity criteria is presented in Attachment A, Table 1b.

Attachment F

Table 9c
Construction Worker: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} \times \frac{(3.14 \times D_A \times T)^{1/2}}{(2 \times \rho_b \times D_A)} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} $(g/m^2\text{-}s)/(kg/m^3)$	π	D_A (cm^2/s)	T (s)	2	ρb (g/cm^3)	10^{-4} (m^2/cm^2)	VF (m^3/kg)
1-Methylnaphthalene	73.32	3.14	1.94E-05	3.15E+07	2	1.38	1.00E-04	6.00E+03
2-Methylnaphthalene	73.32	3.14	2.17E-05	3.15E+07	2	1.38	1.00E-04	5.68E+03
Acenaphthene	73.32	3.14	5.82E-06	3.15E+07	2	1.38	1.00E-04	1.10E+04
Acenaphthylene	73.32	3.14	4.15E-06	3.15E+07	2	1.38	1.00E-04	1.30E+04
Benzo(a)anthracene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Benzo(a)pyrene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Benzo(b)fluoranthene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Benzo(k)fluoranthene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Chrysene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Dibenzo(a,h)anthracene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Dibenzofuran	73.32	3.14	8.46E-06	3.15E+07	2	1.38	1.00E-04	9.09E+03
Fluoranthene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Fluorene	73.32	3.14	2.50E-06	3.15E+07	2	1.38	1.00E-04	1.67E+04
Indeno(1,2,3-cd)pyrene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Naphthalene	73.32	3.14	2.54E-05	3.15E+07	2	1.38	1.00E-04	5.25E+03
Pyrene	73.32	3.14	2.25E-07	3.15E+07	2	1.38	1.00E-04	5.57E+04
1,2,4-Trichlorobenzene	73.32	3.14	1.02E-06	3.15E+07	2	1.38	1.00E-04	2.62E+04
1,2,4-Trimethylbenzene	73.32	3.14	7.01E-04	3.15E+07	2	1.38	1.00E-04	9.98E+02
1,3,5-Trimethylbenzene	73.32	3.14	1.02E-03	3.15E+07	2	1.38	1.00E-04	8.26E+02
Benzene	73.32	3.14	2.05E-03	3.15E+07	2	1.38	1.00E-04	5.83E+02
Ethylbenzene	73.32	3.14	1.27E-03	3.15E+07	2	1.38	1.00E-04	7.41E+02
sec-Butyl benzene	73.32	3.14	1.18E-03	3.15E+07	2	1.38	1.00E-04	7.70E+02
Toluene	73.32	3.14	1.75E-03	3.15E+07	2	1.38	1.00E-04	6.32E+02
Xylenes (total)	73.32	3.14	1.07E-03	3.15E+07	2	1.38	1.00E-04	8.09E+02

Notes:

Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

VF – Volatilization Factor (m^3/kg) (calculated)

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source $(g/m^2\text{-}s)/(kg/m^3)$(Value used is for Minneapolis, MN.)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T – Exposure interval (s)

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated

Attachment F

Table 9d
Construction Worker: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical	VOC?	θa	Di	H'	θw	Dw	η	ρb	ρs	Kd	D_A
Units		(Lair /Lsoil)	(cm^2/s)	unitless	(Lwater /Lsoil)	(cm^2/s)	(Lpore /Lsoil)	(g/cm^3)	(g/cm^3)	(cm^3/g)	(cm^2/s)
1-Methylnaphthalene	*Yes*	3.29E-01	6.31E-02	1.64E-02	0.15	7.13E-06	4.79E-01	1.38	2.65	3.75E+01	1.948E-05
2-Methylnaphthalene	*Yes*	3.29E-01	4.80E-02	2.12E-02	0.15	7.84E-06	4.79E-01	1.38	2.65	1.79E+01	2.166E-05
Acenaphthene	*Yes*	3.29E-01	4.21E-02	7.44E-03	0.15	7.69E-06	4.79E-01	1.38	2.65	3.67E+01	5.819E-06
Acenaphthylene	*Yes*	3.29E-01	4.39E-02	5.11E-03	0.15	7.53E-06	4.79E-01	1.38	2.65	3.67E+01	4.148E-06
Benzo(a)anthracene	No	3.29E-01	5.10E-02	4.91E-04	0.15	9.00E-06	4.79E-01	1.38	2.65	1.39E+03	NC
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Benzo(b)fluoranthene	No	3.29E-01	2.26E-02	2.69E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.82E+03	NC
Benzo(k)fluoranthene	No	3.29E-01	2.26E-02	2.39E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Chrysene	No	3.29E-01	2.48E-02	2.14E-04	0.15	6.21E-06	4.79E-01	1.38	2.65	1.42E+03	NC
Dibenzo(a,h)anthracene	No	3.29E-01	2.02E-02	5.03E-06	0.15	5.18E-06	4.79E-01	1.38	2.65	1.57E+04	NC
Dibenzofuran	*Yes*	3.29E-01	5.51E-02	8.71E-03	0.15	7.04E-06	4.79E-01	1.38	2.65	6.78E+01	8.463E-06
Fluoranthene	No	3.29E-01	3.02E-02	3.62E-04	0.15	6.35E-06	4.79E-01	1.38	2.65	4.25E+02	NC
Fluorene	*Yes*	3.29E-01	3.63E-02	3.93E-03	0.15	7.88E-06	4.79E-01	1.38	2.65	6.78E+01	2.499E-06
Indeno(1,2,3-cd)pyrene	No	3.29E-01	1.90E-02	1.42E-05	0.15	5.66E-06	4.79E-01	1.38	2.65	1.61E+04	NC
Naphthalene	*Yes*	3.29E-01	5.90E-02	1.80E-02	0.15	7.50E-06	4.79E-01	1.38	2.65	1.10E+01	2.537E-05
Pyrene	*Yes*	3.29E-01	2.72E-02	4.87E-04	0.15	7.24E-06	4.79E-01	1.38	2.65	4.16E+02	2.254E-07
1,2,4-Trichlorobenzene	NV	3.29E-01	3.00E-02	1.42E-03	0.15	8.23E-06	4.79E-01	1.38	2.65	1.07E+01	1.02E-06
1,2,4-Trimethylbenzene	*Yes*	3.29E-01	6.44E-02	2.52E-01	0.15	7.92E-06	4.79E-01	1.38	2.65	4.31E+00	7.01E-04
1,3,5-Trimethylbenzene	*Yes*	3.29E-01	6.02E-02	3.59E-01	0.15	8.67E-06	4.79E-01	1.38	2.65	4.22E+00	1.02E-03
Benzene	*Yes*	3.29E-01	8.80E-02	2.27E-01	0.15	9.80E-06	4.79E-01	1.38	2.65	9.93E-01	2.05E-03
Ethylbenzene	*Yes*	3.29E-01	7.50E-02	3.22E-01	0.15	7.80E-06	4.79E-01	1.38	2.65	3.11E+00	1.27E-03
sec-Butyl benzene	*Yes*	3.29E-01	5.76E-02	5.07E-01	0.15	6.75E-06	4.79E-01	1.38	2.65	1.25E+01	1.18E-03
Toluene	*Yes*	3.29E-01	8.70E-02	2.71E-01	0.15	8.60E-06	4.79E-01	1.38	2.65	1.61E+00	1.75E-03
Xylenes (total)	*Yes*	3.29E-01	7.14E-02	2.71E-01	0.15	9.34E-06	4.79E-01	1.38	2.65	2.66E+00	1.07E-03

Notes:

D_A – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's Law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User'S Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density
Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm^3/g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)
VOC? – Volatile organic compounds; If no an apparent diffusivity was not calculated.
NV – no value available
NC – not calculated

ATTACHMENT G

Calculation of Site-specific Particulate Emission Factors

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Attachment G
Calculation of Site-specific Particulate Emission Factors for the Commercial/Industrial and Construction Scenarios

Based on comments provided by USEPA, a site-specific particulate emission factor (PEF) and volatilization factor (VF) was calculated for the residential, commercial/industrial, and construction scenarios. Guidance provided in *Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites* (USEPA, 2002), Sections 4 and 5 and Appendix E were used to estimate the PEF factor for the commercial/industrial and construction worker scenario. The sections below outline the procedures used for estimating the PEF.

The following assumptions were made for receptor population based on the size of the unit and the predominant soil type.

Residential Scenario

- The areal extent of the site is the 0.5 acre default value presented in the Soil Screening Guidance (USEPA, 1996; USEPA 2002).
- The fraction vegetative cover value is based on the assumption that 10% of the available surface at residential properties are bare (garden beds). The fraction vegetative cover (V) is therefore 90%.
- The predominant soil type is silty clay.

Table 1 presents the PEF calculation for the residential scenario.

Commercial/Industrial Scenario – Maintenance Workers and General Industrial Workers

- The areal extent of the site was considered to be NSPW facility and the NSPW storage yard on St.Claire Street for the industrial worker. The total acreage for the NSPW facility is approximately 2.75 acres.
- The areal extent of the site was considered to be Kreher Park for maintenance workers. The total acreage for Kreher Park is 13 acres.
- The fraction vegetative cover value is based on the amount of vegetative cover and nonerodible elements that may prevent or restrict the amount of fugitive dusts generated.[1] The surface cover at Kreher Park, is predominantly vegetation and at the Marina Parking Lot the cover is gravel. The wastewater treatment plant surface cover is predominantly hard surface, buildings and vegetation (**Figures 3** and **5**). Therefore, the fraction of vegetative cover or nonerodible element cover is conservatively estimated to be 90%. The surface cover at the NSPW facility and the NSPW storage yard on St.Claire Street is predominantly buildings, asphalt, concrete, gravel, and some vegetation. Therefore, the fraction of vegetative cover or nonerodible element cover is conservatively estimated to be 90% at the NSPW facility and the NSPW storage yard.
- The predominant soil type at all exposure areas is silty clay.

Tables 2 and **3** present the PEF estimated for the residential scenario.

[1] According to the Soil Screening Guidance Technical Background Document (USEPA, 1996), nonerodible elements are described as clumps of grass or stones (larger than 1 cm in diameter) on the surface (that will) consume part of the shear stress of the wind which otherwise would be transferred to erodible soil.

Construction Scenario

The PEF for the construction scenario was calculated using the approach presented in Appendix E of USEPA 2002. PEF values were calculated for fugitive dusts emitted from unpaved road traffic (PEF_{sc}) as well as other construction related activities (PEF_{sc}') as listed below:

- wind erosion (Equation E-20)
- dumping of excavated soils (Equation E-21)
- dozing operations (Equation E-22)
- grading operations (Equation E-23)
- tilling operations (Equation E-24)

There are no defined plans available for future construction work at the Site. Therefore, assumptions regarding construction activities (unpaved road traffic, excavation, dozing, grading, and tilling) were necessary to complete the calculations. When Site-specific information was unavailable, default values provided in Appendix E of USEPA 2002 were used. Default values are as presented in **Attachment G, Tables 4** to **14**.

Assumptions regarding Site-specific values are presented below.

- Construction would be limited to half of Kreher Park (6.5 acres).
- The time period is 6 months.

The selected PEF is based on the PEF value that will generate the more conservative risk value. In this HHRA, the PEF used for the construction scenario is based on unpaved road traffic. **Tables G-4** to **G-14** outline the equations used to estimate the construction worker PEFs.

Attachment G

Table 1
Residential Receptors at the Upper Bluff: Particulate Emission Factor Calculations

$$PEF = Q/C \times \frac{3600\ s/h}{0.036 \times (1-V) \times (U_m/U_t)^3 \times F(x)}$$

PEF – Particulate emission factor
Q/C – Inverse of mean concentration at center of a 0.5-acre-square source (see calculation presented below)
V – Fraction of vegetative cover. It is assumed that 10% of the surface cover at residential properties are bare (garden beds)
Um – Mean annual windspeed
Ut – Equivalent threshold value of windspeed at 7 m
F(x) – Function dependent on UmUt derived using Cowherd

Equation	PEF	=	Q/C	× [	3600	÷ (	0.036	× (	1	-	V	) × (	Um	/	Ut	) ^{3} ×	F(x)	)
Units	m^3/kg		g/m^2-s per kg/m^3		s/h		unitless				unitless		m/s		m/s		unitless	
All Chemicals	6.58E+09	=	90.8	× [	3600	÷	0.036	× (	1	-	0.9	) × [	4.69	/	11.32	) ^{3} ×	0.194	)

Default values are as presented in Soil Screening Technical Background Document (USEPA 1996).

Attachment G

Table 2
Industrial Worker at Excel Energy Site: Particulate Emission Factor Calculations

$$PEF = Q/C_{wind} \times \frac{3600\ s/h}{0.036 \times (1-V) \times (U_m/U_t)^3 \times F(x)}$$

PEFwind – Particulate emission factor
Q/Cwind – Inverse of mean concentration at center of a 0.5-acre-square source (see calculation presented below)
V – Fraction of vegetative cover. Because the NSPW facility and storage yard are predominantly covered with vegetation, buildings, asphalt, concrete, or gravel, 90% was used for V.
Um – Mean annual windspeed
Ut – Equivalent threshold value of windspeed at 7 m
F(x) – Function dependent on UmUt derived using Cowherd

Equation	PEF_{wind}	=	Q/Cwind	×	[	3600	÷	(	0.036	×	(	1	-	V	)	×	(	Um	/	Ut	)³	×	F(x)	)
Units	m^3/kg		g/m^2-s per kg/m^3			s/h			unitless					unitless				m/s		m/s			unitless	
All Chemicals	5.07E+09	=	69.9226	×	[	3600	÷	(	0.036	×	(	1	-	0.9	)	×	[	4.69	/	11.32	)³	×	0.194	)

Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

$$Q/C_{wind} = A \times \exp\left[\frac{(\ln A_{site} - B)^2}{C}\right]$$

Q/C_{wind} – Inverse of mean concentration at center of a 0.5-acre-square source
A, B, C – Constants based on air dispersion for the Zone 5 Minneapolis climate zone.

Equation	Q/C_{wind}	=	A	×	exp	[	(	*ln*	A site	-	B	)²	÷	C	)]
Units	unitless		unitless						acres		unitless			unitless	
All Chemicals	69.9226	=	16.2302	×	exp	[	(	*ln*	2.75	-	18.7762	)²	÷	216.108	)]

Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

Attachment G

Table 3
Maintenance Worker at Kreher Park: Particulate Emission Factor Calculations

$$PEF = Q/C_{wind} \times \frac{3600\ s/h}{0.036 \times (1-V) \times (U_m/U_t)^3 \times F(x)}$$

PEFwind – Particulate emission factor
Q/Cwind – Inverse of mean concentration at center of a 0.5-acre-square source (see calculation presented below)
V – Fraction of vegetative cover. Because Kreher Park is predominantly covered with vegetation and gravel, 90% was used for V.
Um – Mean annual windspeed
Ut – Equivalent threshold value of windspeed at 7 m
F(x) – Function dependent on UmUt derived using Cowherd

Equation	PEFwind	=	Q/Cwind	× [	3600	÷ (	0.036	× (	1	-	V	) × (	Um	/	Ut	)³ ×	F(x)	)
Units	m³/kg		g/m²-s per kg/m³		s/h		unitless				unitless		m/s		m/s		unitless	
All Chemicals	3.97E+09	=	54.7597	× [	3600	÷	0.036	× (	1	-	0.9	) × [	4.69	/	11.32	)³ ×	0.194	)

Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

$$Q/C_{wind} = A \times \exp\left[\frac{(\ln A_{site} - B)^2}{C}\right]$$

Q/Cwind – Inverse of mean concentration at center of a 0.5-acre-square source
A, B, C – Constants based on air dispersion for the Zone 5 Minneapolis climate zone.

Equation	Q/Cwind	=	A	× exp	[(	*ln*	A site	- B	)²	÷	C	)]
Units	unitless		unitless				*acres*	unitless			unitless	
All Chemicals	54.7597	=	16.2302	× exp	[(	*ln*	13.00	- 18.7762	)²	÷	216.108	)]

Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

Attachment G

Table 4
Calculation of Particulate Emission Factor for Unpaved Road Traffic

Equation E-18:

$$PEF_{sc} = Q/C_{sr} \times \frac{1}{F_D} \times \frac{T \times A_R}{\frac{2.6 \times (s/12)^{0.8} (W/3)^{0.4}}{(M_{dry}/0.2)^{0.3}} \times \left[\frac{(365-p)}{365}\right] \times 281.9 \times \sum VKT}$$

PEF_{sc} =	Subchronic particulate emission factor for unpaved road traffic (m^3/kg)	Calculated	
Q/c_{sr} =	Inverse of 1-h, average air concentration along a straight road segment bisecting a square site (g/m^2-s per kg/m^3)	Calculated, see Equation E-19	
F_D =	Dispersion correction factor (unitless)	Calculated, see Equation E-16	
T =	Total time over which construction occurs (s)	1.08E+07	Assumed time period over which traffic will occur is 6 month.
A_R =	Surface area of contaminated road segment (m^2) $A_R = L_R \times W_R \times 0.092903\ m^2/ft^2$	1.06E+04	
L_R =	Length of road segment (ft)	5.32E+02	Assumes construction is limited to half of Kreher Park; therefore, exposure area is limted to the 6.5 acres or one-half the acreage of Kreher Park.
	L_R = square root of site surface contamination configured as a square		
W_R =	Width of road segment (ft)	2.00E+01	Default
s =	Road surface silt content (%)	8.50E+00	
W =	Mean vehicle weight (tons)	8.00E+00	Value presented in Supplemental Soil Screening Guidance
M_{dry} =	Road surface material moisture content under dry, uncontrolled conditions (%)	2.00E-01	Default
p =	Number of days per year with at least 0.01 inches of precipitation	1.20E+02	From Exhibit E-1
ΣVKT=	Sum of fleet vehicle kilometers traveled during the exposure duration (km) ΣVKT= 30 vehicles × 0.162 km/day × (52 weeks/year ÷ 2) × 5 days/week	6.33E+02	Assumes area of surface contamination is limited to one half of Kreher Park of 6.5 acres or 0.1621862 km.

PEF_{sc}	=	Q/c_{sr}	×	(1 + F_D)	×	[(T	×	A_R)	+	[2.6	×	(s	+ 12) $^{0.8}$	×	(W	+ 3) $^{0.4}$	) ÷ ((M_{dry}	+ 0.2) $^{0.3}$	)	×	((365	- p) ÷ 365)	×	281.9	×	ΣVKT]
(m^3/kg)		(g/m^2-s per kg/m^3)		unitless				m^2/ft^2				%			tons			%				days/year				km
1.98E+07	=	15.931	×	(1 + 1.87E-01)	×	[(1.08E+07	×	1.06E+04)	+	[2.6	×	(8.50E+00	+ 12) $^{0.8}$	×	(8	+ 3) $^{0.4}$	) ÷ ((0.2	+ 0.2) $^{0.3}$	)	×	((365	- 120) ÷ 365)	×	281.9	×	893.1]

Attachment G

Table 5
Calculation of Subchronic Dispersion Factor for On-site Exposure to Unpaved Road Traffic

Equation E-19: $$Q/C_{sr} = A \times \exp\left[\frac{(\ln A_s - B)^2}{C}\right]$$

Q/C_{sr} =	Inverse of 1-h. average air concentration along a straight road segment bisecting a square site (g/m^2-s per kg/m^3)	Calculated
A =	Constant	12.9351
B =	Constant	5.7383
C =	Constant	71.7711
A_s =	Areal extent of site surface contamination (acres)	6.5

Q/C_{sr}	=	A	×	exp	[(	ln	A_s	-	B	)²	÷	C	]
15.93062	=	12.9351	×	exp	[(	ln	6.5	-	5.7383	)²	÷	71.7711	]

Attachment G

Table 6
Calculation of Dispersion Correction Factor

Equation E-16:

$$F_D = 0.1852 + \frac{5.3537}{t_c} + \frac{-9.6318}{t_c^2}$$

F_D = Dispersion correction factor (unitless)
t_c = Duration of construction (hr),
t_c = T in units of hours

Calculated
3000

F_D	=	0.1852	+	(	5.3537	÷	t_c	)	+	(	-9.6318	÷	$(t_c)^2$	)
0.186983	=	0.1852	+	(	5.3537	÷	3.00E+03	)	+	(	-9.6318	÷	9.00E+06	)

Attachment G

Table 7
Calculation of Unit Mass Emitted from the Wind Erosion of Contaminated Soil Surface

Equation E-20:

$$M_{wind} = 0.036 \times (1 - V) \times \left(\frac{U_m}{U_t}\right)^3 \times F(x) \times A_{surf} \times ED \times 8{,}760\ hr/yr$$

M_{wind} =	Unit mass emitted from wind erosion (g)	Calculated	
V =	Fraction of vegetative cover (unitless)	0.9	
U_m =	Mean windspeed during contruction (m/s)	4.69	Default
U_t =	Equivalent threshold value of windspeed at 7m (m/s)	11.32	Default
F(x) =	Function dependent on U_m/U_t derived from Cowherd et al. (1985) (unitless)	0.194	Default
A_{surf} =	Areal extent of site with surface soil contamination (m^2)	2.63E+04	Construction is limited to one half of Kreher Park and the entire surface of the exposure area is contaminated (6.5 acres).
ED =	Exposure duration (yr)	0.5	Assumes exposure duration is 6 months

M_{wind}	=	0.036	×	(	1	-	V	)	×	(	U_m	÷	U_t	$)^3$	×	F(x)	×	A_{surf}	×	ED	×	8760
5.72E+03	=	0.036	×	(	1	-	0.9	)	×	(	4.69	+	11.32	$)^3$	×	0.194	×	2.63E+04	×	0.5	×	8760

Attachment G

Table 8
Calculation of Unit Mass from the Dumping of Excavated Soils

Equation E-21:

$$M_{excav} = 0.35 \times 0.0016 \times \frac{\left(\frac{U_m}{2.2}\right)^{1.3}}{\left(\frac{M}{2}\right)^{1.4}} \times \rho_{soil} \times A_{excav} \times d_{excav} \times N_A \times 10^3 \text{ g/kg}$$

M_{excav} =	Unit mass emitted from excavation soil dumping (g)	Calculated	
0.35 =	PM_{10} particle size multiplier (unitless)	0.35	Constant
U_m =	Mean windspeed during construction (m/s)	4.69	Default
M =	Gravimetric soil moisture content (%),	0.12	Default based on EPA (1985) Table 13.2.4-1, mean value for municipal landfill cover
ρ_{soil} =	In situ soil density (includes water) (Mg/m^3)	1.68	Default
A_{excav} =	Areal extent of excavation (m^2)	2.63E+04	Assumed construction is limited to one half of Kreher Park (6.5 acres)
d_{excav} =	Average depth of excavation (m)	3.048	Site-specific default; risks were estimated assuming excavations could potentially be as deep as 10 feet
N_A =	Number of times soil is dumped (unitless)	2	Default

M_{excav}	=	0.35	×	0.0016	× ((	U_m	÷	2.2	$)^{1.3}$	÷ (	M	÷	2	$)^{1.4}$	) ×	ρ_{soil}	×	A_{excav}	×	d_{excav}	×	N_A	×	1000
2.40E+03	=	0.35	×	0.0016	× ((	4.69	÷	2.2	$)^{1.3}$	÷ (	0.12	÷	2	$)^{1.4}$	) ×	1.68	×	3.048	×	3.048	×	2	×	1000

Attachment G

Table 9
Calculation of Unit Mass Emitted from Dozing Operations

Equation E-22:

$$M_{doz} = 0.75 \times \frac{0.45(s)^{1.5}}{(M)^{1.4}} \times \left(\frac{\sum VKT}{S} \right) \times 10^3 \text{ g/kg}$$

M_{doz} =	Unit mass emitted from grading operations (g)	
0.75	PM_{10} scaling factor (unitless)	
s =	Soil silt content (%)	
M =	Gravimetric soil moisture content (%)	
ΣVKT=	Sum of grading kilometers traveled (km)	
S =	Average dozing speed (kph)	

Calculated	
0.75	Constant
0.069	Default presented in EPA (1985) Table 11.9-3, mean value for overburden
0.079	Default presented in EPA (1985) Table 11.9-3, mean value for overburden
632.5	Calculated
11.4	Default presented in EPA (1985) Table 11.9-3, mean value for graders

M_{doz}	=	0.75	×	((	0.45	× (	s	) $^{1.5}$) ÷ (	M	) $^{1.4}$)	×	(	ΣVKT	÷	S	) ×	1000
1.19E+04	=	0.75	×	((	0.45	× (	0.069	) $^{1.5}$) ÷ (	0.079	) $^{1.4}$)	×	(	632.5262	÷	11.4	) ×	1000

Attachment G

Table 10
Calculation of Unit Mass Emitted from Grading Operations

Equation E-23: $$M_{grade} = 0.60 \times 0.0056 (S)^{2.0} \times \sum VKT \times 10^3 \text{ g/kg}$$

M_{grade} =	Unit mass emitted from grading operations (g)	Calculated	
0.60 =	PM_{10} scaling factor (unitless)	0.60	Constant
S =	Average grading speed (kph)	11.4	Default presented in EPA (1985) Table 11.9-3 mean value for graders
ΣVKT=	Sum of grading kilometers traveled (km)	632.5	Calculated

M_{grade}	=	0.60 ×	0.0056 ×	S ^{2}	× ΣVKT	×	1000
2.76E+05	=	0.60 ×	0.0056 ×	11.4 ^{2}	× 632.5	×	1000

Attachment G

Table 11
Calculation of Unit Mass Emitted from Tilling or Similar Operations

Equation E-24:

$$M_{till} = 1.1(s)^{0.6} \times A_{till} \times 4{,}074\ m^2/acre \times 10^{-4}\ ha/m^2 \times 10^3\ g/kg \times N_A$$

M_{till} =	Unit mass emitted from tilling or similar operations (g)	Calculated	
s =	Soil silt content (%)	0.18	Default presented in EPA (1992a) Section 2.6.1.1
A_{till} =	Areal extent of tilling (acres)	6.5	Assumed construction is limited to one half of Kreher Park
N_A =	Number of times soil is tilled (unitless)	2	Default

M_{till}	=	1.1	× (	s	) $^{0.6}$	×	A_{till}	×	4074	×	1E-04	×	1000
1.04E+03	=	1.1	× (	0.18	) $^{0.6}$	×	6.5	×	4074	×	1E-04	×	1000

Attachment G

Table 12
Calculation of Total Time-averaged Unit Emission Flux from Wind Erosion, Exacavation Soil Dumping, Dozing, Grading, and Tilling Operations

Equation E-25:

$$< J'_T > = \frac{M_{wind} + M_{excav} + M_{doz} + M_{grade} + M_{till}}{A_c \times T}$$

$<J'_T>$ =	Total time-averaged PM_{10} unit emission flux for construction activities other than traffic on unpaved roads (g/m^2-s)	Calculated
M_{wind} =	Unit mass emitted from wind erosion (g)	Calculated, see Equation E-20
M_{excav} =	Unit mass emitted from excavation soil dumping (g)	Calculated, see Equation E-21
M_{doz} =	Unit mass emitted from grading operations (g)	Calculated, see Equation E-22
M_{grade} =	Unit mass emitted from grading operations (g)	Calculated, see Equation E-23
M_{till} =	Unit mass emitted from tilling or similar operations (g)	Calculated, see Equation E-24
A_c =	Areal extent of site soil contamination (m^2)	2.63E+04
T =	Duration of construction (s)	1.08E+07 Assumed time period over which traffic will occur is 6 months.

$<J'_T>$	=	(	M_{wind}	+	M_{excav}	+	M_{doz}	+	M_{grade}	+	M_{till}	) ÷ (	A_c	×	T	)
1.05E-06	=	(	5.72E+03	+	2.40E+03	+	1.19E+04	+	2.76E+05	+	1.04E+03	) ÷ (	2.63E+04	×	1.08E+07	)

Attachment G

Table 13
Calculation of Subchronic Particulate Emission Factor for Construction Activities other than Traffic on Unpaved Roads

Equation E-26:

$$PEF'_{sc} = Q/C_{sa} \times \frac{1}{F_D} \times \frac{1}{< J'_T >}$$

PEF'_{sc} =	Subchronic particulate emission factor for construction activities other than traffic on unpaved roads (m^3/kg)	Calculated
Q/C_{sa} =	Inverse of 1 hour average air concentration at the center of the square emission source (g/m^2-s per kg/m^3)	Calculated, See Equation E-15
F_D=	Dispersion correction factor (unitless)	1.87E-01
$<J'_T>$ =	Total time-averaged PM_{10} unit emission flux for construction activities other than traffic on unpaved roads (g/m^2-s)	1.05E-06

PEF'_{sc}	=	Q/C_{sa}	×	(	1	÷	F_D	)	×	(	1	÷	$<J'_T>$	)
4.62E+07	=	9.03E+00	×	(	1	÷	0.186983	)	×	(	1	÷	1.05E-06	)

Attachment G

Table 14
Calculation of the On-site Subchronic Dispersion Factor for a Ground-level Area Emission Source

Equation E-15: $$Q/C_{sa} = A \times \exp\left[\frac{(\ln A_c - B)^2}{C}\right]$$

Q/C_{sa} = Inverse of 1- hour average air concentration at the center of the square emission source (g/m^2-s per kg/m^3)

A =	Constant	2.4538
B =	Constant	17.566
C =	Constant	189.0426
A_c =	Areal extent of site soil contamination (acres)	6.5

Q/C_{sa}	=	A	× exp [(ln	A_c	-	B	)² ÷	C	]
9.03E+00	=	2.454	× exp [(ln	6.5	-	17.566	)² ÷	189.0426	]

ATTACHMENT H

Evaluation of Data Excluding Concentrations Exceeding Csat

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ATTACHMENT H1

Calculations of Csat Values

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Attachment H1

Table 1
Soil Saturation Concentration Calculations for Surface Soil

Equation:

$$C_{sat} = \frac{S}{\rho_b}\left(\left(K_d \times \rho_b\right) + \theta_w + \left(H' \times \theta_a\right)\right)$$

C_{sat} = Soil Saturation Concentration (mg/kg)	Calculated	
S = Solubility in Water (mg/L)	Chemical-specific	
ρ_b = Dry Soil Bulk Density (kg/L)	1.38	Default for Silty Soil; Value obtained from *User's Guide for Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
K_d = Soil-water Partition Coefficient (L/kg) $K_d = K_{oc} \times f_{oc}$	Calculated	
K_{oc} = Organic Carbon Partition Coefficient (L/kg)	Chemical-specific	
f_{oc} = Fraction Organic Carbon in Soil (g/g)	0.002	Default value for surface soil presented in Supplemental Soil Screening Guidance (USEPA, 2002)
θ_w = Water-filled Soil Porosity (L_{water}/L_{soil})	0.15	Default value presented in Supplemental Soil Screening Guidance (USEPA, 2002)
H' = Dimensionless Henry's Law Constant	Chemical-specific	
θ_a = Air-filled Soil Porosity (L_{air}/L_{soil})	0.33	Calculated as outlined in Equation 4-9 in Supplemental Soil Screening Guidance (USEPA, 2002)

CAS Number	Chemical	C_{sat} mg/kg	=	(	S mg/L	÷	ρ_b kg/L	) × ((	K_{oc} L/kg	×	f_{oc} g/g	) ×	ρ_b kg/L	) +	θ_w L_{water}/L_{soil}	+	(	H' Unitless	×	θ_a L_{air}/L_{soil}	)
90120	1-Methylnaphthalene	9.47E+01	=	(	2.50E+01	+	1.38	) × ((	1.84E+03	×	0.002	) ×	1.38	) +	0.15	+	(	1.64E-02	×	0.33	)
832699	1-Methylphenanthrene	NA	=	(	NV	+	1.38	) × ((	NV	×	0.002	) ×	1.38	) +	0.15	+	(	NA	×	0.33	)
2245387	2,3,5-Trimethylphthalene	NA	=	(	NV	+	1.38	) × ((	NV	×	0.002	) ×	1.38	) +	0.15	+	(	NA	×	0.33	)
581420	2,6-Dimethylphthalene	NA	=	(	NV	+	1.38	) × ((	NV	×	0.002	) ×	1.38	) +	0.15	+	(	NA	×	0.33	)
91576	2-Methylphthalene	1.49E+02	=	(	2.46E+01	+	1.38	) × ((	2.98E+03	×	0.002	) ×	1.38	) +	0.15	+	(	2.12E-02	×	0.33	)
83329	Acephthene	4.82E+01	=	(	3.90E+00	+	1.38	) × ((	6.12E+03	×	0.002	) ×	1.38	) +	0.15	+	(	7.44E-03	×	0.33	)
208968	Acephthylene	1.99E+02	=	(	1.61E+01	+	1.38	) × ((	6.12E+03	×	0.002	) ×	1.38	) +	0.15	+	(	5.11E-03	×	0.33	)
120127	Anthracene	1.78E+00	=	(	4.34E-02	+	1.38	) × ((	2.04E+04	×	0.002	) ×	1.38	) +	0.15	+	(	2.27E-03	×	0.33	)
56553	Benzo(a)anthracene	4.34E+00	=	(	9.40E-03	+	1.38	) × ((	2.31E+05	×	0.002	) ×	1.38	) +	0.15	+	(	4.91E-04	×	0.33	)
50328	Benzo(a)pyrene	2.55E+00	=	(	1.62E-03	+	1.38	) × ((	7.87E+05	×	0.002	) ×	1.38	) +	0.15	+	(	4.63E-05	×	0.33	)
205992	Benzo(b)fluoranthene	2.41E+00	=	(	1.50E-03	+	1.38	) × ((	8.03E+05	×	0.002	) ×	1.38	) +	0.15	+	(	2.69E-05	×	0.33	)
192972	Benzo(e)pyrene	2.73E+00	=	(	8.60E-04	+	1.38	) × ((	1.58E+06	×	0.002	) ×	1.38	) +	0.15	+	(	2.38E-05	×	0.33	)
191242	Benzo(g,h,i)perylene	1.39E+00	=	(	2.60E-04	+	1.38	) × ((	2.68E+06	×	0.002	) ×	1.38	) +	0.15	+	(	1.35E-05	×	0.33	)
207089	Benzo(k)fluoranthene	1.26E+00	=	(	8.00E-04	+	1.38	) × ((	7.87E+05	×	0.002	) ×	1.38	) +	0.15	+	(	2.39E-05	×	0.33	)
92524	Biphenyl	8.75E+01	=	(	6.94E+00	+	1.38	) × ((	6.25E+03	×	0.002	) ×	1.38	) +	0.15	+	(	1.26E-02	×	0.33	)
218019	Chrysene	9.44E-01	=	(	2.00E-03	+	1.38	) × ((	2.36E+05	×	0.002	) ×	1.38	) +	0.15	+	(	2.14E-04	×	0.33	)
53703	Dibenzo(a,h)anthracene	5.40E+00	=	(	1.03E-03	+	1.38	) × ((	2.62E+06	×	0.002	) ×	1.38	) +	0.15	+	(	5.03E-06	×	0.33	)
132649	Dibenzofuran	7.04E+01	=	(	3.10E+00	+	1.38	) × ((	1.13E+04	×	0.002	) ×	1.38	) +	0.15	+	(	8.71E-03	×	0.33	)
206440	Fluoranthene	3.69E+01	=	(	2.60E-01	+	1.38	) × ((	7.09E+04	×	0.002	) ×	1.38	) +	0.15	+	(	3.62E-04	×	0.33	)
86737	Fluorene	4.29E+01	=	(	1.89E+00	+	1.38	) × ((	1.13E+04	×	0.002	) ×	1.38	) +	0.15	+	(	3.93E-03	×	0.33	)
193395	Indeno(1,2,3-cd)pyrene	1.02E+00	=	(	1.90E-04	+	1.38	) × ((	2.68E+06	×	0.002	) ×	1.38	) +	0.15	+	(	1.42E-05	×	0.33	)
108394	m -Cresols	2.22E+04	=	(	2.27E+04	+	1.38	) × ((	4.34E+02	×	0.002	) ×	1.38	) +	0.15	+	(	4.09E-05	×	0.33	)
106445	p-Cresols	2.10E+04	=	(	2.15E+04	+	1.38	) × ((	4.34E+02	×	0.002	) ×	1.38	) +	0.15	+	(	4.09E-05	×	0.33	)
91203	phthalene	1.17E+02	=	(	3.10E+01	+	1.38	) × ((	1.84E+03	×	0.002	) ×	1.38	) +	0.15	+	(	1.80E-02	×	0.33	)

Attachment H1

Table 1
Soil Saturation Concentration Calculations for Surface Soil

Equation:

$$C_{sat} = \frac{S}{\rho_b}\left(\left(K_d \times \rho_b\right) + \theta_w + \left(H' \times \theta_a\right)\right)$$

C_{sat} = Soil Saturation Concentration (mg/kg)	Calculated	
S = Solubility in Water (mg/L)	Chemical-specific	
ρ_b = Dry Soil Bulk Density (kg/L)	1.38	Default for Silty Soil; Value obtained from *User's Guide for Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
K_d = Soil-water Partition Coefficient (L/kg) $K_d = K_{oc} \times f_{oc}$	Calculated	
K_{oc} = Organic Carbon Partition Coefficient (L/kg)	Chemical-specific	
f_{oc} = Fraction Organic Carbon in Soil (g/g)	0.002	Default value for surface soil presented in Supplemental Soil Screening Guidance (USEPA, 2002)
θ_w = Water-filled Soil Porosity (L_{water}/L_{soil})	0.15	Default value presented in Supplemental Soil Screening Guidance (USEPA, 2002)
H' = Dimensionless Henry's Law Constant	Chemical-specific	
θ_a = Air-filled Soil Porosity (L_{air}/L_{soil})	0.33	Calculated as outlined in Equation 4-9 in Supplemental Soil Screening Guidance (USEPA, 2002)

CAS Number	Chemical	C_{sat} mg/kg	= (	S mg/L	+	ρ_b kg/L	) × ((	K_{oc} L/kg	×	f_{oc} g/g	) ×	ρ_b kg/L	) +	θ_w L_{water}/L_{soil}	+ (	H' Unitless	×	θ_a L_{air}/L_{soil})
95487	o-Cresol	2.58E+04	= (	2.59E+04	+	1.38	) × ((	4.43E+02	×	0.002	) ×	1.38	) +	0.15	+ (	4.91E-05	×	0.33)
106445	p-Cresol	2.10E+04	= (	2.15E+04	+	1.38	) × ((	4.34E+02	×	0.002	) ×	1.38	) +	0.15	+ (	4.09E-05	×	0.33)
198550	Perylene (Dibenz[de,kl]anthracene)	1.02E+00	= (	1.31E-04	+	1.38	) × ((	3.89E+06	×	0.002	) ×	1.38	) +	0.15	+ (	3.50E-13	×	0.33)
85018	Phenthrene	4.60E+01	= (	1.15E+00	+	1.38	) × ((	2.08E+04	×	0.002	) ×	1.38	) +	0.15	+ (	1.73E-03	×	0.33)
108952	Phenol	5.34E+04	= (	8.28E+04	+	1.38	) × ((	2.68E+02	×	0.002	) ×	1.38	) +	0.15	+ (	1.36E-05	×	0.33)
129000	Pyrene	1.88E+01	= (	1.35E-01	+	1.38	) × ((	6.94E+04	×	0.002	) ×	1.38	) +	0.15	+ (	4.87E-04	×	0.33)
71556	1,1,1-Trichloroethane	4.82E+02	= (	1.29E+03	+	1.38	) × ((	4.86E+01	×	0.002	) ×	1.38	) +	0.15	+ (	7.03E-01	×	0.33)
526738	1,2,3-Trimethylbenzene	9.91E+01	= (	7.52E+01	+	1.38	) × ((	5.89E+02	×	0.002	) ×	1.38	) +	0.15	+ (	1.33E-01	×	0.33)
120821	1,2,4-Trichlorobenzene	1.80E+02	= (	4.90E+01	+	1.38	) × ((	1.78E+03	×	0.002	) ×	1.38	) +	0.15	+ (	1.42E-03	×	0.33)
95636	1,2,4-Trimethylbenzene	9.14E+01	= (	5.70E+01	+	1.38	) × ((	7.18E+02	×	0.002	) ×	1.38	) +	0.15	+ (	2.52E-01	×	0.33)
108678	1,3,5-Trimethylbenzene	7.71E+01	= (	4.82E+01	+	1.38	) × ((	7.03E+02	×	0.002	) ×	1.38	) +	0.15	+ (	3.59E-01	×	0.33)
106467	1,4-Dichlorobenzene	8.13E+01	= (	8.13E+01	+	1.38	) × ((	4.34E+02	×	0.002	) ×	1.38	) +	0.15	+ (	9.85E-02	×	0.33)
71432	Benzene	6.84E+02	= (	1.79E+03	+	1.38	) × ((	1.66E+02	×	0.002	) ×	1.38	) +	0.15	+ (	2.27E-01	×	0.33)
56235	Carbon tetrachloride	3.77E+02	= (	7.93E+02	+	1.38	) × ((	4.86E+01	×	0.002	) ×	1.38	) +	0.15	+ (	1.13E+00	×	0.33)
74873	Chloromethane	1.19E+03	= (	5.32E+03	+	1.38	) × ((	1.43E+01	×	0.002	) ×	1.38	) +	0.15	+ (	3.61E-01	×	0.33)
75718	Dichlorodifluoromethane	9.93E+02	= (	2.80E+02	+	1.38	) × ((	4.86E+01	×	0.002	) ×	1.38	) +	0.15	+ (	1.40E+01	×	0.33)
100414	Ethylbenzene	2.06E+02	= (	1.69E+02	+	1.38	) × ((	5.18E+02	×	0.002	) ×	1.38	) +	0.15	+ (	3.22E-01	×	0.33)
75092	Methylene chloride	2.44E+03	= (	1.30E+04	+	1.38	) × ((	2.37E+01	×	0.002	) ×	1.38	) +	0.15	+ (	1.33E-01	×	0.33)
108383	m-Xylenes	1.71E+02	= (	1.61E+02	+	1.38	) × ((	4.43E+02	×	0.002	) ×	1.38	) +	0.15	+ (	2.71E-01	×	0.33)
106423	p-Xylenes	1.72E+02	= (	1.62E+02	+	1.38	) × ((	4.43E+02	×	0.002	) ×	1.38	) +	0.15	+ (	2.71E-01	×	0.33)
104518	n-Butyl benzene	5.66E+01	= (	1.08E+01	+	1.38	) × ((	2.51E+03	×	0.002	) ×	1.38	) +	0.15	+ (	5.57E-01	×	0.33)
95476	o-Xylene	1.11E+02	= (	1.06E+02	+	1.38	) × ((	4.43E+02	×	0.002	) ×	1.38	) +	0.15	+ (	2.12E-01	×	0.33)
135988	sec-Butyl benzene	7.98E+01	= (	1.81E+01	+	1.38	) × ((	2.09E+03	×	0.002	) ×	1.38	) +	0.15	+ (	5.07E-01	×	0.33)
100425	Styrene	3.63E+02	= (	3.10E+02	+	1.38	) × ((	5.18E+02	×	0.002	) ×	1.38	) +	0.15	+ (	1.12E-01	×	0.33)

Attachment H1

Table 1
Soil Saturation Concentration Calculations for Surface Soil

Equation:

$$C_{sat} = \frac{S}{\rho_b}\left(\left(K_d \times \rho_b\right) + \theta_w + \left(H' \times \theta_a\right)\right)$$

C_{sat} = Soil Saturation Concentration (mg/kg)	Calculated	
S = Solubility in Water (mg/L)	Chemical-specific	
ρ_b = Dry Soil Bulk Density (kg/L)	1.38	Default for Silty Soil; Value obtained from *User's Guide for Evaluating Subsurface Vapor Intrusion Into Buildings (USEPA, 2003).*
K_d = Soil-water Partition Coefficient (L/kg) $K_d = K_{oc} \times f_{oc}$	Calculated	
K_{oc} = Organic Carbon Partition Coefficient (L/kg)	Chemical-specific	
f_{oc} = Fraction Organic Carbon in Soil (g/g)	0.002	Default value for surface soil presented in Supplemental Soil Screening Guidance (USEPA, 2002)
θ_w = Water-filled Soil Porosity (L_{water}/L_{soil})	0.15	Default value presented in Supplemental Soil Screening Guidance (USEPA, 2002)
H' = Dimensionless Henry's Law Constant	Chemical-specific	
θ_a = Air-filled Soil Porosity (L_{air}/L_{soil})	0.33	Calculated as outlined in Equation 4-9 in Supplemental Soil Screening Guidance (USEPA, 2002)

CAS Number	Chemical	C_{sat} mg/kg	=	(	S mg/L	÷	ρ_b kg/L	) × ((	K_{oc} L/kg	×	f_{oc} g/g	) ×	ρ_b kg/L	) +	θ_w L_{water}/L_{soil}	+	(	H' Unitless	×	θ_a L_{air}/L_{soil}	)
108883	Toluene	3.73E+02	=	(	5.26E+02	÷	1.38	) × ((	2.68E+02	×	0.002	) ×	1.38	) +	0.15	+	(	2.71E-01	×	0.33	)
79016	Trichloroethene	4.36E+02	=	(	1.28E+03	÷	1.38	) × ((	6.77E+01	×	0.002	) ×	1.38	) +	0.15	+	(	4.03E-01	×	0.33	)
75694	Trichlorofluoromethane	1.27E+03	=	(	1.10E+03	÷	1.38	) × ((	4.86E+01	×	0.002	) ×	1.38	) +	0.15	+	(	3.97E+00	×	0.33	)
1330207	Xylenes (total)	1.12E+02	=	(	1.06E+02	÷	1.38	) × ((	4.43E+02	×	0.002	) ×	1.38	) +	0.15	+	(	2.71E-01	×	0.33	)

Attachment H1

Table 2
Soil Saturation Concentration Calculations for Subsurface Soil

Equation:

$$C_{sat} = \frac{S}{\rho_b}\left(\left(K_d \times \rho_b\right) + \theta_w + \left(H' \times \theta_a\right)\right)$$

C_{sat} = Soil Saturation Concentration (mg/kg)	Calculated	
S = Solubility in Water (mg/L)	Chemical-specific	
ρ_b = Dry Soil Bulk Density (kg/L)	1.38	Default for Silty Soil; Value obtained from *User's Guide for Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
K_d = Soil-water Partition Coefficient (L/kg) $K_d = K_{oc} \times f_{oc}$	Calculated	
K_{oc} = Organic Carbon Partition Coefficient (L/kg)	Chemical-specific	
f_{oc} = Fraction Organic Carbon in Soil (g/g)	0.006	Default value for subsurface soil presented in Supplemental Soil Screening Guidance (USEPA, 2002)
θ_w = Water-filled Soil Porosity (L_{water}/L_{soil})	0.15	Default value presented in Supplemental Soil Screening Guidance (USEPA, 2002)
H' = Dimensionless Henry's Law Constant	Chemical-specific	
θ_a = Air-filled Soil Porosity (L_{air}/L_{soil})	0.33	Calculated as outlined in Equation 4-9 in Supplemental Soil Screening Guidance (USEPA, 2002)

CAS Number	Chemical	C_{sat} mg/kg	= (	S mg/L	÷	ρ_b kg/L	) × ((	K_{oc} L/kg	×	f_{oc} g/g	) ×	ρ_b kg/L	) +	θ_w L_{water}/L_{soil}	+ (	H' Unitless	×	θ_a L_{air}/L_{soil}	)
90120	1-Methylnaphthalene	2.78E+02	= (	2.50E+01	+	1.38	) × ((	1.84E+03	×	0.006	) ×	1.38	) +	0.15	+ (	1.64E-02	×	0.33	)
832699	1-Methylphenanthrene	NA	= (	NV	+	1.38	) × ((	NV	×	0.006	) ×	1.38	) +	0.15	+ (	NA	×	0.33	)
2245387	2,3,5-Trimethylphthalene	NA	= (	NV	+	1.38	) × ((	NV	×	0.006	) ×	1.38	) +	0.15	+ (	NA	×	0.33	)
581420	2,6-Dimethylphthalene	NA	= (	NV	+	1.38	) × ((	NV	×	0.006	) ×	1.38	) +	0.15	+ (	NA	×	0.33	)
91576	2-Methylphthalene	4.42E+02	= (	2.46E+01	+	1.38	) × ((	2.98E+03	×	0.006	) ×	1.38	) +	0.15	+ (	2.12E-02	×	0.33	)
83329	Acephthene	1.44E+02	= (	3.90E+00	+	1.38	) × ((	6.12E+03	×	0.006	) ×	1.38	) +	0.15	+ (	7.44E-03	×	0.33	)
208968	Acephthylene	5.93E+02	= (	1.61E+01	+	1.38	) × ((	6.12E+03	×	0.006	) ×	1.38	) +	0.15	+ (	5.11E-03	×	0.33	)
120127	Anthracene	5.32E+00	= (	4.34E-02	+	1.38	) × ((	2.04E+04	×	0.006	) ×	1.38	) +	0.15	+ (	2.27E-03	×	0.33	)
56553	Benzo(a)anthracene	1.30E+01	= (	9.40E-03	+	1.38	) × ((	2.31E+05	×	0.006	) ×	1.38	) +	0.15	+ (	4.91E-04	×	0.33	)
50328	Benzo(a)pyrene	7.65E+00	= (	1.62E-03	+	1.38	) × ((	7.87E+05	×	0.006	) ×	1.38	) +	0.15	+ (	4.63E-05	×	0.33	)
205992	Benzo(b)fluoranthene	7.23E+00	= (	1.50E-03	+	1.38	) × ((	8.03E+05	×	0.006	) ×	1.38	) +	0.15	+ (	2.69E-05	×	0.33	)
192972	Benzo(e)pyrene	8.18E+00	= (	8.60E-04	+	1.38	) × ((	1.58E+06	×	0.006	) ×	1.38	) +	0.15	+ (	2.38E-05	×	0.33	)
191242	Benzo(g,h,i)perylene	4.18E+00	= (	2.60E-04	+	1.38	) × ((	2.68E+06	×	0.006	) ×	1.38	) +	0.15	+ (	1.35E-05	×	0.33	)
207089	Benzo(k)fluoranthene	3.78E+00	= (	8.00E-04	+	1.38	) × ((	7.87E+05	×	0.006	) ×	1.38	) +	0.15	+ (	2.39E-05	×	0.33	)
92524	Biphenyl	2.61E+02	= (	6.94E+00	+	1.38	) × ((	6.25E+03	×	0.006	) ×	1.38	) +	0.15	+ (	1.26E-02	×	0.33	)
218019	Chrysene	2.83E+00	= (	2.00E-03	+	1.38	) × ((	2.36E+05	×	0.006	) ×	1.38	) +	0.15	+ (	2.14E-04	×	0.33	)
53703	Dibenzo(a,h)anthracene	1.62E+01	= (	1.03E-03	+	1.38	) × ((	2.62E+06	×	0.006	) ×	1.38	) +	0.15	+ (	5.03E-06	×	0.33	)
132649	Dibenzofuran	2.11E+02	= (	3.10E+00	+	1.38	) × ((	1.13E+04	×	0.006	) ×	1.38	) +	0.15	+ (	8.71E-03	×	0.33	)
206440	Fluoranthene	1.11E+02	= (	2.60E-01	+	1.38	) × ((	7.09E+04	×	0.006	) ×	1.38	) +	0.15	+ (	3.62E-04	×	0.33	)
86737	Fluorene	1.28E+02	= (	1.89E+00	+	1.38	) × ((	1.13E+04	×	0.006	) ×	1.38	) +	0.15	+ (	3.93E-03	×	0.33	)
193395	Indeno(1,2,3-cd)pyrene	3.06E+00	= (	1.90E-04	+	1.38	) × ((	2.68E+06	×	0.006	) ×	1.38	) +	0.15	+ (	1.42E-05	×	0.33	)
108394	m -Cresols	6.16E+04	= (	2.27E+04	+	1.38	) × ((	4.34E+02	×	0.006	) ×	1.38	) +	0.15	+ (	4.09E-05	×	0.33	)
106445	p-Cresols	5.83E+04	= (	2.15E+04	+	1.38	) × ((	4.34E+02	×	0.006	) ×	1.38	) +	0.15	+ (	4.09E-05	×	0.33	)
91203	phthalene	3.45E+02	= (	3.10E+01	+	1.38	) × ((	1.84E+03	×	0.006	) ×	1.38	) +	0.15	+ (	1.80E-02	×	0.33	)
95487	o-Cresol	7.17E+04	= (	2.59E+04	+	1.38	) × ((	4.43E+02	×	0.006	) ×	1.38	) +	0.15	+ (	4.91E-05	×	0.33	)

Attachment H1

Table 2
Soil Saturation Concentration Calculations for Subsurface Soil

Equation:

$$C_{sat} = \frac{S}{\rho_b}\left(\left(K_d \times \rho_b\right) + \theta_w + \left(H' \times \theta_a\right)\right)$$

C_{sat} = Soil Saturation Concentration (mg/kg)	Calculated	
S = Solubility in Water (mg/L)	Chemical-specific	
ρ_b = Dry Soil Bulk Density (kg/L)	1.38	Default for Silty Soil; Value obtained from *User's Guide for Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
K_d = Soil-water Partition Coefficient (L/kg) $K_d = K_{oc} \times f_{oc}$	Calculated	
K_{oc} = Organic Carbon Partition Coefficient (L/kg)	Chemical-specific	
f_{oc} = Fraction Organic Carbon in Soil (g/g)	0.006	Default value for subsurface soil presented in Supplemental Soil Screening Guidance (USEPA, 2002)
θ_w = Water-filled Soil Porosity (L_{water}/L_{soil})	0.15	Default value presented in Supplemental Soil Screening Guidance (USEPA, 2002)
H' = Dimensionless Henry's Law Constant	Chemical-specific	
θ_a = Air-filled Soil Porosity (L_{air}/L_{soil})	0.33	Calculated as outlined in Equation 4-9 in Supplemental Soil Screening Guidance (USEPA, 2002)

CAS Number	Chemical	C_{sat} mg/kg	= (	S mg/L	÷	ρ_b kg/L	) × ((	K_{oc} L/kg	×	f_{oc} g/g	) ×	ρ_b kg/L	) +	θ_w L_{water}/L_{soil}	+ (	H' Unitless	×	θ_a L_{air}/L_{soil}	)
106445	p-Cresol	5.83E+04	= (	2.15E+04	÷	1.38	) × ((	4.34E+02	×	0.006	) ×	1.38	) +	0.15	+ (	4.09E-05	×	0.33	)
198550	Perylene (Dibenz[de,kl]anthracene)	3.06E+00	= (	1.31E-04	÷	1.38	) × ((	3.89E+06	×	0.006	) ×	1.38	) +	0.15	+ (	3.50E-13	×	0.33	)
85018	Phenthrene	1.44E+02	= (	1.15E+00	÷	1.38	) × ((	2.08E+04	×	0.006	) ×	1.38	) +	0.15	+ (	1.73E-03	×	0.33	)
108952	Phenol	1.42E+05	= (	8.28E+04	÷	1.38	) × ((	2.68E+02	×	0.006	) ×	1.38	) +	0.15	+ (	1.36E-05	×	0.33	)
129000	*Pyrene*	5.62E+01	= (	*1.35E-01*	÷	*1.38*	) × ((	*6.94E+04*	×	*0.006*	) ×	*1.38*	) +	*0.15*	+ (	*4.87E-04*	×	*0.33*	)
71556	1,1,1-Trichloroethane	7.33E+02	= (	1.29E+03	÷	1.38	) × ((	4.86E+01	×	0.006	) ×	1.38	) +	0.15	+ (	7.03E-01	×	0.33	)
526738	1,2,3-Trimethylbenzene	2.76E+02	= (	7.52E+01	÷	1.38	) × ((	5.89E+02	×	0.006	) ×	1.38	) +	0.15	+ (	1.33E-01	×	0.33	)
120821	1,2,4-Trichlorobenzene	5.29E+02	= (	4.90E+01	÷	1.38	) × ((	1.78E+03	×	0.006	) ×	1.38	) +	0.15	+ (	1.42E-03	×	0.33	)
95636	1,2,4-Trimethylbenzene	2.55E+02	= (	5.70E+01	÷	1.38	) × ((	7.18E+02	×	0.006	) ×	1.38	) +	0.15	+ (	2.52E-01	×	0.33	)
108678	1,3,5-Trimethylbenzene	2.13E+02	= (	4.82E+01	÷	1.38	) × ((	7.03E+02	×	0.006	) ×	1.38	) +	0.15	+ (	3.59E-01	×	0.33	)
106467	1,4-Dichlorobenzene	2.22E+02	= (	8.13E+01	÷	1.38	) × ((	4.34E+02	×	0.006	) ×	1.38	) +	0.15	+ (	9.85E-02	×	0.33	)
71432	Benzene	2.07E+03	= (	1.79E+03	÷	1.38	) × ((	1.66E+02	×	0.006	) ×	1.38	) +	0.15	+ (	2.27E-01	×	0.33	)
56235	Carbon tetrachloride	5.31E+02	= (	7.93E+02	÷	1.38	) × ((	4.86E+01	×	0.006	) ×	1.38	) +	0.15	+ (	1.13E+00	×	0.33	)
74873	Chloromethane	1.49E+03	= (	5.32E+03	÷	1.38	) × ((	1.43E+01	×	0.006	) ×	1.38	) +	0.15	+ (	3.61E-01	×	0.33	)
75718	Dichlorodifluoromethane	1.05E+03	= (	2.80E+02	÷	1.38	) × ((	4.86E+01	×	0.006	) ×	1.38	) +	0.15	+ (	1.40E+01	×	0.33	)
100414	Ethylbenzene	5.56E+02	= (	1.69E+02	÷	1.38	) × ((	5.18E+02	×	0.006	) ×	1.38	) +	0.15	+ (	3.22E-01	×	0.33	)
75092	Methylene chloride	3.68E+03	= (	1.30E+04	÷	1.38	) × ((	2.37E+01	×	0.006	) ×	1.38	) +	0.15	+ (	1.33E-01	×	0.33	)
108383	m-Xylenes	4.56E+02	= (	1.61E+02	÷	1.38	) × ((	4.43E+02	×	0.006	) ×	1.38	) +	0.15	+ (	2.71E-01	×	0.33	)
106423	p-Xylenes	4.59E+02	= (	1.62E+02	÷	1.38	) × ((	4.43E+02	×	0.006	) ×	1.38	) +	0.15	+ (	2.71E-01	×	0.33	)
104518	n-Butyl benzene	1.65E+02	= (	1.08E+01	÷	1.38	) × ((	2.51E+03	×	0.006	) ×	1.38	) +	0.15	+ (	5.57E-01	×	0.33	)
95476	o-Xylene	2.99E+02	= (	1.06E+02	÷	1.38	) × ((	4.43E+02	×	0.006	) ×	1.38	) +	0.15	+ (	2.12E-01	×	0.33	)
135988	sec-Butyl benzene	2.31E+02	= (	1.81E+01	÷	1.38	) × ((	2.09E+03	×	0.006	) ×	1.38	) +	0.15	+ (	5.07E-01	×	0.33	)
100425	*Styrene*	1.01E+03	= (	3.10E+02	÷	1.38	) × ((	5.18E+02	×	0.006	) ×	1.38	) +	0.15	+ (	1.12E-01	×	0.33	)
108883	Toluene	9.37E+02	= (	5.26E+02	÷	1.38	) × ((	2.68E+02	×	0.006	) ×	1.38	) +	0.15	+ (	2.71E-01	×	0.33	)
79016	Trichloroethene	7.82E+02	= (	1.28E+03	÷	1.38	) × ((	6.77E+01	×	0.006	) ×	1.38	) +	0.15	+ (	4.03E-01	×	0.33	)

Attachment H1

Table 2
Soil Saturation Concentration Calculations for Subsurface Soil

Equation:

$$C_{sat} = \frac{S}{\rho_b}\left(\left(K_d \times \rho_b\right) + \theta_w + \left(H' \times \theta_a\right)\right)$$

C_{sat} = Soil Saturation Concentration (mg/kg)	Calculated	
S = Solubility in Water (mg/L)	Chemical-specific	
ρ_b = Dry Soil Bulk Density (kg/L)	1.38	Default for Silty Soil; Value obtained from *User's Guide for Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
K_d = Soil-water Partition Coefficient (L/kg) $K_d = K_{oc} \times f_{oc}$	Calculated	
K_{oc} = Organic Carbon Partition Coefficient (L/kg)	Chemical-specific	
f_{oc} = Fraction Organic Carbon in Soil (g/g)	0.006	Default value for subsurface soil presented in Supplemental Soil Screening Guidance (USEPA, 2002)
θ_w = Water-filled Soil Porosity (L_{water}/L_{soil})	0.15	Default value presented in Supplemental Soil Screening Guidance (USEPA, 2002)
H' = Dimensionless Henry's Law Constant	Chemical-specific	
θ_a = Air-filled Soil Porosity (L_{air}/L_{soil})	0.33	Calculated as outlined in Equation 4-9 in Supplemental Soil Screening Guidance (USEPA, 2002)

CAS Number	Chemical	C_{sat} mg/kg	=	(	S mg/L	÷	ρ_b kg/L	) × ((	K_{oc} L/kg	×	f_{oc} g/g	) ×	ρ_b kg/L	) +	θ_w L_{water}/L_{soil}	+	(	H' Unitless	×	θ_a L_{air}/L_{soil}	)
75694	Trichlorofluoromethane	1.48E+03	=	(	1.10E+03	÷	1.38	) × ((	4.86E+01	×	0.006	) ×	1.38	) +	0.15	+	(	3.97E+00	×	0.33	)
1330207	Xylenes (total)	3.00E+02	=	(	1.06E+02	÷	1.38	) × ((	4.43E+02	×	0.006	) ×	1.38	) +	0.15	+	(	2.71E-01	×	0.33	)

ATTACHMENT H2

Exposure Point Concentration Summary

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Attachment H2

Table 1
Exposure Point Concentration
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 feet)
Excluding VOC Exceeding Csat Values

Analyte	Detection Range (mg/kg)	Frequency of Detection	Maximum Concentration (mg/kg)	Average Concentration (mg/kg)	95% UCL (mg/kg)	Distribution	Statistic used for 95% UCL	Rationale	Selected EPC (mg/kg)
Inorganics									
Arsenic	0.87 - 23.4	87 / 103	23.4	4.30	5.07	lognormal	Standard Boostrap		5.07
Lead	6 - 4000	82 / 103	4000	90.48	-	-	-	Per EPA Guidance	90.48
Thallium	1.5 - 1.8	2 / 86	1.8	0.78	0.82	normal	Student's-t UCL		0.82
SVOCs									
1-Methylnaphthalene	0.051 - 3800	36 / 86	3800	75.31	150	non-parametric	Standard Boostrap		150.12
2-Methylnaphthalene	0.0076 - 3300	47 / 102	3300	80.47	144	non-parametric	Standard Boostrap		143.91
Acenaphthene	0.00059 - 670	33 / 101	670	21.78	36	non-parametric	Standard Boostrap		36.42
Benzo(a)anthracene	0.044 - 520	50 / 102	520	14.63	24.6	non-parametric	Standard Boostrap		24.59
Benzo(a)pyrene	0.06 - 340	50 / 104	340	12.27	20	non-parametric	Standard Boostrap		19.51
Benzo(b)fluoranthene	0.07 - 410	50 / 102	410	13.03	21.3	non-parametric	Standard Boostrap		21.28
Benzo(k)fluoranthene	0.045 - 170	35 / 102	170	6.35	10.1	non-parametric	Standard Boostrap		10.12
Chrysene	0.059 - 470	47 / 102	470	14.01	23.4	non-parametric	Standard Boostrap		23.38
Dibenzo(a,h)anthracene	0.12 - 3.8	6 / 102	3.8	2.03	3.1	non-parametric	Standard Boostrap		3.12
Dibenzofuran	0.079 - 280	14 / 86	280	4.67	9.9	non-parametric	Standard Boostrap		9.93
Fluoranthene	0.047 - 1400	57 / 103	1400	36.74	64	non-parametric	Standard Boostrap		63.62
Fluorene	0.0015 - 1200	34 / 101	1200	25.35	46	non-parametric	Standard Boostrap		45.88
Indeno(1,2,3-cd)pyrene	0.037 - 100	32 / 102	100	3.44	5.3	non-parametric	Standard Boostrap		5.34
Naphthalene	0.00024 - 2900	62 / 123	2900	121.18	186	non-parametric	Standard Boostrap		186.15
Phenanthrene	0.0054 - 3700	60 / 104	3700	79.45	144	non-parametric	Standard Boostrap		143.81
Pyrene	0.048 - 2000	64 / 104	2000	49.18	86	non-parametric	Standard Boostrap		85.60
VOCs									
1,2,4-Trichlorobenzene	0.0097 - 120	7 / 16	120	15.44	29.64	non-parametric	Standard Boostrap		29.64
1,2,4-Trimethylbenzene	0.02 - 100	43 / 87	100	3.77	6.05	non-parametric	Standard Boostrap		6.05
1,3,5-Trimethylbenzene	0.0079 - 30	36 / 102	30	1.46	2.22	non-parametric	Standard Boostrap		2.22
Benzene	0.016 - 230	49 / 104	230	8.40	14.14	non-parametric	Standard Boostrap		14.14
Xylenes (total)	0.046 - 170	6 / 17	170	5.88	13.03	non-parametric	Standard Boostrap		13.03

All units are milligrams per kilogram (mg/kg).

EPC– Exposure Point Concentration
mg/kg – milligrams per kilogram
SVOC– Semi-volatile organic compound
UCL– Upper Confidence Limit
VOC– Volatile organic compound

Attachment H2

Table 2
Exposure Point Concentration
Construction Worker Receptor Exposed to Surface and Subsurface Soil
Excluding VOC Exceeding Csat Values

Analyte	Detection Range (mg/kg)	Frequency of Detection	Maximum Concentration (mg/kg)	Average Concentration (mg/kg)	95% UCL (mg/kg)	Distribution	Statistic used for 95% UCL	Rationale	Selected EPC (mg/kg)
Inorganics									
Arsenic	0.83 - 36	140 / 190	36	4.22	4.90	non-parametric	Standard Bootstrap		4.90
Lead	3.32 - 4000	173 / 207	4000	88.74	-	-	-	Per EPA Guidance	88.74
SVOCs									
1-Methylnaphthalene	0.04 - 21000	75 / 181	21000	899.28	1,313.53	non-parametric	Standard Bootstrap		1,313.53
2-Methylnaphthalene	0.0076 - 30000	97 / 209	30000	965.35	1,412.33	non-parametric	Standard Bootstrap		1,412.33
Acenaphthene	0.00059 - 8200	84 / 211	8200	317.16	440.69	non-parametric	Standard Bootstrap		440.69
Benzo(a)anthracene	0.0173 - 2400	128 / 224	2400	146.29	197.30	non-parametric	Standard Bootstrap		197.30
Benzo(a)pyrene	0.0219 - 3000	130 / 241	3000	126.85	172.82	non-parametric	Standard Bootstrap		172.82
Benzo(b)fluoranthene	0.0149 - 1300	128 / 210	1300	76.78	101.95	non-parametric	Standard Bootstrap		101.95
Benzo(k)fluoranthene	0.00669 - 1600	96 / 216	1600	87.17	118.65	non-parametric	Standard Bootstrap		118.65
Chrysene	0.0118 - 2300	120 / 219	2300	134.76	181.33	non-parametric	Standard Bootstrap		181.33
Dibenzo(a,h)anthracene	0.12 - 350	44 / 188	350	19.43	26.19	non-parametric	Standard Bootstrap		26.19
Dibenzofuran	0.042 - 1400	50 / 181	1400	63.08	89.23	non-parametric	Standard Bootstrap		89.23
Fluoranthene	0.047 - 5400	142 / 227	5400	245.24	329.11	non-parametric	Standard Bootstrap		329.11
Fluorene	0.0015 - 4600	89 / 214	4600	206.67	282.16	non-parametric	Standard Bootstrap		282.16
Indeno(1,2,3-cd)pyrene	0.0113 - 1500	98 / 220	1500	68.43	93.43	non-parametric	Standard Bootstrap		93.43
Naphthalene	0.00024 - 37000	146 / 278	37000	800.64	1,172.94	non-parametric	Standard Bootstrap		1,172.94
Pyrene	0.042 - 8400	153 / 241	8400	360.14	484.99	non-parametric	Standard Bootstrap		484.99
VOCs									
1,2,4-Trichlorobenzene	0.0097 - 157	22 / 45	157	9.19	16.87	non-parametric	Standard Bootstrap		16.87
1,2,4-Trimethylbenzene	0.019 - 100	51 / 149	100	2.23	3.56	non-parametric	Standard Bootstrap		3.56
1,3,5-Trimethylbenzene	0.0079 - 30	48 / 174	30	0.97	1.44	non-parametric	Standard Bootstrap		1.44
Benzene	0.005 - 645	68 / 194	645	7.91	14.22	non-parametric	Standard Bootstrap		14.22

All units are milligrams per kilogram (mg/kg).

EPC– Exposure Point Concentration
mg/kg – milligrams per kilogram
SVOC– Semi-volatile organic compound
UCL– Upper Confidence Limit
VOC– Volatile organic compound

Attachment H2

Table 3
Exposure Point Concentration
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 feet)
Excluding VOCs Exceeding Csat Values

Analyte	Detection Range (mg/kg)	Frequency of Detection	Maximum Concentration (mg/kg)	Average Concentration (mg/kg)	95% UCL (mg/kg)	Distribution	Statistic used for 95% UCL	Rationale	Selected EPC (mg/kg)
Inorganics									
Arsenic	0.87 - 13	29 / 40	13	2.97	3.74	gamma	Standard Boostrap		3.74
Lead	9.6 - 4000	26 / 40	4000	176.19	-	-	-	Per EPA Guidance	176.19
SVOCs									
1-Methylnaphthalene	0.051 - 230	8 / 40	230	7.21	16.61	non-parametric	Standard Boostrap		16.61
Benzo(a)anthracene	0.044 - 190	18 / 40	190	5.77	13.58	non-parametric	Standard Boostrap		13.58
Benzo(a)pyrene	0.060 - 220	18 / 40	220	6.97	16.13	non-parametric	Standard Boostrap		16.13
Benzo(b)fluoranthene	0.070 - 180	21 / 40	180	6.12	13.47	non-parametric	Standard Boostrap		13.47
Benzo(k)fluoranthene	0.069 - 56	13 / 40	56	1.98	4.23	non-parametric	Standard Boostrap		4.23
Dibenzo(a,h)anthracene	0.12 - 3.8	3 / 40	3.8	0.39	0.76	non-parametric	Standard Boostrap		0.76
Fluoranthene	0.047 - 390	21 / 40	390	11.18	26.47	non-parametric	Standard Boostrap		26.47
Indeno(1,2,3-cd)pyrene	0.037 - 45	12 / 40	45	1.54	3.39	non-parametric	Standard Boostrap		3.39
Naphthalene	0.051 - 91	7 / 40	91	2.82	6.46	non-parametric	Standard Boostrap		6.46
Pyrene	0.046 - 670	24 / 40	670	19.10	46.98	non-parametric	Standard Boostrap		46.98
VOCs									
1,2,4-Trimethylbenzene	0.020 - 15	4 / 40	15	0.61	1.32	non-parametric	Standard Boostrap		1.32
1,3,5-Trimethylbenzene	0.074 - 5.4	13 / 40	5.4	0.23	0.49	non-parametric	Standard Boostrap		0.49
Benzene	0.018 - 25	7 / 40	25	0.89	1.95	non-parametric	Standard Boostrap		1.95

All units are milligrams per kilogram (mg/kg).

EPC– Exposure Point Concentration
mg/kg – milligrams per kilogram
SVOC– Semi-volatile organic compound
UCL– Upper Confidence Limit
VOC– Volatile organic compound

ATTACHMENT H3

ProUCL Output Tables

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Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil
1,2,4-Trimethylbenzene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	14
Minimum	7.5
Maximum	15000
Mean	613.3375
Median	7.5
Standard Deviation	2706.627
Variance	7325829
Coefficient of Variation	4.412949
Skewness	4.762315

Gamma Statistics	
k hat	0.206001
k star (bias corrected)	0.207217
Theta hat	2977.358
Theta star	2959.877
nu hat	16.48005
nu star	16.57738
Approx.Chi Square Value (.05)	8.369755
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	8.15066

Log-transformed Statistics	
Minimum of log data	2.014903
Maximum of log data	9.615805
Mean of log data	2.862975
Standard Deviation of log data	1.739353
Variance of log data	3.025348

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are microgram per kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.248484
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	1334.389

Gamma Distribution Test	
A-D Test Statistic	11.39951
A-D 5% Critical Value	0.900121
K-S Test Statistic	0.416167
K-S 5% Critical Value	0.154241
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	1214.794
Adjusted Gamma UCL	1247.448

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.556659
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	200.1478
95% Chebyshev (MVUE) UCL	191.6996
97.5% Chebyshev (MVUE) UCL	243.1038
99% Chebyshev (MVUE) UCL	344.0774

95% Non-parametric UCLs	
CLT UCL	1317.261
Adj-CLT UCL (Adjusted for skewness)	1661.585
Mod-t UCL (Adjusted for skewness)	1388.096
Jackknife UCL	1334.389
Standard Bootstrap UCL	1320.463
Bootstrap-t UCL	52495.61
Hall's Bootstrap UCL	43570.2
Percentile Bootstrap UCL	1362.425
BCA Bootstrap UCL	1733.888
95% Chebyshev (Mean, Sd) UCL	2478.751
97.5% Chebyshev (Mean, Sd) UCL	3285.917
99% Chebyshev (Mean, Sd) UCL	4871.439

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil
1,3,5-Trimethylbenzene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	5
Minimum	8
Maximum	5400
Mean	232.8
Median	8
Standard Deviation	971.549732
Variance	943908.882
Coefficient of Variation	4.17332359
Skewness	4.74240511

Gamma Statistics	
k hat	0.24544169
k star (bias corrected)	0.24370023
Theta hat	948.494111
Theta star	955.271966
nu hat	19.6353354
nu star	19.4960186
Approx.Chi Square Value (.05)	10.4790035
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	10.2305484

Log-transformed Statistics	
Minimum of log data	2.07944154
Maximum of log data	8.59415423
Mean of log data	2.547663
Standard Deviation of log data	1.52230197
Variance of log data	2.31740328

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are microgram per kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.26142057
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	491.622884

Gamma Distribution Test	
A-D Test Statistic	13.7192926
A-D 5% Critical Value	0.88231308
K-S Test Statistic	0.55922326
K-S 5% Critical Value	0.15306584
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	433.120681
Adjusted Gamma UCL	443.639278

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.35128409
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	84.9584884
95% Chebyshev (MVUE) UCL	91.0735805
97.5% Chebyshev (MVUE) UCL	113.862084
99% Chebyshev (MVUE) UCL	158.625685

95% Non-parametric UCLs	
CLT UCL	485.475014
Adj-CLT UCL (Adjusted for skewness)	608.554056
Mod-t UCL (Adjusted for skewness)	510.820727
Jackknife UCL	491.622884
Standard Bootstrap UCL	485.535922
Bootstrap-t UCL	3204.32156
Hall's Bootstrap UCL	3886.93638
Percentile Bootstrap UCL	511.8
BCA Bootstrap UCL	646.6
95% Chebyshev (Mean, Sd) UCL	902.394444
97.5% Chebyshev (Mean, Sd) UCL	1192.12849
99% Chebyshev (Mean, Sd) UCL	1761.25493

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil
1-Methylnaphthalene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	14
Minimum	16
Maximum	230000
Mean	7205.6875
Median	31.5
Standard Deviation	37158.4285
Variance	1380748806
Coefficient of Variation	5.15681931
Skewness	5.8679174

Gamma Statistics	
k hat	0.16073387
k star (bias corrected)	0.1653455
Theta hat	44829.9247
Theta star	43579.5801
nu hat	12.85871
nu star	13.2276401
Approx.Chi Square Value (.05)	6.04501687
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	5.86285734

Log-transformed Statistics	
Minimum of log data	2.77258872
Maximum of log data	12.3458346
Mean of log data	4.14918914
Standard Deviation of log data	2.02965103
Variance of log data	4.11948329

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are microgram per kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.21120548
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	17104.7707

Gamma Distribution Test	
A-D Test Statistic	10.8857694
A-D 5% Critical Value	0.9262601
K-S Test Statistic	0.46537446
K-S 5% Critical Value	0.15586107
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	15767.4069
Adjusted Gamma UCL	16257.3017

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.6632246
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	1670.64634
95% Chebyshev (MVUE) UCL	1290.22717
97.5% Chebyshev (MVUE) UCL	1661.36575
99% Chebyshev (MVUE) UCL	2390.39563

95% Non-parametric UCLs	
CLT UCL	16869.6358
Adj-CLT UCL (Adjusted for skewness)	22694.1775
Mod-t UCL (Adjusted for skewness)	18013.2815
Jackknife UCL	17104.7707
Standard Bootstrap UCL	16930.9742
Bootstrap-t UCL	2114429.67
Hall's Bootstrap UCL	1681084.88
Percentile Bootstrap UCL	18685.0375
BCA Bootstrap UCL	25817.8375
95% Chebyshev (Mean, Sd) UCL	32815.367
97.5% Chebyshev (Mean, Sd) UCL	43896.6957
99% Chebyshev (Mean, Sd) UCL	65663.8203

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil
Arsenic (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	37
Minimum	0.325
Maximum	13
Mean	2.970375
Median	2.1
Standard Deviation	2.99074414
Variance	8.9445505
Coefficient of Variation	1.00685743
Skewness	1.60788608

Gamma Statistics	
k hat	1.10376882
k star (bias corrected)	1.03765282
Theta hat	2.6911206
Theta star	2.86259039
nu hat	88.3015055
nu star	83.0122259
Approx.Chi Square Value (.05)	63.0107351
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	62.3577453

Log-transformed Statistics	
Minimum of log data	-1.1239301
Maximum of log data	2.56494936
Mean of log data	0.57159141
Standard Deviation of log data	1.09451021
Variance of log data	1.19795261

RECOMMENDATION

Data follow gamma distribution (0.05)

Use Approximate Gamma UCL

All units are milligram per kilogram (mg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.81332856
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	3.7671155

Gamma Distribution Test	
A-D Test Statistic	0.62439236
A-D 5% Critical Value	0.77605069
K-S Test Statistic	0.12623353
K-S 5% Critical Value	0.14336926
Data follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	3.91326081
Adjusted Gamma UCL	3.9542392

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.92921742
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	4.97678314
95% Chebyshev (MVUE) UCL	5.98186692
97.5% Chebyshev (MVUE) UCL	7.20700042
99% Chebyshev (MVUE) UCL	9.61353794

95% Non-parametric UCLs	
CLT UCL	3.74819037
Adj-CLT UCL (Adjusted for skewness)	3.87664654
Mod-t UCL (Adjusted for skewness)	3.78715207
Jackknife UCL	3.7671155
Standard Bootstrap UCL	3.73289606
Bootstrap-t UCL	4.0036382
Hall's Bootstrap UCL	3.90431721
Percentile Bootstrap UCL	3.75825
BCA Bootstrap UCL	3.843125
95% Chebyshev (Mean, Sd) UCL	5.03160315
97.5% Chebyshev (Mean, Sd) UCL	5.92349822
99% Chebyshev (Mean, Sd) UCL	7.67545337

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil
Benzo(a)anthracene (0-3ft)

Raw Statistics	
Number of Valid Samples	38
Number of Unique Samples	19
Minimum	17
Maximum	2900
Mean	338.657895
Median	76
Standard Deviation	638.297324
Variance	407423.474
Coefficient of Variation	1.88478501
Skewness	2.77781273

Gamma Statistics	
k hat	0.46087024
k star (bias corrected)	0.4420296
Theta hat	734.822662
Theta star	766.143016
nu hat	35.0261381
nu star	33.59425
Approx.Chi Square Value (.05)	21.3381787
Adjusted Level of Significance	0.0434
Adjusted Chi Square Value	20.9326121

Log-transformed Statistics	
Minimum of log data	2.83321334
Maximum of log data	7.97246602
Mean of log data	4.42908351
Standard Deviation of log data	1.66609426
Variance of log data	2.7758701

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are microgram per kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.57332552
Shapiro-Wilk 5% Critical Value	0.938
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	513.348811

Gamma Distribution Test	
A-D Test Statistic	2.95263694
A-D 5% Critical Value	0.82145872
K-S Test Statistic	0.22726762
K-S 5% Critical Value	0.1521746
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	533.173807
Adjusted Gamma UCL	543.50398

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.84227682
Shapiro-Wilk 5% Critical Value	0.938
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	815.12583
95% Chebyshev (MVUE) UCL	797.917918
97.5% Chebyshev (MVUE) UCL	1008.93599
99% Chebyshev (MVUE) UCL	1423.44012

95% Non-parametric UCLs	
CLT UCL	508.975085
Adj-CLT UCL (Adjusted for skewness)	558.831702
Mod-t UCL (Adjusted for skewness)	521.125436
Jackknife UCL	513.348811
Standard Bootstrap UCL	502.406277
Bootstrap-t UCL	617.439816
Hall's Bootstrap UCL	686.215139
Percentile Bootstrap UCL	513.394737
BCA Bootstrap UCL	578.078947
95% Chebyshev (Mean, Sd) UCL	790.002261
97.5% Chebyshev (Mean, Sd) UCL	985.299329
99% Chebyshev (Mean, Sd) UCL	1368.9226

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil
Pyrene (0-3)

Raw Statistics	
Number of Valid Samples	38
Number of Unique Samples	22
Minimum	18
Maximum	7300
Mean	814.907895
Median	155
Standard Deviation	1.66E+03
Variance	2756053.94
Coefficient of Variation	2.03720781
Skewness	3.07227547

Gamma Statistics	
k hat	0.38254669
k star (bias corrected)	0.3698895
Theta hat	2130.21813
Theta star	2203.11175
nu hat	29.0735485
nu star	28.1116017
Approx.Chi Square Value (.05)	17.0130343
Adjusted Level of Significance	0.0434
Adjusted Chi Square Value	16.6544481

Log-transformed Statistics	
Minimum of log data	2.89037176
Maximum of log data	8.89562963
Mean of log data	4.97048697
Standard Deviation of log data	1.98910949
Variance of log data	3.95655655

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are microgram per kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.53558468
Shapiro-Wilk 5% Critical Value	0.938
Data not normal at 5% significance level	
95% UCL (Assuming Normal Distribution)	
Student's-t UCL	1269.25855

Gamma Distribution Test	
A-D Test Statistic	2.22290295
A-D 5% Critical Value	0.83885438
K-S Test Statistic	0.18756945
K-S 5% Critical Value	0.15374107
Data do not follow gamma distribution	
at 5% significance level	
95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	1346.51854
Adjusted Gamma UCL	1375.51038

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.8628843
Shapiro-Wilk 5% Critical Value	0.938
Data not lognormal at 5% significance level	
95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	3491.73336
95% Chebyshev (MVUE) UCL	2696.03613
97.5% Chebyshev (MVUE) UCL	3469.50498
99% Chebyshev (MVUE) UCL	4988.83476

95% Non-parametric UCLs	
CLT UCL	1257.883
Adj-CLT UCL (Adjusted for skewness)	1401.30006
Mod-t UCL (Adjusted for skewness)	1291.62871
Jackknife UCL	1269.25855
Standard Bootstrap UCL	1244.29779
Bootstrap-t UCL	1700.00474
Hall's Bootstrap UCL	3104.83501
Percentile Bootstrap UCL	1308.82895
BCA Bootstrap UCL	1429.60526
95% Chebyshev (Mean, Sd) UCL	1988.80183
97.5% Chebyshev (Mean, Sd) UCL	2496.74667
99% Chebyshev (Mean, Sd) UCL	3494.50596

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil
Dibenz(a,h)anthracene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	10
Minimum	17
Maximum	8500
Mean	394.725
Median	34
Standard Deviation	1450.06194
Variance	2102679.64
Coefficient of Variation	3.67360047
Skewness	5.05090365

Gamma Statistics	
k hat	0.33476519
k star (bias corrected)	0.32632447
Theta hat	1179.11004
Theta star	1209.60895
nu hat	26.7812156
nu star	26.1059577
Approx.Chi Square Value (.05)	15.459147
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	15.1512206

Log-transformed Statistics	
Minimum of log data	2.83321334
Maximum of log data	9.04782144
Mean of log data	3.95488067
Standard Deviation of log data	1.5278663
Variance of log data	2.33437543

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are microgram per kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.29347434
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	781.024539

Gamma Distribution Test	
A-D Test Statistic	7.0848659
A-D 5% Critical Value	0.84993431
K-S Test Statistic	0.33464504
K-S 5% Critical Value	0.15076556
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	666.574562
Adjusted Gamma UCL	680.121715

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.74994656
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	351.557859
95% Chebyshev (MVUE) UCL	375.960787
97.5% Chebyshev (MVUE) UCL	470.22173
99% Chebyshev (MVUE) UCL	655.3791

95% Non-parametric UCLs	
CLT UCL	771.848691
Adj-CLT UCL (Adjusted for skewness)	967.496984
Mod-t UCL (Adjusted for skewness)	811.541719
Jackknife UCL	781.024539
Standard Bootstrap UCL	775.622923
Bootstrap-t UCL	3019.44576
Hall's Bootstrap UCL	3581.59926
Percentile Bootstrap UCL	808.2
BCA Bootstrap UCL	1200.575
95% Chebyshev (Mean, Sd) UCL	1394.11123
97.5% Chebyshev (Mean, Sd) UCL	1826.54645
99% Chebyshev (Mean, Sd) UCL	2675.9817

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil
Indeno(1,2,3-c,d)pyrene (0-3ft)

Raw Statistics	
Number of Valid Samples	38
Number of Unique Samples	15
Minimum	15.5
Maximum	2700
Mean	238.934211
Median	31
Standard Deviation	612.987183
Variance	375753.286
Coefficient of Variation	2.56550613
Skewness	3.55751777

Gamma Statistics	
k hat	0.43386709
k star (bias corrected)	0.41715828
Theta hat	550.708309
Theta star	572.76631
nu hat	32.9738987
nu star	31.7040295
Approx.Chi Square Value (.05)	19.8353995
Adjusted Level of Significance	0.0434
Adjusted Chi Square Value	19.4455724

Log-transformed Statistics	
Minimum of log data	2.74084002
Maximum of log data	7.90100705
Mean of log data	3.97913753
Standard Deviation of log data	1.4775233
Variance of log data	2.1830751

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are microgram per kilogram (μg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.405927
Shapiro-Wilk 5% Critical Value	0.938
Data not normal at 5% significance level	
95% UCL (Assuming Normal Distribution)	
Student's-t UCL	406.69818

Gamma Distribution Test	
A-D Test Statistic	4.7678372
A-D 5% Critical Value	0.82745612
K-S Test Statistic	0.26868355
K-S 5% Critical Value	0.15271466
Data do not follow gamma distribution	
at 5% significance level	
95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	381.901927
Adjusted Gamma UCL	389.557947

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.80666992
Shapiro-Wilk 5% Critical Value	0.938
Data not lognormal at 5% significance level	
95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	328.335702
95% Chebyshev (MVUE) UCL	353.496357
97.5% Chebyshev (MVUE) UCL	441.277222
99% Chebyshev (MVUE) UCL	613.705733

95% Non-parametric UCLs	
CLT UCL	402.497883
Adj-CLT UCL (Adjusted for skewness)	463.816915
Mod-t UCL (Adjusted for skewness)	416.262709
Jackknife UCL	406.69818
Standard Bootstrap UCL	404.097888
Bootstrap-t UCL	711.787964
Hall's Bootstrap UCL	1075.5611
Percentile Bootstrap UCL	409.368421
BCA Bootstrap UCL	480.210526
95% Chebyshev (Mean, Sd) UCL	672.381604
97.5% Chebyshev (Mean, Sd) UCL	859.934638
99% Chebyshev (Mean, Sd) UCL	1228.34625

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil
Fluoranthene (0-3ft)

Raw Statistics	
Number of Valid Samples	39
Number of Unique Samples	24
Minimum	18.5
Maximum	40000
Mean	1468.89744
Median	100
Standard Deviation	6381.29627
Variance	40720942
Coefficient of Variation	4.34427626
Skewness	6.09949005

Gamma Statistics	
k hat	0.28609603
k star (bias corrected)	0.28118266
Theta hat	5134.28101
Theta star	5223.99715
nu hat	22.3154907
nu star	21.9322478
Approx.Chi Square Value (.05)	12.2859071
Adjusted Level of Significance	0.0437
Adjusted Chi Square Value	12.0003212

Log-transformed Statistics	
Minimum of log data	2.91777073
Maximum of log data	10.5966347
Mean of log data	4.86328683
Standard Deviation of log data	1.98778319
Variance of log data	3.95128199

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are microgram per kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.23377681
Shapiro-Wilk 5% Critical Value	0.939
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	3191.64791

Gamma Distribution Test	
A-D Test Statistic	4.05100801
A-D 5% Critical Value	0.8636538
K-S Test Statistic	0.22209646
K-S 5% Critical Value	0.15384063
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	2622.20951
Adjusted Gamma UCL	2684.61336

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.86518586
Shapiro-Wilk 5% Critical Value	0.939
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	3060.72995
95% Chebyshev (MVUE) UCL	2408.50975
97.5% Chebyshev (MVUE) UCL	3097.25016
99% Chebyshev (MVUE) UCL	4450.14732

95% Non-parametric UCLs	
CLT UCL	3149.65031
Adj-CLT UCL (Adjusted for skewness)	4216.04566
Mod-t UCL (Adjusted for skewness)	3357.98404
Jackknife UCL	3191.64791
Standard Bootstrap UCL	3148.9371
Bootstrap-t UCL	14437.9619
Hall's Bootstrap UCL	9342.00921
Percentile Bootstrap UCL	3468.03846
BCA Bootstrap UCL	4784.17949
95% Chebyshev (Mean, Sd) UCL	5922.93018
97.5% Chebyshev (Mean, Sd) UCL	7850.1937
99% Chebyshev (Mean, Sd) UCL	11635.9297

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil
Benzo(a)pyrene (0-3ft)

Raw Statistics	
Number of Valid Samples	37
Number of Unique Samples	17
Minimum	17
Maximum	4900
Mean	435.081081
Median	70
Standard Deviation	961.162299
Variance	923832.966
Coefficient of Variation	2.20915673
Skewness	3.42405993

Gamma Statistics	
k hat	0.4041217
k star (bias corrected)	0.38937309
Theta hat	1076.60906
Theta star	1117.38867
nu hat	29.9050056
nu star	28.8136088
Approx.Chi Square Value (.05)	17.5608039
Adjusted Level of Significance	0.0431
Adjusted Chi Square Value	17.1784824

Log-transformed Statistics	
Minimum of log data	2.83321334
Maximum of log data	8.49699048
Mean of log data	4.44990278
Standard Deviation of log data	1.7464232
Variance of log data	3.049994

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are microgram per kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.50655106
Shapiro-Wilk 5% Critical Value	0.936
Data not normal at 5% significance level	
95% UCL (Assuming Normal Distribution)	
Student's-t UCL	701.8559

Gamma Distribution Test	
A-D Test Statistic	3.32078751
A-D 5% Critical Value	0.83385301
K-S Test Statistic	0.25150924
K-S 5% Critical Value	0.15525433
Data do not follow gamma distribution	
at 5% significance level	
95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	713.877116
Adjusted Gamma UCL	729.765049

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.83894779
Shapiro-Wilk 5% Critical Value	0.936
Data not lognormal at 5% significance level	
95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	1046.41604
95% Chebyshev (MVUE) UCL	961.885022
97.5% Chebyshev (MVUE) UCL	1223.14326
99% Chebyshev (MVUE) UCL	1736.33449

95% Non-parametric UCLs	
CLT UCL	694.991161
Adj-CLT UCL (Adjusted for skewness)	790.033425
Mod-t UCL (Adjusted for skewness)	716.680573
Jackknife UCL	701.8559
Standard Bootstrap UCL	689.312249
Bootstrap-t UCL	952.698815
Hall's Bootstrap UCL	1026.26538
Percentile Bootstrap UCL	715.108108
BCA Bootstrap UCL	815.405405
95% Chebyshev (Mean, Sd) UCL	1123.84861
97.5% Chebyshev (Mean, Sd) UCL	1421.87887
99% Chebyshev (Mean, Sd) UCL	2007.30161

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil
Benzene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	8
Minimum	7.5
Maximum	25000
Mean	891.7375
Median	7.5
Standard Deviation	4070.682
Variance	16570452
Coefficient of Variation	4.56488821
Skewness	5.65837552

Gamma Statistics	
k hat	0.18213946
k star (bias corrected)	0.18514566
Theta hat	4895.90512
Theta star	4816.41038
nu hat	14.5711566
nu star	14.8116532
Approx.Chi Square Value (.05)	7.12954248
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	6.92942447

Log-transformed Statistics	
Minimum of log data	2.01490302
Maximum of log data	10.1266311
Mean of log data	2.69394106
Standard Deviation of log data	1.89640789
Variance of log data	3.59636288

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are microgram per kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.24375089
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	1976.17571

Gamma Distribution Test	
A-D Test Statistic	13.0322635
A-D 5% Critical Value	0.91348739
K-S Test Statistic	0.47631005
K-S 5% Critical Value	0.15507548
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	1852.58824
Adjusted Gamma UCL	1906.08998

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.41304453
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	261.448187
95% Chebyshev (MVUE) UCL	225.02581
97.5% Chebyshev (MVUE) UCL	287.872169
99% Chebyshev (MVUE) UCL	411.321671

95% Non-parametric UCLs	
CLT UCL	1950.41684
Adj-CLT UCL (Adjusted for skewness)	2565.70615
Mod-t UCL (Adjusted for skewness)	2072.14841
Jackknife UCL	1976.17571
Standard Bootstrap UCL	1945.03466
Bootstrap-t UCL	4712.35163
Hall's Bootstrap UCL	4981.57619
Percentile Bootstrap UCL	2140
BCA Bootstrap UCL	3020.5375
95% Chebyshev (Mean, Sd) UCL	3697.26146
97.5% Chebyshev (Mean, Sd) UCL	4911.21392
99% Chebyshev (Mean, Sd) UCL	7295.78845

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil
Napthalene (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	13
Minimum	15.5
Maximum	91000
Mean	2815.7375
Median	30.5
Standard Deviation	14579.2552
Variance	212554682
Coefficient of Variation	5.17777499
Skewness	5.99655251

Gamma Statistics	
k hat	0.19003325
k star (bias corrected)	0.19244742
Theta hat	14817.0781
Theta star	14631.204
nu hat	15.20266
nu star	15.3957938
Approx.Chi Square Value (.05)	7.53644883
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	7.32993938

Log-transformed Statistics	
Minimum of log data	2.74084002
Maximum of log data	11.4186148
Mean of log data	4.03955324
Standard Deviation of log data	1.89585897
Variance of log data	3.59428124

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are microgram per kilogram (μg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.20809109
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	
95% UCL (Assuming Normal Distribution)	
Student's-t UCL	6699.68162

Gamma Distribution Test	
A-D Test Statistic	9.8423071
A-D 5% Critical Value	0.90877716
K-S Test Statistic	0.41924945
K-S 5% Critical Value	0.15478578
Data do not follow gamma distribution	
at 5% significance level	
95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	5752.11416
Adjusted Gamma UCL	5914.17089

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.70231267
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	
95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	1002.50625
95% Chebyshev (MVUE) UCL	863.202966
97.5% Chebyshev (MVUE) UCL	1104.25124
99% Chebyshev (MVUE) UCL	1577.7439

95% Non-parametric UCLs	
CLT UCL	6607.42555
Adj-CLT UCL (Adjusted for skewness)	8942.80472
Mod-t UCL (Adjusted for skewness)	7063.95358
Jackknife UCL	6699.68162
Standard Bootstrap UCL	6599.60041
Bootstrap-t UCL	246251.947
Hall's Bootstrap UCL	212510.741
Percentile Bootstrap UCL	7323.7375
BCA Bootstrap UCL	10074.8
95% Chebyshev (Mean, Sd) UCL	12863.7957
97.5% Chebyshev (Mean, Sd) UCL	17211.5986
99% Chebyshev (Mean, Sd) UCL	25752.0153

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil
Benzo(k)fluoranthene (0-3ft)

Raw Statistics	
Number of Valid Samples	38
Number of Unique Samples	16
Minimum	19
Maximum	2100
Mean	214.842105
Median	38
Standard Deviation	408.125479
Variance	166566.407
Coefficient of Variation	1.89965314
Skewness	3.22842732

Gamma Statistics	
k hat	0.53931686
k star (bias corrected)	0.51428307
Theta hat	398.359705
Theta star	417.750683
nu hat	40.9880814
nu star	39.0855136
Approx.Chi Square Value (.05)	25.7625896
Adjusted Level of Significance	0.0434
Adjusted Chi Square Value	*25.3136208*

Log-transformed Statistics	
Minimum of log data	2.94443898
Maximum of log data	7.64969262
Mean of log data	4.20577464
Standard Deviation of log data	1.44276058
Variance of log data	2.08155808

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are microgram per kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.55414149
Shapiro-Wilk 5% Critical Value	0.938
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	326.538976

Gamma Distribution Test	
A-D Test Statistic	3.44592794
A-D 5% Critical Value	0.80895647
K-S Test Statistic	0.24586024
K-S 5% Critical Value	0.15098185
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	325.946039
Adjusted Gamma UCL	331.7271

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	*0.82082541*
Shapiro-Wilk 5% Critical Value	0.938
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	380.633411
95% Chebyshev (MVUE) UCL	415.718077
97.5% Chebyshev (MVUE) UCL	517.598847
99% Chebyshev (MVUE) UCL	717.723892

95% Non-parametric UCLs	
CLT UCL	323.742428
Adj-CLT UCL (Adjusted for skewness)	360.791859
Mod-t UCL (Adjusted for skewness)	332.317939
Jackknife UCL	326.538976
Standard Bootstrap UCL	320.57361
Bootstrap-t UCL	411.279717
Hall's Bootstrap UCL	421.923364
Percentile Bootstrap UCL	328.421053
BCA Bootstrap UCL	369.710526
95% Chebyshev (Mean, Sd) UCL	503.430399
97.5% Chebyshev (Mean, Sd) UCL	628.302785
99% Chebyshev (Mean, Sd) UCL	873.590406

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil
Lead (0-3ft)

Raw Statistics	
Number of Valid Samples	40
Number of Unique Samples	34
Minimum	1.95
Maximum	4000
Mean	176.1938
Median	28.5
Standard Deviation	632.1934
Variance	399668.4
Coefficient of Variation	3.588058
Skewness	5.966169

Gamma Statistics	
k hat	0.331352
k star (bias corrected)	0.323168
Theta hat	531.7412
Theta star	545.2085
nu hat	26.5082
nu star	25.85341
Approx.Chi Square Value (.05)	15.26472
Adjusted Level of Significance	0.044
Adjusted Chi Square Value	14.95892

Log-transformed Statistics	
Minimum of log data	0.667829
Maximum of log data	8.29405
Mean of log data	3.124016
Standard Deviation of log data	2.025891
Variance of log data	4.104236

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are milligram per kilogram (mg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.281285
Shapiro-Wilk 5% Critical Value	0.94
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	344.6114

Gamma Distribution Test	
A-D Test Statistic	2.506158
A-D 5% Critical Value	0.850695
K-S Test Statistic	0.174415
K-S 5% Critical Value	0.150832
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	298.4143
Adjusted Gamma UCL	304.5147

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.903341
Shapiro-Wilk 5% Critical Value	0.94
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	592.3865
95% Chebyshev (MVUE) UCL	458.997
97.5% Chebyshev (MVUE) UCL	590.9265
99% Chebyshev (MVUE) UCL	850.0767

95% Non-parametric UCLs	
CLT UCL	340.6109
Adj-CLT UCL (Adjusted for skewness)	441.3658
Mod-t UCL (Adjusted for skewness)	360.3271
Jackknife UCL	344.6114
Standard Bootstrap UCL	340.2487
Bootstrap-t UCL	957.04
Hall's Bootstrap UCL	880.2691
Percentile Bootstrap UCL	374.22
BCA Bootstrap UCL	473.625
95% Chebyshev (Mean, Sd) UCL	611.903
97.5% Chebyshev (Mean, Sd) UCL	800.4347
99% Chebyshev (Mean, Sd) UCL	1170.769

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil
Benzo(b)fluoranthene (0-3ft)

Raw Statistics	
Number of Valid Samples	37
Number of Unique Samples	19
Minimum	19
Maximum	5300
Mean	515.554054
Median	95
Standard Deviation	1052.56181
Variance	1107886.36
Coefficient of Variation	2.0416129
Skewness	3.2066989

Gamma Statistics	
k hat	0.4167167
k star (bias corrected)	0.40094688
Theta hat	1237.18116
Theta star	1285.84129
nu hat	30.8370359
nu star	29.6700691
Approx.Chi Square Value (.05)	18.2316494
Adjusted Level of Significance	0.0431
Adjusted Chi Square Value	17.8414371

Log-transformed Statistics	
Minimum of log data	2.94443898
Maximum of log data	8.5754621
Mean of log data	4.67649822
Standard Deviation of log data	1.78745613
Variance of log data	3.19499943

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are microgram per kilogram (mg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.54385603
Shapiro-Wilk 5% Critical Value	0.936
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	807.697208

Gamma Distribution Test	
A-D Test Statistic	2.78559095
A-D 5% Critical Value	0.83106007
K-S Test Statistic	0.21793381
K-S 5% Critical Value	0.15499865
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	839.009353
Adjusted Gamma UCL	857.359434

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.84810402
Shapiro-Wilk 5% Critical Value	0.936
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	1469.42659
95% Chebyshev (MVUE) UCL	1312.53432
97.5% Chebyshev (MVUE) UCL	1672.92808
99% Chebyshev (MVUE) UCL	2380.85185

95% Non-parametric UCLs	
CLT UCL	800.179682
Adj-CLT UCL (Adjusted for skewness)	897.652715
Mod-t UCL (Adjusted for skewness)	822.901031
Jackknife UCL	807.697208
Standard Bootstrap UCL	789.445645
Bootstrap-t UCL	1055.9454
Hall's Bootstrap UCL	1039.97926
Percentile Bootstrap UCL	824.148649
BCA Bootstrap UCL	935.878378
95% Chebyshev (Mean, Sd) UCL	1269.81834
97.5% Chebyshev (Mean, Sd) UCL	1596.1891
99% Chebyshev (Mean, Sd) UCL	2237.28126

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
1,2,4 Trichlorobenzene

Raw Statistics	
Number of Valid Samples	16
Number of Unique Samples	10
Minimum	9.7
Maximum	120000
Mean	15438.73125
Median	75
Standard Deviation	35798.06404
Variance	1281501389
Coefficient of Variation	2.318717999
Skewness	2.491489234

Gamma Statistics	
k hat	0.20110297
k star (bias corrected)	0.20506283
Theta hat	76770.27956
Theta star	75287.80934
nu hat	6.435295049
nu star	6.562010561
Approx.Chi Square Value (.05)	1.932941561
Adjusted Level of Significance	0.03348
Adjusted Chi Square Value	1.660843758

Log-transformed Statistics	
Minimum of log data	2.272125886
Maximum of log data	11.69524702
Mean of log data	5.988352967
Standard Deviation of log data	3.044199778
Variance of log data	9.267152286

RECOMMENDATION

Data are Non-parametric (0.05)

Use Hall's Bootstrap UCL

All units are in microgram per kilogram (µg/kg)

In case Hall's Bootstrap method yields
an erratic, unreasonably large UCL value,
use 99% Chebyshev (Mean, Sd) UCL

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.503955082
Shapiro-Wilk 5% Critical Value	0.887
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	31127.68147

Gamma Distribution Test	
A-D Test Statistic	1.953542108
A-D 5% Critical Value	0.877883407
K-S Test Statistic	0.321437764
K-S 5% Critical Value	0.237548602
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	52411.88847
Adjusted Gamma UCL	60998.58402

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.821602963
Shapiro-Wilk 5% Critical Value	0.887
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	7050860.156
95% Chebyshev (MVUE) UCL	68392.41816
97.5% Chebyshev (MVUE) UCL	91529.12203
99% Chebyshev (MVUE) UCL	136976.6966

95% Non-parametric UCLs	
CLT UCL	30159.37513
Adj-CLT UCL (Adjusted for skewness)	36115.70836
Mod-t UCL (Adjusted for skewness)	32056.74909
Jackknife UCL	31127.68147
Standard Bootstrap UCL	29643.29969
Bootstrap-t UCL	92031.34244
Hall's Bootstrap UCL	124880.0965
Percentile Bootstrap UCL	31616.85625
BCA Bootstrap UCL	36791.875
95% Chebyshev (Mean, Sd) UCL	54448.76713
97.5% Chebyshev (Mean, Sd) UCL	71328.44081
99% Chebyshev (Mean, Sd) UCL	104485.2912

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Xylenes (total)

Raw Statistics	
Number of Valid Samples	17
Number of Unique Samples	11
Minimum	2.5
Maximum	75000
Mean	5882.5
Median	75
Standard Deviation	18307.35619
Variance	335159290.8
Coefficient of Variation	3.112172748
Skewness	3.796958788

Gamma Statistics	
k hat	0.215306218
k star (bias corrected)	0.216526689
Theta hat	27321.55189
Theta star	27167.5516
nu hat	7.320411403
nu star	7.36190743
Approx.Chi Square Value (.05)	2.370683381
Adjusted Level of Significance	0.03461
Adjusted Chi Square Value	2.084632196

Log-transformed Statistics	
Minimum of log data	0.916290732
Maximum of log data	11.22524339
Mean of log data	5.301071042
Standard Deviation of log data	2.52695363
Variance of log data	6.385494646

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

an erratic, unreasonably large UCL value,
use 99% Chebyshev (Mean, Sd) UCL

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.369622555
Shapiro-Wilk 5% Critical Value	0.892
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	13634.54774

Gamma Distribution Test	
A-D Test Statistic	2.598225362
A-D 5% Critical Value	0.876402818
K-S Test Statistic	0.360636116
K-S 5% Critical Value	0.230756016
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	18267.48388
Adjusted Gamma UCL	20774.1301

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.865279734
Shapiro-Wilk 5% Critical Value	0.892
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	150639.9264
95% Chebyshev (MVUE) UCL	11515.90919
97.5% Chebyshev (MVUE) UCL	15285.87782
99% Chebyshev (MVUE) UCL	22691.2512

95% Non-parametric UCLs	
CLT UCL	13185.95618
Adj-CLT UCL (Adjusted for skewness)	17555.06647
Mod-t UCL (Adjusted for skewness)	14316.04065
Jackknife UCL	13634.54774
Standard Bootstrap UCL	13026.67965
Bootstrap-t UCL	74852.77198
Hall's Bootstrap UCL	79501.63004
Percentile Bootstrap UCL	14355.23529
BCA Bootstrap UCL	20460
95% Chebyshev (Mean, Sd) UCL	25236.8224
97.5% Chebyshev (Mean, Sd) UCL	33611.45316
99% Chebyshev (Mean, Sd) UCL	50061.79365

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
1-Methylnaphthalene

Raw Statistics	
Number of Valid Samples	83
Number of Unique Samples	37
Minimum	16
Maximum	230000
Mean	12976.24699
Median	80
Standard Deviation	3.48E+04
Variance	1208464326
Coefficient of Variation	2.678969776
Skewness	3.905380757

Gamma Statistics	
k hat	0.182213363
k star (bias corrected)	0.183659466
Theta hat	71214.57396
Theta star	70653.84253
nu hat	30.24741819
nu star	30.48747135
Approx.Chi Square Value (.05)	18.87441777
Adjusted Level of Significance	0.047108434
Adjusted Chi Square Value	18.71278965

Log-transformed Statistics	
Minimum of log data	2.772588722
Maximum of log data	12.34583459
Mean of log data	5.373561898
Standard Deviation of log data	3.078341738
Variance of log data	9.476187857

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.389515125
Lilliefors 5% Critical Value	0.097251134
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	19324.28545

Gamma Distribution Test	
A-D Test Statistic	10.45217514
A-D 5% Critical Value	0.927428289
K-S Test Statistic	0.306179779
K-S 5% Critical Value	0.109334094
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	20960.27348
Adjusted Gamma UCL	21141.31381

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.201260241
Lilliefors 5% Critical Value	0.097251134
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	124494.5474
95% Chebyshev (MVUE) UCL	67531.77765
97.5% Chebyshev (MVUE) UCL	88748.76538
99% Chebyshev (MVUE) UCL	130425.4294

95% Non-parametric UCLs	
CLT UCL	19252.56771
Adj-CLT UCL (Adjusted for skewness)	21000.33103
Mod-t UCL (Adjusted for skewness)	19596.9012
Jackknife UCL	19324.28545
Standard Bootstrap UCL	19148.50236
Bootstrap-t UCL	22552.44411
Hall's Bootstrap UCL	23877.20007
Percentile Bootstrap UCL	19484.86145
BCA Bootstrap UCL	21565.09036
95% Chebyshev (Mean, Sd) UCL	29608.63743
97.5% Chebyshev (Mean, Sd) UCL	36805.48607
99% Chebyshev (Mean, Sd) UCL	50942.30162

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Dibenzofuran

Raw Statistics	
Number of Valid Samples	85
Number of Unique Samples	27
Minimum	16
Maximum	31500
Mean	1433.841176
Median	31.5
Standard Deviation	4230.022885
Variance	17893093.61
Coefficient of Variation	2.950133498
Skewness	5.126421613

Gamma Statistics	
k hat	0.26363513
k star (bias corrected)	0.262173498
Theta hat	5438.733351
Theta star	5469.054597
nu hat	44.81797217
nu star	44.56949472
Approx.Chi Square Value (.05)	30.25440184
Adjusted Level of Significance	0.047176471
Adjusted Chi Square Value	30.05111807

Log-transformed Statistics	
Minimum of log data	2.772588722
Maximum of log data	10.35774282
Mean of log data	4.596930226
Standard Deviation of log data	2.233335526
Variance of log data	4.987787573

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.368742746
Lilliefors 5% Critical Value	0.096100193
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	2196.932982

Gamma Distribution Test	
A-D Test Statistic	10.23466035
A-D 5% Critical Value	0.882577821
K-S Test Statistic	0.272582638
K-S 5% Critical Value	0.106063208
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	2112.273682
Adjusted Gamma UCL	2126.562366

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.237395232
Lilliefors 5% Critical Value	0.096100193
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	2915.545759
95% Chebyshev (MVUE) UCL	2967.764153
97.5% Chebyshev (MVUE) UCL	3779.466141
99% Chebyshev (MVUE) UCL	5373.89752

95% Non-parametric UCLs	
CLT UCL	2188.517128
Adj-CLT UCL (Adjusted for skewness)	2461.112531
Mod-t UCL (Adjusted for skewness)	2239.452356
Jackknife UCL	2196.932982
Standard Bootstrap UCL	2189.620505
Bootstrap-t UCL	2875.9809
Hall's Bootstrap UCL	5164.45346
Percentile Bootstrap UCL	2256.047059
BCA Bootstrap UCL	2608.388235
95% Chebyshev (Mean, Sd) UCL	3433.749347
97.5% Chebyshev (Mean, Sd) UCL	4299.111209
99% Chebyshev (Mean, Sd) UCL	5998.947022

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
1,2,4 Trimethylbenzene

Raw Statistics	
Number of Valid Samples	87
Number of Unique Samples	40
Minimum	7.5
Maximum	100000
Mean	3773.701149
Median	20
Standard Deviation	12722.38469
Variance	161859072.1
Coefficient of Variation	3.371328089
Skewness	5.946097365

Gamma Statistics	
k hat	0.188205122
k star (bias corrected)	0.189378125
Theta hat	20051.00135
Theta star	19926.80593
nu hat	32.74769118
nu star	32.95179379
Approx.Chi Square Value (.05)	20.82613959
Adjusted Level of Significance	0.047241379
Adjusted Chi Square Value	20.66367371

Log-transformed Statistics	
Minimum of log data	2.014903021
Maximum of log data	11.51292546
Mean of log data	4.288590529
Standard Deviation of log data	2.93236233
Variance of log data	8.598748836

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.383603841
Lilliefors 5% Critical Value	0.094989171
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	6041.684255

Gamma Distribution Test	
A-D Test Statistic	11.64245037
A-D 5% Critical Value	0.922521837
K-S Test Statistic	0.303316098
K-S 5% Critical Value	0.106648159
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	5970.872402
Adjusted Gamma UCL	6017.817733

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.275194603
Lilliefors 5% Critical Value	0.094989171
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	22618.15037
95% Chebyshev (MVUE) UCL	14724.24257
97.5% Chebyshev (MVUE) UCL	19255.12535
99% Chebyshev (MVUE) UCL	28155.16723

95% Non-parametric UCLs	
CLT UCL	6017.253222
Adj-CLT UCL (Adjusted for skewness)	6946.351598
Mod-t UCL (Adjusted for skewness)	6186.604826
Jackknife UCL	6041.684255
Standard Bootstrap UCL	6045.583864
Bootstrap-t UCL	9040.551724
Hall's Bootstrap UCL	15935.69639
Percentile Bootstrap UCL	6208.87931
BCA Bootstrap UCL	6930.885057
95% Chebyshev (Mean, Sd) UCL	9719.164377
97.5% Chebyshev (Mean, Sd) UCL	12291.77106
99% Chebyshev (Mean, Sd) UCL	17345.15875

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Dibenzo(a,h)anthracene

Raw Statistics	
Number of Valid Samples	96
Number of Unique Samples	29
Minimum	0.11
Maximum	8500
Mean	530.1365625
Median	77.5
Standard Deviation	1188.05328
Variance	1411470.596
Coefficient of Variation	2.241032526
Skewness	4.104595176

Gamma Statistics	
k hat	0.377231377
k star (bias corrected)	0.372387341
Theta hat	1405.335279
Theta star	1423.615962
nu hat	72.42842437
nu star	71.49836945
Approx.Chi Square Value (.05)	53.02632
Adjusted Level of Significance	0.0475
Adjusted Chi Square Value	52.78465159

Log-transformed Statistics	
Minimum of log data	-2.207274913
Maximum of log data	9.047821442
Mean of log data	4.512147705
Standard Deviation of log data	1.955391495
Variance of log data	3.823555898

RECOMMENDATION

Data are Non-parametric (0.05)

Use 97.5% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.3448254
Lilliefors 5% Critical Value	0.090426996
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	731.5476559

Gamma Distribution Test	
A-D Test Statistic	7.026632412
A-D 5% Critical Value	0.848700287
K-S Test Statistic	0.215023406
K-S 5% Critical Value	0.098174389
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	714.8129419
Adjusted Gamma UCL	718.0856302

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.2109744
Lilliefors 5% Critical Value	0.090426996
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	1184.676038
95% Chebyshev (MVUE) UCL	1372.430721
97.5% Chebyshev (MVUE) UCL	1713.845546
99% Chebyshev (MVUE) UCL	2384.488861

95% Non-parametric UCLs	
CLT UCL	729.5835854
Adj-CLT UCL (Adjusted for skewness)	783.8605347
Mod-t UCL (Adjusted for skewness)	740.0137631
Jackknife UCL	731.5476559
Standard Bootstrap UCL	725.7956069
Bootstrap-t UCL	827.8564978
Hall's Bootstrap UCL	881.093344
Percentile Bootstrap UCL	738.804375
BCA Bootstrap UCL	805.8229167
95% Chebyshev (Mean, Sd) UCL	1058.675639
97.5% Chebyshev (Mean, Sd) UCL	1287.37492
99% Chebyshev (Mean, Sd) UCL	1736.610372

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Chrysene

Raw Statistics	
Number of Valid Samples	80
Number of Unique Samples	37
Minimum	0.11
Maximum	2400
Mean	386.638875
Median	110
Standard Deviation	574.6146198
Variance	330181.9613
Coefficient of Variation	1.486179112
Skewness	1.625742587

Gamma Statistics	
k hat	0.468197086
k star (bias corrected)	0.458973029
Theta hat	825.8036762
Theta star	842.3999902
nu hat	74.9115338
nu star	73.43568461
Approx.Chi Square Value (.05)	54.69805776
Adjusted Level of Significance	0.047
Adjusted Chi Square Value	54.4021435

Log-transformed Statistics	
Minimum of log data	-2.207274913
Maximum of log data	7.783224016
Mean of log data	4.58683809
Standard Deviation of log data	1.885602349
Variance of log data	3.555496217

RECOMMENDATION

Data are Non-parametric (0.05)

Use 97.5% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.301592241
Lilliefors 5% Critical Value	0.099057811
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	493.5645082

Gamma Distribution Test	
A-D Test Statistic	4.571278764
A-D 5% Critical Value	0.826246719
K-S Test Statistic	0.225524877
K-S 5% Critical Value	0.105928421
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	519.0877271
Adjusted Gamma UCL	521.9112457

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.228358647
Lilliefors 5% Critical Value	0.099057811
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	1150.446695
95% Chebyshev (MVUE) UCL	1306.691652
97.5% Chebyshev (MVUE) UCL	1634.970048
99% Chebyshev (MVUE) UCL	2279.809388

95% Non-parametric UCLs	
CLT UCL	492.3106336
Adj-CLT UCL (Adjusted for skewness)	504.7878837
Mod-t UCL (Adjusted for skewness)	495.5107071
Jackknife UCL	493.5645082
Standard Bootstrap UCL	494.0649617
Bootstrap-t UCL	510.764769
Hall's Bootstrap UCL	505.9078351
Percentile Bootstrap UCL	488.18125
BCA Bootstrap UCL	501.66175
95% Chebyshev (Mean, Sd) UCL	666.6714013
97.5% Chebyshev (Mean, Sd) UCL	787.8416992
99% Chebyshev (Mean, Sd) UCL	1025.857286

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Benzo(k)fluoranthene

Raw Statistics	
Number of Valid Samples	85
Number of Unique Samples	34
Minimum	0.11
Maximum	3600
Mean	347.6365882
Median	69
Standard Deviation	618.1288318
Variance	382083.2527
Coefficient of Variation	1.77808911
Skewness	2.853061525

Gamma Statistics	
k hat	0.464871306
k star (bias corrected)	0.456307221
Theta hat	747.8125311
Theta star	761.8476593
nu hat	79.02812207
nu star	77.57222757
Approx.Chi Square Value (.05)	58.2790894
Adjusted Level of Significance	0.047176471
Adjusted Chi Square Value	57.99154578

Log-transformed Statistics	
Minimum of log data	-2.207274913
Maximum of log data	8.188689124
Mean of log data	4.469149146
Standard Deviation of log data	1.797798094
Variance of log data	3.232077987

RECOMMENDATION

Data are Non-parametric (0.05)

Use 97.5% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.287677712
Lilliefors 5% Critical Value	0.096100193
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	459.1463978

Gamma Distribution Test	
A-D Test Statistic	5.192645809
A-D 5% Critical Value	0.827071706
K-S Test Statistic	0.208631325
K-S 5% Critical Value	0.103030385
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	462.7207599
Adjusted Gamma UCL	465.0151013

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.213573246
Lilliefors 5% Critical Value	0.096100193
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	806.6936345
95% Chebyshev (MVUE) UCL	947.3942089
97.5% Chebyshev (MVUE) UCL	1176.031834
99% Chebyshev (MVUE) UCL	1625.146176

95% Non-parametric UCLs	
CLT UCL	457.9165979
Adj-CLT UCL (Adjusted for skewness)	480.0858798
Mod-t UCL (Adjusted for skewness)	462.6043578
Jackknife UCL	459.1463978
Standard Bootstrap UCL	458.6186288
Bootstrap-t UCL	500.3858188
Hall's Bootstrap UCL	489.1355582
Percentile Bootstrap UCL	458.6235294
BCA Bootstrap UCL	487.7411765
95% Chebyshev (Mean, Sd) UCL	639.881083
97.5% Chebyshev (Mean, Sd) UCL	766.3355093
99% Chebyshev (Mean, Sd) UCL	1014.730743

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
2-Methylnaphthalene

Raw Statistics	
Number of Valid Samples	98
Number of Unique Samples	50
Minimum	7.6
Maximum	380000
Mean	17527.77143
Median	130
Standard Deviation	5.86E+04
Variance	3435599869
Coefficient of Variation	3.344064054
Skewness	4.908086566

Gamma Statistics	
k hat	0.178639578
k star (bias corrected)	0.17997374
Theta hat	98118.07461
Theta star	97390.71592
nu hat	35.01335726
nu star	35.27485313
Approx.Chi Square Value (.05)	22.68347451
Adjusted Level of Significance	0.04755102
Adjusted Chi Square Value	22.53279205

Log-transformed Statistics	
Minimum of log data	2.028148247
Maximum of log data	12.84792653
Mean of log data	5.579609061
Standard Deviation of log data	3.081319841
Variance of log data	9.494531964

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.382505311
Lilliefors 5% Critical Value	0.089499515
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	27360.7063

Gamma Distribution Test	
A-D Test Statistic	10.80414169
A-D 5% Critical Value	0.934672296
K-S Test Statistic	0.279069897
K-S 5% Critical Value	0.100979018
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	27257.26884
Adjusted Gamma UCL	27439.54506

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.178691659
Lilliefors 5% Critical Value	0.089499515
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	132552.5117
95% Chebyshev (MVUE) UCL	84106.7851
97.5% Chebyshev (MVUE) UCL	110184.2917
99% Chebyshev (MVUE) UCL	161408.5038

95% Non-parametric UCLs	
CLT UCL	27266.79704
Adj-CLT UCL (Adjusted for skewness)	30403.4599
Mod-t UCL (Adjusted for skewness)	27849.96232
Jackknife UCL	27360.7063
Standard Bootstrap UCL	27297.75023
Bootstrap-t UCL	34406.22941
Hall's Bootstrap UCL	45495.708
Percentile Bootstrap UCL	28043.79082
BCA Bootstrap UCL	31362.90306
95% Chebyshev (Mean, Sd) UCL	43336.40736
97.5% Chebyshev (Mean, Sd) UCL	54503.82475
99% Chebyshev (Mean, Sd) UCL	76440.05377

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Indeno(1,2,3-c,d)pyrene

Raw Statistics	
Number of Valid Samples	87
Number of Unique Samples	37
Minimum	0.11
Maximum	2900
Mean	355.1851724
Median	57
Standard Deviation	640.2420775
Variance	409909.9178
Coefficient of Variation	1.802558573
Skewness	2.448291762

Gamma Statistics	
k hat	0.433297519
k star (bias corrected)	0.426019061
Theta hat	819.7258392
Theta star	833.7307067
nu hat	75.39376831
nu star	74.12731653
Approx.Chi Square Value (.05)	55.29573236
Adjusted Level of Significance	0.047241379
Adjusted Chi Square Value	55.02258103

Log-transformed Statistics	
Minimum of log data	-2.207274913
Maximum of log data	7.972466016
Mean of log data	4.373306799
Standard Deviation of log data	1.856411697
Variance of log data	3.446264387

RECOMMENDATION

Data are Non-parametric (0.05)

Use 97.5% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.303522524
Lilliefors 5% Critical Value	0.094989171
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	469.3192951

Gamma Distribution Test	
A-D Test Statistic	5.46135494
A-D 5% Critical Value	0.834741339
K-S Test Statistic	0.189766031
K-S 5% Critical Value	0.102278817
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	476.1474815
Adjusted Gamma UCL	478.5112441

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.189709167
Lilliefors 5% Critical Value	0.094989171
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	836.8915693
95% Chebyshev (MVUE) UCL	973.9894117
97.5% Chebyshev (MVUE) UCL	1212.796472
99% Chebyshev (MVUE) UCL	1681.8867

95% Non-parametric UCLs	
CLT UCL	468.0898263
Adj-CLT UCL (Adjusted for skewness)	487.3415024
Mod-t UCL (Adjusted for skewness)	472.3221676
Jackknife UCL	469.3192951
Standard Bootstrap UCL	467.7592021
Bootstrap-t UCL	494.1081707
Hall's Bootstrap UCL	484.1453821
Percentile Bootstrap UCL	471.0012644
BCA Bootstrap UCL	485.2241379
95% Chebyshev (Mean, Sd) UCL	654.3850333
97.5% Chebyshev (Mean, Sd) UCL	783.8490521
99% Chebyshev (Mean, Sd) UCL	1038.156048

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Benzo(b)fluoranthene

Raw Statistics	
Number of Valid Samples	87
Number of Unique Samples	38
Minimum	0.11
Maximum	7100
Mean	788.3288506
Median	180
Standard Deviation	1380.032374
Variance	1904489.355
Coefficient of Variation	1.750579563
Skewness	2.677243653

Gamma Statistics	
k hat	0.398734221
k star (bias corrected)	0.3926476
Theta hat	1977.07849
Theta star	2007.726141
nu hat	69.37975436
nu star	68.32068237
Approx.Chi Square Value (.05)	50.29221092
Adjusted Level of Significance	0.047241379
Adjusted Chi Square Value	50.03234976

Log-transformed Statistics	
Minimum of log data	-2.207274913
Maximum of log data	8.867850063
Mean of log data	5.018756075
Standard Deviation of log data	2.095361261
Variance of log data	4.390538814

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.2958841
Lilliefors 5% Critical Value	0.094989171
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	1034.343272

Gamma Distribution Test	
A-D Test Statistic	3.934902552
A-D 5% Critical Value	0.843110496
K-S Test Statistic	0.191468166
K-S 5% Critical Value	0.102745594
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	1070.924583
Adjusted Gamma UCL	1076.486818

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.206718469
Lilliefors 5% Critical Value	0.094989171
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	2967.469136
95% Chebyshev (MVUE) UCL	3218.269443
97.5% Chebyshev (MVUE) UCL	4065.844693
99% Chebyshev (MVUE) UCL	5730.742147

95% Non-parametric UCLs	
CLT UCL	1031.69317
Adj-CLT UCL (Adjusted for skewness)	1077.070437
Mod-t UCL (Adjusted for skewness)	1041.421209
Jackknife UCL	1034.343272
Standard Bootstrap UCL	1034.040938
Bootstrap-t UCL	1115.118701
Hall's Bootstrap UCL	1109.551813
Percentile Bootstrap UCL	1042.275862
BCA Bootstrap UCL	1077.541494
95% Chebyshev (Mean, Sd) UCL	1433.249747
97.5% Chebyshev (Mean, Sd) UCL	1712.307534
99% Chebyshev (Mean, Sd) UCL	2260.46252

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Benzo(a)anthracene

Raw Statistics	
Number of Valid Samples	91
Number of Unique Samples	50
Minimum	0.11
Maximum	11000
Mean	1221.64956
Median	160
Standard Deviation	2516.546726
Variance	6333007.422
Coefficient of Variation	2.059957951
Skewness	2.616484932

Gamma Statistics	
k hat	0.325460397
k star (bias corrected)	0.32205694
Theta hat	3753.604352
Theta star	3793.271959
nu hat	59.23379216
nu star	58.61436311
Approx.Chi Square Value (.05)	42.00931985
Adjusted Level of Significance	0.047362637
Adjusted Chi Square Value	41.78359449

Log-transformed Statistics	
Minimum of log data	-2.207274913
Maximum of log data	9.305650552
Mean of log data	5.017207056
Standard Deviation of log data	2.278453693
Variance of log data	5.191351229

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.316785281
Lilliefors 5% Critical Value	0.092878037
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	1660.084422

Gamma Distribution Test	
A-D Test Statistic	5.390354909
A-D 5% Critical Value	0.861602517
K-S Test Statistic	0.18191028
K-S 5% Critical Value	0.101415941
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	1704.531546
Adjusted Gamma UCL	1713.73985

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.20473164
Lilliefors 5% Critical Value	0.092878037
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	4893.333473
95% Chebyshev (MVUE) UCL	5007.977765
97.5% Chebyshev (MVUE) UCL	6378.803148
99% Chebyshev (MVUE) UCL	9071.524169

95% Non-parametric UCLs	
CLT UCL	1655.57145
Adj-CLT UCL (Adjusted for skewness)	1732.886183
Mod-t UCL (Adjusted for skewness)	1672.143958
Jackknife UCL	1660.084422
Standard Bootstrap UCL	1661.100046
Bootstrap-t UCL	1795.763807
Hall's Bootstrap UCL	1704.959372
Percentile Bootstrap UCL	1684.52989
BCA Bootstrap UCL	1728.120879
95% Chebyshev (Mean, Sd) UCL	2371.552285
97.5% Chebyshev (Mean, Sd) UCL	2869.116112
99% Chebyshev (Mean, Sd) UCL	3846.483903

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
1,3,5 Trimethylbenzene

Raw Statistics	
Number of Valid Samples	102
Number of Unique Samples	41
Minimum	7.9
Maximum	30000
Mean	1460.739216
Median	8
Standard Deviation	4696.191587
Variance	22054215.42
Coefficient of Variation	3.214941816
Skewness	4.758496096

Gamma Statistics	
k hat	0.215407138
k star (bias corrected)	0.215607582
Theta hat	6781.294382
Theta star	6774.990024
nu hat	43.94305618
nu star	*43.98394668*
Approx.Chi Square Value (.05)	29.7717359
Adjusted Level of Significance	0.047647059
Adjusted Chi Square Value	29.60437216

Log-transformed Statistics	
Minimum of log data	2.066862759
Maximum of log data	10.30895266
Mean of log data	3.909864869
Standard Deviation of log data	*2.547070927*
Variance of log data	6.487570308

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (μg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.378521856
Lilliefors 5% Critical Value	0.087727072
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	2232.663685

Gamma Distribution Test	
A-D Test Statistic	14.90458923
A-D 5% Critical Value	0.905461472
K-S Test Statistic	0.310292964
K-S 5% Critical Value	0.098202199
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	2158.056084
Adjusted Gamma UCL	*2170.25632*

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.322641773
Lilliefors 5% Critical Value	0.087727072
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	3503.815718
95% Chebyshev (MVUE) UCL	*3309.470974*
97.5% Chebyshev (MVUE) UCL	4252.985947
99% Chebyshev (MVUE) UCL	6106.338412

95% Non-parametric UCLs	
CLT UCL	2225.583415
Adj-CLT UCL (Adjusted for skewness)	2459.680371
Mod-t UCL (Adjusted for skewness)	2269.178079
Jackknife UCL	2232.663685
Standard Bootstrap UCL	*2215.008369*
Bootstrap-t UCL	*2836.78846*
Hall's Bootstrap UCL	2422.645994
Percentile Bootstrap UCL	2277.887255
BCA Bootstrap UCL	2504.342157
95% Chebyshev (Mean, Sd) UCL	3487.59347
97.5% Chebyshev (Mean, Sd) UCL	4364.614925
99% Chebyshev (Mean, Sd) UCL	6087.353748

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Lead

Raw Statistics	
Number of Valid Samples	103
Number of Unique Samples	80
Minimum	1.95
Maximum	4000
Mean	90.48417476
Median	12
Standard Deviation	401.3691189
Variance	161097.1696
Coefficient of Variation	4.435793552
Skewness	9.267837134

Gamma Statistics	
k hat	0.404839779
k star (bias corrected)	0.399520821
Theta hat	223.5061359
Theta star	226.4817499
nu hat	83.39699455
nu star	82.30128921
Approx.Chi Square Value (.05)	62.39101708
Adjusted Level of Significance	0.047669903
Adjusted Chi Square Value	62.1460266

Log-transformed Statistics	
Minimum of log data	0.667829373
Maximum of log data	8.29404964
Mean of log data	2.882892277
Standard Deviation of log data	1.540440121
Variance of log data	2.372955767

RECOMMENDATION

Data are Non-parametric (0.05)

Use 97.5% Chebyshev (Mean, Sd) UCL

All units are in milligram per kilogram (mg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.412709604
Lilliefors 5% Critical Value	0.087300174
Data not normal at 5% significance level	
95% UCL (Assuming Normal Distribution)	
Student's-t UCL	156.1311978

Gamma Distribution Test	
A-D Test Statistic	8.580892616
A-D 5% Critical Value	0.841890854
K-S Test Statistic	0.224221407
K-S 5% Critical Value	0.094957108
Data do not follow gamma distribution	
at 5% significance level	
95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	119.3595582
Adjusted Gamma UCL	119.8300944

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.118777459
Lilliefors 5% Critical Value	0.087300174
Data not lognormal at 5% significance level	
95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	89.07606002
95% Chebyshev (MVUE) UCL	110.1602046
97.5% Chebyshev (MVUE) UCL	133.1157017
99% Chebyshev (MVUE) UCL	178.2073307

95% Non-parametric UCLs	
CLT UCL	155.5349685
Adj-CLT UCL (Adjusted for skewness)	194.1241474
Mod-t UCL (Adjusted for skewness)	162.1503298
Jackknife UCL	156.1311978
Standard Bootstrap UCL	155.7063698
Bootstrap-t UCL	330.2965731
Hall's Bootstrap UCL	374.8710898
Percentile Bootstrap UCL	168.7479612
BCA Bootstrap UCL	214.0456311
95% Chebyshev (Mean, Sd) UCL	262.8702346
97.5% Chebyshev (Mean, Sd) UCL	337.4618204
99% Chebyshev (Mean, Sd) UCL	483.9825469

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Arsenic

Raw Statistics	
Number of Valid Samples	103
Number of Unique Samples	67
Minimum	0.325
Maximum	23.4
Mean	4.296893204
Median	2.6
Standard Deviation	4.771122495
Variance	22.76360986
Coefficient of Variation	1.110365622
Skewness	2.029987787

Gamma Statistics	
k hat	1.103206044
k star (bias corrected)	1.077546321
Theta hat	3.894914488
Theta star	3.987664493
nu hat	227.2604451
nu star	221.9745421
Approx.Chi Square Value (.05)	188.4842573
Adjusted Level of Significance	0.047669903
Adjusted Chi Square Value	188.0496384

Log-transformed Statistics	
Minimum of log data	-1.123930097
Maximum of log data	3.152736022
Mean of log data	0.940502462
Standard Deviation of log data	1.050057534
Variance of log data	1.102620825

RECOMMENDATION

Data are lognormal (0.05)

Use H-UCL

All units are in milligram per kilogram (mg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.248809114
Lilliefors 5% Critical Value	0.087300174
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	5.077247181

Gamma Distribution Test	
A-D Test Statistic	1.946118027
A-D 5% Critical Value	0.780264844
K-S Test Statistic	0.135737275
K-S 5% Critical Value	0.091137708
Data do not follow gamma distribution at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	5.060374353
Adjusted Gamma UCL	5.07206985

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.065026215
Lilliefors 5% Critical Value	0.087300174
Data are lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	5.616091524
95% Chebyshev (MVUE) UCL	6.829863547
97.5% Chebyshev (MVUE) UCL	7.877401727
99% Chebyshev (MVUE) UCL	9.935087638

95% Non-parametric UCLs	
CLT UCL	5.070159732
Adj-CLT UCL (Adjusted for skewness)	5.170634539
Mod-t UCL (Adjusted for skewness)	5.09291922
Jackknife UCL	5.077247181
Standard Bootstrap UCL	5.07118494
Bootstrap-t UCL	5.212102068
Hall's Bootstrap UCL	5.142070821
Percentile Bootstrap UCL	5.07961165
BCA Bootstrap UCL	5.120825243
95% Chebyshev (Mean, Sd) UCL	6.346066817
97.5% Chebyshev (Mean, Sd) UCL	7.232745877
99% Chebyshev (Mean, Sd) UCL	8.974455195

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Benzo(a)pyrene

Raw Statistics	
Number of Valid Samples	87
Number of Unique Samples	43
Minimum	0.11
Maximum	6800
Mean	660.7254023
Median	120
Standard Deviation	1204.06175
Variance	1449764.698
Coefficient of Variation	1.822333069
Skewness	2.820330628

Gamma Statistics	
k hat	0.389940595
k star (bias corrected)	0.384157203
Theta hat	1694.425794
Theta star	1719.934957
nu hat	67.84966353
nu star	66.84335329
Approx.Chi Square Value (.05)	49.02463719
Adjusted Level of Significance	0.047241379
Adjusted Chi Square Value	48.76824609

Log-transformed Statistics	
Minimum of log data	-2.207274913
Maximum of log data	8.824677891
Mean of log data	4.79885663
Standard Deviation of log data	2.076478241
Variance of log data	4.311761884

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.313087363
Lilliefors 5% Critical Value	0.094989171
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	875.3700443

Gamma Distribution Test	
A-D Test Statistic	4.486610444
A-D 5% Critical Value	0.845239784
K-S Test Statistic	0.192624708
K-S 5% Critical Value	0.102864352
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	900.8756419
Adjusted Gamma UCL	905.6118485

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.207395051
Lilliefors 5% Critical Value	0.094989171
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	2261.643114
95% Chebyshev (MVUE) UCL	2469.213243
97.5% Chebyshev (MVUE) UCL	3116.21945
99% Chebyshev (MVUE) UCL	4387.137858

95% Non-parametric UCLs	
CLT UCL	873.0578621
Adj-CLT UCL (Adjusted for skewness)	914.7649575
Mod-t UCL (Adjusted for skewness)	881.8755084
Jackknife UCL	875.3700443
Standard Bootstrap UCL	870.7063749
Bootstrap-t UCL	940.1960105
Hall's Bootstrap UCL	930.3371286
Percentile Bootstrap UCL	880.4955172
BCA Bootstrap UCL	921.1174713
95% Chebyshev (Mean, Sd) UCL	1223.411175
97.5% Chebyshev (Mean, Sd) UCL	1466.885758
99% Chebyshev (Mean, Sd) UCL	1945.144432

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Benzene

Raw Statistics	
Number of Valid Samples	104
Number of Unique Samples	51
Minimum	2.5
Maximum	230000
Mean	8403.408654
Median	21
Standard Deviation	35849.72715
Variance	1285202937
Coefficient of Variation	4.266093514
Skewness	5.384344676

Gamma Statistics	
k hat	0.165479525
k star (bias corrected)	0.167116334
Theta hat	50782.16566
Theta star	50284.7835
nu hat	34.41974121
nu star	34.76019739
Approx.Chi Square Value (.05)	22.27062543
Adjusted Level of Significance	0.047692308
Adjusted Chi Square Value	22.13017908

Log-transformed Statistics	
Minimum of log data	0.916290732
Maximum of log data	12.34583459
Mean of log data	4.458562919
Standard Deviation of log data	3.017199807
Variance of log data	9.103494675

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.420176099
Lilliefors 5% Critical Value	0.086879448
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	14238.13124

Gamma Distribution Test	
A-D Test Statistic	14.30611452
A-D 5% Critical Value	0.950486663
K-S Test Statistic	0.272887841
K-S 5% Critical Value	0.099322176
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	13116.11766
Adjusted Gamma UCL	13199.35743

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.233311765
Lilliefors 5% Critical Value	0.086879448
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	31955.0551
95% Chebyshev (MVUE) UCL	22478.06293
97.5% Chebyshev (MVUE) UCL	29356.9151
99% Chebyshev (MVUE) UCL	42869.08817

95% Non-parametric UCLs	
CLT UCL	14185.65303
Adj-CLT UCL (Adjusted for skewness)	16168.84969
Mod-t UCL (Adjusted for skewness)	14547.46984
Jackknife UCL	14238.13124
Standard Bootstrap UCL	14138.96785
Bootstrap-t UCL	18220.29265
Hall's Bootstrap UCL	13361.88072
Percentile Bootstrap UCL	14756.01442
BCA Bootstrap UCL	17393.36058
95% Chebyshev (Mean, Sd) UCL	23726.48571
97.5% Chebyshev (Mean, Sd) UCL	30356.79339
99% Chebyshev (Mean, Sd) UCL	43380.74895

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Napthalene

Raw Statistics	
Number of Valid Samples	115
Number of Unique Samples	62
Minimum	0.24
Maximum	280000
Mean	15526.03687
Median	130
Standard Deviation	4.86E+04
Variance	2363108257
Coefficient of Variation	3.130986505
Skewness	4.13453456

Gamma Statistics	
k hat	0.182299291
k star (bias corrected)	0.183340759
Theta hat	85167.8401
Theta star	84684.04391
nu hat	41.92883694
nu star	42.16837453
Approx.Chi Square Value (.05)	28.27963769
Adjusted Level of Significance	0.047913043
Adjusted Chi Square Value	28.13549904

Log-transformed Statistics	
Minimum of log data	-1.427116356
Maximum of log data	12.54254488
Mean of log data	5.555186364
Standard Deviation of log data	3.091495106
Variance of log data	9.557341991

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (*Mean, Sd*) UCL

All units are in microgram per kilogram (μg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.38089739
Lilliefors 5% Critical Value	0.082619926
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	23043.36943

Gamma Distribution Test	
A-D Test Statistic	11.76182044
A-D 5% Critical Value	0.933723805
K-S Test Statistic	0.24845928
K-S 5% Critical Value	0.095519526
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	23151.2067
Adjusted Gamma UCL	23269.81074

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.146536019
Lilliefors 5% Critical Value	0.082619926
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	117756.4993
95% Chebyshev (MVUE) UCL	84561.98279
97.5% Chebyshev (MVUE) UCL	110438.8356
99% Chebyshev (MVUE) UCL	161268.9022

95% Non-parametric UCLs	
CLT UCL	22982.28146
Adj-CLT UCL (Adjusted for skewness)	24849.74017
Mod-t UCL (Adjusted for skewness)	23334.65525
Jackknife UCL	23043.36943
Standard Bootstrap UCL	23159.34758
Bootstrap-t UCL	25873.94671
Hall's Bootstrap UCL	23848.46633
Percentile Bootstrap UCL	23689.95426
BCA Bootstrap UCL	25058.03913
95% *Chebyshev (Mean, Sd)* UCL	35285.25198
97.5% Chebyshev (Mean, Sd) UCL	43835.08014
99% Chebyshev (Mean, Sd) UCL	60629.56199

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Thallium

Raw Statistics	
Number of Valid Samples	86
Number of Unique Samples	15
Minimum	0.485
Maximum	1.8
Mean	0.782790698
Median	0.8
Standard Deviation	0.191295283
Variance	0.036593885
Coefficient of Variation	0.244376029
Skewness	2.26028677

Gamma Statistics	
k hat	20.30379954
k star (bias corrected)	19.6032794
Theta hat	0.038553902
Theta star	0.03993162
nu hat	3492.253521
nu star	3371.764057
Approx.Chi Square Value (.05)	3237.808294
Adjusted Level of Significance	0.047209302
Adjusted Chi Square Value	3235.595453

Log-transformed Statistics	
Minimum of log data	-0.723606388
Maximum of log data	0.587786665
Mean of log data	-0.269717956
Standard Deviation of log data	0.217979957
Variance of log data	0.047515262

RECOMMENDATION

Data are Non-parametric (0.05)

Use Student's-t UCL
or Modified-t UCL

All units are in milligram per kilogram (mg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.132895031
Lilliefors 5% Critical Value	0.095539837
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	0.817094446

Gamma Distribution Test	
A-D Test Statistic	1.173695715
A-D 5% Critical Value	0.750021215
K-S Test Statistic	0.106826338
K-S 5% Critical Value	0.096111757
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	0.815176595
Adjusted Gamma UCL	0.815734098

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.100022581
Lilliefors 5% Critical Value	0.095539837
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	0.814167224
95% Chebyshev (MVUE) UCL	0.862684499
97.5% Chebyshev (MVUE) UCL	0.897712575
99% Chebyshev (MVUE) UCL	0.966518447

95% Non-parametric UCLs	
CLT UCL	0.816720575
Adj-CLT UCL (Adjusted for skewness)	0.822092745
Mod-t UCL (Adjusted for skewness)	0.817932396
Jackknife UCL	0.817094446
Standard Bootstrap UCL	0.816127267
Bootstrap-t UCL	0.821242157
Hall's Bootstrap UCL	0.830998359
Percentile Bootstrap UCL	0.816104651
BCA Bootstrap UCL	0.821337209
95% Chebyshev (Mean, Sd) UCL	0.872705633
97.5% Chebyshev (Mean, Sd) UCL	0.911611897
99% Chebyshev (Mean, Sd) UCL	0.988035719

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Fluorene

Raw Statistics	
Number of Valid Samples	96
Number of Unique Samples	43
Minimum	1.5
Maximum	100000
Mean	4904.359375
Median	80
Standard Deviation	1.58E+04
Variance	248079980.8
Coefficient of Variation	3.211541759
Skewness	5.015163096

Gamma Statistics	
k hat	0.213791878
k star (bias corrected)	0.214055326
Theta hat	22939.87697
Theta star	22911.64375
nu hat	41.04804054
nu star	41.09862261
Approx.Chi Square Value (.05)	27.40377927
Adjusted Level of Significance	0.0475
Adjusted Chi Square Value	27.23347146

Log-transformed Statistics	
Minimum of log data	0.405465108
Maximum of log data	11.51292546
Mean of log data	5.091486303
Standard Deviation of log data	2.690887274
Variance of log data	7.240874322

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.377793307
Lilliefors 5% Critical Value	0.090426996
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	7574.556533

Gamma Distribution Test	
A-D Test Statistic	10.30758801
A-D 5% Critical Value	0.905815231
K-S Test Statistic	0.258675793
K-S 5% Critical Value	0.100907749
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	7355.278012
Adjusted Gamma UCL	7401.275132

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.204382575
Lilliefors 5% Critical Value	0.090426996
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	19302.80954
95% Chebyshev (MVUE) UCL	16220.63102
97.5% Chebyshev (MVUE) UCL	20996.54196
99% Chebyshev (MVUE) UCL	30377.8942

95% Non-parametric UCLs	
CLT UCL	7548.51797
Adj-CLT UCL (Adjusted for skewness)	8427.722875
Mod-t UCL (Adjusted for skewness)	7711.694731
Jackknife UCL	7574.556533
Standard Bootstrap UCL	7503.904712
Bootstrap-t UCL	10316.81489
Hall's Bootstrap UCL	16722.6518
Percentile Bootstrap UCL	7803.848958
BCA Bootstrap UCL	8735
95% Chebyshev (Mean, Sd) UCL	11911.43886
97.5% Chebyshev (Mean, Sd) UCL	14943.40775
99% Chebyshev (Mean, Sd) UCL	20899.12352

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Acenaphthene

Raw Statistics	
Number of Valid Samples	97
Number of Unique Samples	42
Minimum	0.59
Maximum	59000
Mean	4226.39268
Median	80
Standard Deviation	11125.14107
Variance	123768763.9
Coefficient of Variation	2.632301803
Skewness	3.351592074

Gamma Statistics	
k hat	0.220683254
k star (bias corrected)	0.220730851
Theta hat	19151.39735
Theta star	19147.26767
nu hat	42.81255121
nu star	42.82178503
Approx.Chi Square Value (.05)	28.81583715
Adjusted Level of Significance	0.047525773
Adjusted Chi Square Value	28.6427296

Log-transformed Statistics	
Minimum of log data	-0.527632742
Maximum of log data	10.98529272
Mean of log data	5.065611667
Standard Deviation of log data	2.686229021
Variance of log data	7.215826351

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.37332769
Lilliefors 5% Critical Value	0.08995967
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	6102.502332

Gamma Distribution Test	
A-D Test Statistic	10.29224671
A-D 5% Critical Value	0.90284556
K-S Test Statistic	0.282796445
K-S 5% Critical Value	0.100242371
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	6280.632343
Adjusted Gamma UCL	6318.590488

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.195095267
Lilliefors 5% Critical Value	0.08995967
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	18373.82436
95% Chebyshev (MVUE) UCL	15584.41145
97.5% Chebyshev (MVUE) UCL	20164.28044
99% Chebyshev (MVUE) UCL	29160.54624

95% Non-parametric UCLs	
CLT UCL	6084.397844
Adj-CLT UCL (Adjusted for skewness)	6495.136296
Mod-t UCL (Adjusted for skewness)	6166.56923
Jackknife UCL	6102.502332
Standard Bootstrap UCL	6085.035702
Bootstrap-t UCL	6758.614579
Hall's Bootstrap UCL	6448.007493
Percentile Bootstrap UCL	6109.492474
BCA Bootstrap UCL	6564.623711
95% Chebyshev (Mean, Sd) UCL	9150.147967
97.5% Chebyshev (Mean, Sd) UCL	11280.66081
99% Chebyshev (Mean, Sd) UCL	15465.64075

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Fluoranthene

Raw Statistics	
Number of Valid Samples	97
Number of Unique Samples	54
Minimum	0.11
Maximum	110000
Mean	5298.41866
Median	200
Standard Deviation	1.62E+04
Variance	262629752.2
Coefficient of Variation	3.058621172
Skewness	5.11852341

Gamma Statistics	
k hat	0.242954002
k star (bias corrected)	0.242312813
Theta hat	21808.32017
Theta star	21866.02762
nu hat	47.13307637
nu star	47.00868569
Approx.Chi Square Value (.05)	32.27218866
Adjusted Level of Significance	0.047525773
Adjusted Chi Square Value	32.0883005

Log-transformed Statistics	
Minimum of log data	-2.207274913
Maximum of log data	11.60823564
Mean of log data	5.638118334
Standard Deviation of log data	2.680087591
Variance of log data	7.182869497

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.371857485
Lilliefors 5% Critical Value	0.08995967
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	8031.3244

Gamma Distribution Test	
A-D Test Statistic	6.509755222
A-D 5% Critical Value	0.892980954
K-S Test Statistic	0.187240602
K-S 5% Critical Value	0.099791611
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	7717.843375
Adjusted Gamma UCL	7762.071956

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.18515848
Lilliefors 5% Critical Value	0.08995967
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	31885.60571
95% Chebyshev (MVUE) UCL	27150.3326
97.5% Chebyshev (MVUE) UCL	35121.13165
99% Chebyshev (MVUE) UCL	50778.22293

95% Non-parametric UCLs	
CLT UCL	8004.951817
Adj-CLT UCL (Adjusted for skewness)	8918.697495
Mod-t UCL (Adjusted for skewness)	8173.85026
Jackknife UCL	8031.3244
Standard Bootstrap UCL	7980.968799
Bootstrap-t UCL	10567.43807
Hall's Bootstrap UCL	20019.18743
Percentile Bootstrap UCL	8063.167216
BCA Bootstrap UCL	9202.064124
95% Chebyshev (Mean, Sd) UCL	12470.79213
97.5% Chebyshev (Mean, Sd) UCL	15574.28386
99% Chebyshev (Mean, Sd) UCL	21670.4924

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Phenanthrene

Raw Statistics	
Number of Valid Samples	97
Number of Unique Samples	55
Minimum	5.4
Maximum	76000
Mean	6522.772165
Median	185
Standard Deviation	1.54E+04
Variance	236142147.4
Coefficient of Variation	2.355887484
Skewness	2.941417398

Gamma Statistics	
k hat	0.232309711
k star (bias corrected)	0.231997727
Theta hat	28077.91435
Theta star	28115.67276
nu hat	45.06808391
nu star	45.00755898
Approx.Chi Square Value (.05)	30.61594257
Adjusted Level of Significance	0.047525773
Adjusted Chi Square Value	30.43714496

Log-transformed Statistics	
Minimum of log data	1.686398954
Maximum of log data	11.23848862
Mean of log data	5.689295232
Standard Deviation of log data	2.729265264
Variance of log data	7.448888881

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.386760085
Lilliefors 5% Critical Value	0.08995967
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	9114.201943

Gamma Distribution Test	
A-D Test Statistic	7.929335036
A-D 5% Critical Value	0.897695737
K-S Test Statistic	0.229231902
K-S 5% Critical Value	0.100007052
Data do not follow gamma distribution at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	9588.927476
Adjusted Gamma UCL	9645.25593

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.164649971
Lilliefors 5% Critical Value	0.08995967
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	39848.76281
95% Chebyshev (MVUE) UCL	32868.99023
97.5% Chebyshev (MVUE) UCL	42595.08941
99% Chebyshev (MVUE) UCL	61700.12791

95% Non-parametric UCLs	
CLT UCL	9089.194605
Adj-CLT UCL (Adjusted for skewness)	9587.10603
Mod-t UCL (Adjusted for skewness)	9191.866064
Jackknife UCL	9114.201943
Standard Bootstrap UCL	9031.073544
Bootstrap-t UCL	9795.576279
Hall's Bootstrap UCL	9478.732159
Percentile Bootstrap UCL	9286.354639
BCA Bootstrap UCL	9587.405155
95% Chebyshev (Mean, Sd) UCL	13323.8491
97.5% Chebyshev (Mean, Sd) UCL	16266.68052
99% Chebyshev (Mean, Sd) UCL	22047.303

Attachment H3

ProUCL Summary Sheet
Residential Receptor Exposed to Surface and Subsurface Soil (0-10 ft)
Excluding VOCs Exceeding Csat Values
Pyrene

Raw Statistics	
Number of Valid Samples	94
Number of Unique Samples	55
Minimum	0.11
Maximum	46000
Mean	3731.304362
Median	220
Standard Deviation	8.60E+03
Variance	73972234.46
Coefficient of Variation	2.305014666
Skewness	3.20955007

Gamma Statistics	
k hat	0.268791681
k star (bias corrected)	0.267305422
Theta hat	13881.77026
Theta star	13958.95504
nu hat	50.53283599
nu star	50.25341924
Approx.Chi Square Value (.05)	34.97309369
Adjusted Level of Significance	0.047446809
Adjusted Chi Square Value	34.77493126

Log-transformed Statistics	
Minimum of log data	-2.207274913
Maximum of log data	10.73639668
Mean of log data	5.612793426
Standard Deviation of log data	2.660618799
Variance of log data	7.078892395

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.33220818
Lilliefors 5% Critical Value	0.091383922
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	5205.127987

Gamma Distribution Test	
A-D Test Statistic	4.884485338
A-D 5% Critical Value	0.881505828
K-S Test Statistic	0.165883911
K-S 5% Critical Value	0.100833146
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	5361.573216
Adjusted Gamma UCL	5392.125753

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.187325668
Lilliefors 5% Critical Value	0.091383922
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	29707.14117
95% Chebyshev (MVUE) UCL	25130.49225
97.5% Chebyshev (MVUE) UCL	32510.51763
99% Chebyshev (MVUE) UCL	47007.14843

95% Non-parametric UCLs	
CLT UCL	5190.446834
Adj-CLT UCL (Adjusted for skewness)	5504.231043
Mod-t UCL (Adjusted for skewness)	5254.071982
Jackknife UCL	5205.127987
Standard Bootstrap UCL	5237.405351
Bootstrap-t UCL	5606.586218
Hall's Bootstrap UCL	5527.540235
Percentile Bootstrap UCL	5264.894787
BCA Bootstrap UCL	5502.325638
95% Chebyshev (Mean, Sd) UCL	7598.064585
97.5% Chebyshev (Mean, Sd) UCL	9271.214823
99% Chebyshev (Mean, Sd) UCL	12557.79448

Attachment H2

ProUCL Summary Sheet
Construction Worker Receptor Exposed to Surface Soil
Excluding VOCs Exceeding Csat Values
1,2,4-Trimethylbenzene

Raw Statistics	
Number of Valid Samples	149
Number of Unique Samples	51
Minimum	7.5
Maximum	100000
Mean	2232.10403
Median	7.5
Standard Deviation	9873.99432
Variance	97495763.9
Coefficient of Variation	4.42362641
Skewness	7.77473297

Gamma Statistics	
k hat	0.17683724
k star (bias corrected)	0.17775103
Theta hat	12622.3642
Theta star	12557.4745
nu hat	52.6974971
nu star	52.969807
Approx.Chi Square Value (.05)	37.2476815
Adjusted Level of Significance	0.04838926
Adjusted Chi Square Value	37.1193264

Log-transformed Statistics	
Minimum of log data	2.01490302
Maximum of log data	11.5129255
Mean of log data	3.46950874
Standard Deviation of log data	2.5064351
Variance of log data	6.28221692

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.41453356
Lilliefors 5% Critical Value	0.07258395
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	3571.02193

Gamma Distribution Test	
A-D Test Statistic	31.9498467
A-D 5% Critical Value	0.94733015
K-S Test Statistic	0.37535454
K-S 5% Critical Value	0.08609188
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	3174.2679
Adjusted Gamma UCL	3185.24421

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.32324602
Lilliefors 5% Critical Value	0.07258395
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	1629.73463
95% Chebyshev (MVUE) UCL	1799.48083
97.5% Chebyshev (MVUE) UCL	2282.15478
99% Chebyshev (MVUE) UCL	3230.27429

95% Non-parametric UCLs	
CLT UCL	3562.64115
Adj-CLT UCL (Adjusted for skewness)	4113.16039
Mod-t UCL (Adjusted for skewness)	3656.8918
Jackknife UCL	3571.02193
Standard Bootstrap UCL	3556.15187
Bootstrap-t UCL	5329.44725
Hall's Bootstrap UCL	9391.34842
Percentile Bootstrap UCL	3701.58389
BCA Bootstrap UCL	4484.61409
95% Chebyshev (Mean, Sd) UCL	5758.05719
97.5% Chebyshev (Mean, Sd) UCL	7283.73994
99% Chebyshev (Mean, Sd) UCL	10280.6483

Attachment H2

ProUCL Summary Sheet
Construction Worker Receptor Exposed to Surface Soil
Excluding VOCs Exceeding Csat Values
Dibenzofuran

Raw Statistics	
Number of Valid Samples	165
Number of Unique Samples	55
Minimum	16
Maximum	210000
Mean	7376.71515
Median	65
Standard Deviation	31168.6904
Variance	971487259
Coefficient of Variation	4.22528046
Skewness	5.30338455

Gamma Statistics	
k hat	0.18321521
k star (bias corrected)	0.18392443
Theta hat	40262.5694
Theta star	40107.3157
nu hat	60.4610197
nu star	60.6950617
Approx.Chi Square Value (.05)	43.7754381
Adjusted Level of Significance	0.04854545
Adjusted Chi Square Value	43.6493418

Log-transformed Statistics	
Minimum of log data	2.77258872
Maximum of log data	12.2548628
Mean of log data	4.83459207
Standard Deviation of log data	2.48094746
Variance of log data	6.1551003

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.42666161
Lilliefors 5% Critical Value	0.06897501
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	11390.5914

Gamma Distribution Test	
A-D Test Statistic	27.4576996
A-D 5% Critical Value	0.9404438
K-S Test Statistic	0.31858755
K-S 5% Critical Value	0.08126159
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	10227.8858
Adjusted Gamma UCL	10257.4326

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.20294851
Lilliefors 5% Critical Value	0.06897501
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	5648.35636
95% Chebyshev (MVUE) UCL	6451.50076
97.5% Chebyshev (MVUE) UCL	8144.26329
99% Chebyshev (MVUE) UCL	11469.3675

95% Non-parametric UCLs	
CLT UCL	11367.9184
Adj-CLT UCL (Adjusted for skewness)	12438.3727
Mod-t UCL (Adjusted for skewness)	11557.5607
Jackknife UCL	11390.5914
Standard Bootstrap UCL	11172.5615
Bootstrap-t UCL	13172.2345
Hall's Bootstrap UCL	11741.9839
Percentile Bootstrap UCL	11599.9758
BCA Bootstrap UCL	12569.4121
95% Chebyshev (Mean, Sd) UCL	17953.493
97.5% Chebyshev (Mean, Sd) UCL	22530.0732
99% Chebyshev (Mean, Sd) UCL	31519.8789

Attachment H2

ProUCL Summary Sheet
Construction Worker Receptor Exposed to Surface Soil
Excluding VOCs Exceeding Csat Values
Benzene

Raw Statistics	
Number of Valid Samples	194
Number of Unique Samples	68
Minimum	2.5
Maximum	645000
Mean	7913.273196
Median	7.5
Standard Deviation	53073.67856
Variance	2816815356
Coefficient of Variation	6.706918521
Skewness	9.938220928

Gamma Statistics	
k hat	0.142744215
k star (bias corrected)	0.143973256
Theta hat	55436.73492
Theta star	54963.49397
nu hat	55.38475534
nu star	55.86162338
Approx.Chi Square Value (.05)	39.6815406
Adjusted Level of Significance	0.048762887
Adjusted Chi Square Value	39.57988128

Log-transformed Statistics	
Minimum of log data	0.916290732
Maximum of log data	13.3770056
Mean of log data	3.553326335
Standard Deviation of log data	2.815714162
Variance of log data	7.92824624

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.45022239
Lilliefors 5% Critical Value	0.06361109
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	14211.1641

Gamma Distribution Test	
A-D Test Statistic	37.9443963
A-D 5% Critical Value	1.0194313
K-S Test Statistic	0.3245145
K-S 5% Critical Value	0.07494029
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	11139.8973
Adjusted Gamma UCL	11168.5097

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.31584183
Lilliefors 5% Critical Value	0.06361109
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	4239.63852
95% Chebyshev (MVUE) UCL	4595.11706
97.5% Chebyshev (MVUE) UCL	5860.35078
99% Chebyshev (MVUE) UCL	8345.65743

95% Non-parametric UCLs	
CLT UCL	14180.9354
Adj-CLT UCL (Adjusted for skewness)	17086.0718
Mod-t UCL (Adjusted for skewness)	14664.3067
Jackknife UCL	14211.1641
Standard Bootstrap UCL	14223.1399
Bootstrap-t UCL	24711.5706
Hall's Bootstrap UCL	30174.5319
Percentile Bootstrap UCL	15060.7758
BCA Bootstrap UCL	18792.9072
95% Chebyshev (Mean, Sd) UCL	24522.7184
97.5% Chebyshev (Mean, Sd) UCL	31709.6386
99% Chebyshev (Mean, Sd) UCL	45826.9516

Attachment H2

ProUCL Summary Sheet
Construction Worker Receptor Exposed to Surface Soil
Excluding VOCs Exceeding Csat Values
1,3,5-Trimethylbenzene

Raw Statistics	
Number of Valid Samples	174
Number of Unique Samples	58
Minimum	7.9
Maximum	30000
Mean	973.568391
Median	8
Standard Deviation	3865.513
Variance	14942190.7
Coefficient of Variation	3.97045861
Skewness	5.71401668

Gamma Statistics	
k hat	0.2092443
k star (bias corrected)	0.20946806
Theta hat	4652.78324
Theta star	4647.81306
nu hat	72.8170178
nu star	72.8948853
Approx.Chi Square Value (.05)	54.2310358
Adjusted Level of Significance	0.04862069
Adjusted Chi Square Value	54.0972654

Log-transformed Statistics	
Minimum of log data	2.06686276
Maximum of log data	10.3089527
Mean of log data	3.38873165
Standard Deviation of log data	2.21498226
Variance of log data	4.90614642

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.41465239
Lilliefors 5% Critical Value	0.06716749
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	1458.17748

Gamma Distribution Test	
A-D Test Statistic	35.6213408
A-D 5% Critical Value	0.90956078
K-S Test Statistic	0.35306001
K-S 5% Critical Value	0.07778901
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	1308.62623
Adjusted Gamma UCL	1311.86217

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.32622375
Lilliefors 5% Critical Value	0.06716749
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	612.983531
95% Chebyshev (MVUE) UCL	744.510477
97.5% Chebyshev (MVUE) UCL	924.466421
99% Chebyshev (MVUE) UCL	1277.95503

95% Non-parametric UCLs	
CLT UCL	1455.58252
Adj-CLT UCL (Adjusted for skewness)	1591.22003
Mod-t UCL (Adjusted for skewness)	1479.33419
Jackknife UCL	1458.17748
Standard Bootstrap UCL	1437.27845
Bootstrap-t UCL	1743.13257
Hall's Bootstrap UCL	1588.39842
Percentile Bootstrap UCL	1462.22414
BCA Bootstrap UCL	1664.67184
95% Chebyshev (Mean, Sd) UCL	2250.91663
97.5% Chebyshev (Mean, Sd) UCL	2803.62624
99% Chebyshev (Mean, Sd) UCL	3889.31723

Attachment H2

ProUCL Summary Sheet
Construction Worker Receptor Exposed to Surface Soil
Excluding VOCs Exceeding Csat Values
Naphthalene

Raw Statistics	
Number of Valid Samples	244
Number of Unique Samples	124
Minimum	0.24
Maximum	280000
Mean	10378.30057
Median	81
Standard Deviation	40185.58677
Variance	1614881384
Coefficient of Variation	3.872077754
Skewness	5.157912143

Gamma Statistics	
k hat	0.184807518
k star (bias corrected)	0.185267535
Theta hat	56157.35064
Theta star	56017.91268
nu hat	90.18606865
nu star	90.41055688
Approx.Chi Square Value (.05)	69.48216658
Adjusted Level of Significance	0.049016393
Adjusted Chi Square Value	69.37387848

Log-transformed Statistics	
Minimum of log data	-1.42711636
Maximum of log data	12.54254488
Mean of log data	5.216410578
Standard Deviation of log data	2.774651424
Variance of log data	7.698690523

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (μg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.41207916
Lilliefors 5% Critical Value	0.05672034
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	14626.0747

Gamma Distribution Test	
A-D Test Statistic	29.5524397
A-D 5% Critical Value	0.94891815
K-S Test Statistic	0.25768569
K-S 5% Critical Value	0.06564633
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	13504.2987
Adjusted Gamma UCL	13525.3781

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.13452742
Lilliefors 5% Critical Value	0.05672034
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	17680.5025
95% Chebyshev (MVUE) UCL	20566.8034
97.5% Chebyshev (MVUE) UCL	25986.608
99% Chebyshev (MVUE) UCL	36632.7647

95% Non-parametric UCLs	
CLT UCL	14609.8816
Adj-CLT UCL (Adjusted for skewness)	15517.5659
Mod-t UCL (Adjusted for skewness)	14767.6551
Jackknife UCL	14626.0747
Standard Bootstrap UCL	14628.9009
Bootstrap-t UCL	15934.3519
Hall's Bootstrap UCL	15330.3987
Percentile Bootstrap UCL	14782.2289
BCA Bootstrap UCL	15735.6398
95% Chebyshev (Mean, Sd) UCL	21592.085
97.5% Chebyshev (Mean, Sd) UCL	26444.2984
99% Chebyshev (Mean, Sd) UCL	35975.5322

Attachment H2

ProUCL Summary Sheet
Construction Worker Receptor Exposed to Surface Soil
Excluding VOCs Exceeding Csat Values
Indeno(1,2,3-c,d)pyrene

Raw Statistics	
Number of Valid Samples	160
Number of Unique Samples	67
Minimum	0.11
Maximum	2900
Mean	327.381313
Median	73.75
Standard Deviation	604.690174
Variance	365650.206
Coefficient of Variation	1.84705159
Skewness	2.6570313

Gamma Statistics	
k hat	0.46498664
k star (bias corrected)	0.46043481
Theta hat	704.06606
Theta star	711.026418
nu hat	148.795725
nu star	147.339139
Approx.Chi Square Value (.05)	120.279771
Adjusted Level of Significance	0.0485
Adjusted Chi Square Value	120.05927

Log-transformed Statistics	
Minimum of log data	-2.20727491
Maximum of log data	7.97246602
Mean of log data	4.40951385
Standard Deviation of log data	1.71591893
Variance of log data	2.94437776

RECOMMENDATION
Data are Non-parametric (0.05)

Use 97.5% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.30217192
Lilliefors 5% Critical Value	0.07004445
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	406.474284

Gamma Distribution Test	
A-D Test Statistic	9.39189969
A-D 5% Critical Value	0.8284335
K-S Test Statistic	0.19108564
K-S 5% Critical Value	0.07859909
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	401.032363
Adjusted Gamma UCL	401.7689

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.18459077
Lilliefors 5% Critical Value	0.07004445
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	529.633829
95% Chebyshev (MVUE) UCL	662.59019
97.5% Chebyshev (MVUE) UCL	797.608382
99% Chebyshev (MVUE) UCL	1062.82547

95% Non-parametric UCLs	
CLT UCL	406.013467
Adj-CLT UCL (Adjusted for skewness)	416.743227
Mod-t UCL (Adjusted for skewness)	408.147909
Jackknife UCL	406.474284
Standard Bootstrap UCL	407.762194
Bootstrap-t UCL	421.268685
Hall's Bootstrap UCL	416.587622
Percentile Bootstrap UCL	408.010063
BCA Bootstrap UCL	426.741313
95% Chebyshev (Mean, Sd) UCL	535.758283
97.5% Chebyshev (Mean, Sd) UCL	625.923165
99% Chebyshev (Mean, Sd) UCL	803.034616

Attachment H2

ProUCL Summary Sheet
Construction Worker Receptor Exposed to Surface Soil
Excluding VOCs Exceeding Csat Values
Dibenz(a,h)anthrancene

Raw Statistics	
Number of Valid Samples	159
Number of Unique Samples	46
Minimum	0.11
Maximum	15000
Mean	793.912642
Median	85
Standard Deviation	2099.66175
Variance	4408579.46
Coefficient of Variation	2.64470124
Skewness	4.195084

Gamma Statistics	
k hat	0.33641948
k star (bias corrected)	0.33426482
Theta hat	2359.88902
Theta star	2375.10083
nu hat	106.981395
nu star	106.296212
Approx.Chi Square Value (.05)	83.4985357
Adjusted Level of Significance	0.04849057
Adjusted Chi Square Value	83.3149145

Log-transformed Statistics	
Minimum of log data	-2.20727491
Maximum of log data	9.61580548
Mean of log data	4.66523247
Standard Deviation of log data	1.98859691
Variance of log data	3.95451768

RECOMMENDATION

Data are Non-parametric (0.05)

Use 97.5% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.35287328
Lilliefors 5% Critical Value	0.07026437
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	1069.41916

Gamma Distribution Test	
A-D Test Statistic	12.9874814
A-D 5% Critical Value	0.85967737
K-S Test Statistic	0.20734795
K-S 5% Critical Value	0.08021063
Data do not follow gamma distribution at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	1010.67528
Adjusted Gamma UCL	1012.90275

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.20519104
Lilliefors 5% Critical Value	0.07026437
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	1268.07252
95% Chebyshev (MVUE) UCL	1565.74524
97.5% Chebyshev (MVUE) UCL	1923.03811
99% Chebyshev (MVUE) UCL	2624.87076

95% Non-parametric UCLs	
CLT UCL	1067.80381
Adj-CLT UCL (Adjusted for skewness)	1126.99721
Mod-t UCL (Adjusted for skewness)	1078.65213
Jackknife UCL	1069.41916
Standard Bootstrap UCL	1066.16736
Bootstrap-t UCL	1150.51656
Hall's Bootstrap UCL	1150.3933
Percentile Bootstrap UCL	1080.4717
BCA Bootstrap UCL	1144.18868
95% Chebyshev (Mean, Sd) UCL	1519.73038
97.5% Chebyshev (Mean, Sd) UCL	1833.79229
99% Chebyshev (Mean, Sd) UCL	2450.7061

Attachment H2

ProUCL Summary Sheet
Construction Worker Receptor Exposed to Surface Soil
Excluding VOCs Exceeding Csat Values
Benzo(b)fluoranthene

Raw Statistics	
Number of Valid Samples	148
Number of Unique Samples	63
Minimum	0.11
Maximum	3750
Mean	595.819662
Median	159
Standard Deviation	892.036716
Variance	795729.503
Coefficient of Variation	1.49715891
Skewness	1.79269422

Gamma Statistics	
k hat	0.45385855
k star (bias corrected)	0.44916322
Theta hat	1312.78713
Theta star	1326.51036
nu hat	134.34213
nu star	132.952313
Approx.Chi Square Value (.05)	107.309503
Adjusted Level of Significance	0.04837838
Adjusted Chi Square Value	107.084585

Log-transformed Statistics	
Minimum of log data	-2.20727491
Maximum of log data	8.22951112
Mean of log data	4.96902891
Standard Deviation of log data	1.92797486
Variance of log data	3.71708707

RECOMMENDATION

Data are Non-parametric (0.05)

Use 97.5% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (μg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.26667582
Lilliefors 5% Critical Value	0.07282875
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	717.193384

Gamma Distribution Test	
A-D Test Statistic	6.30164408
A-D 5% Critical Value	0.83086559
K-S Test Statistic	0.19369214
K-S 5% Critical Value	0.08200756
Data do not follow gamma distribution at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	738.197456
Adjusted Gamma UCL	739.747944

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.21127482
Lilliefors 5% Critical Value	0.07282875
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	1516.91074
95% Chebyshev (MVUE) UCL	1871.14205
97.5% Chebyshev (MVUE) UCL	2295.05225
99% Chebyshev (MVUE) UCL	3127.74178

95% Non-parametric UCLs	
CLT UCL	716.428499
Adj-CLT UCL (Adjusted for skewness)	727.973864
Mod-t UCL (Adjusted for skewness)	718.994228
Jackknife UCL	717.193384
Standard Bootstrap UCL	715.224057
Bootstrap-t UCL	730.37143
Hall's Bootstrap UCL	730.328963
Percentile Bootstrap UCL	722.164865
BCA Bootstrap UCL	723.64527
95% Chebyshev (Mean, Sd) UCL	915.435781
97.5% Chebyshev (Mean, Sd) UCL	1053.73393
99% Chebyshev (Mean, Sd) UCL	1325.39387

Attachment H2

ProUCL Summary Sheet
Construction Worker Receptor Exposed to Surface Soil
Excluding VOCs Exceeding Csat Values
Benzo(a)pyrene

Raw Statistics	
Number of Valid Samples	185
Number of Unique Samples	84
Minimum	0.11
Maximum	7400
Mean	716.272487
Median	85
Standard Deviation	1398.44644
Variance	1955652.44
Coefficient of Variation	1.95239447
Skewness	2.70302345

Gamma Statistics	
k hat	0.35793948
k star (bias corrected)	0.35573866
Theta hat	2001.0994
Theta star	2013.47944
nu hat	132.437609
nu star	131.623306
Approx.Chi Square Value (.05)	106.115152
Adjusted Level of Significance	0.0487027
Adjusted Chi Square Value	105.936707

Log-transformed Statistics	
Minimum of log data	-2.20727491
Maximum of log data	8.90923528
Mean of log data	4.70227394
Standard Deviation of log data	2.08843435
Variance of log data	4.36155804

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.30428598
Lilliefors 5% Critical Value	0.06514002
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	886.245226

Gamma Distribution Test	
A-D Test Statistic	10.7700873
A-D 5% Critical Value	0.85491832
K-S Test Statistic	0.17963989
K-S 5% Critical Value	0.07276947
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	888.451375
Adjusted Gamma UCL	889.947928

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.19297359
Lilliefors 5% Critical Value	0.06514002
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	1612.76511
95% Chebyshev (MVUE) UCL	1998.98876
97.5% Chebyshev (MVUE) UCL	2456.87291
99% Chebyshev (MVUE) UCL	3356.29766

95% Non-parametric UCLs	
CLT UCL	885.389473
Adj-CLT UCL (Adjusted for skewness)	907.222016
Mod-t UCL (Adjusted for skewness)	889.650662
Jackknife UCL	886.245226
Standard Bootstrap UCL	883.887553
Bootstrap-t UCL	904.992798
Hall's Bootstrap UCL	900.360468
Percentile Bootstrap UCL	885.148216
BCA Bootstrap UCL	924.254108
95% Chebyshev (Mean, Sd) UCL	1164.43629
97.5% Chebyshev (Mean, Sd) UCL	1358.35712
99% Chebyshev (Mean, Sd) UCL	1739.27705

Attachment H2

ProUCL Summary Sheet
Construction Worker Receptor Exposed to Surface Soil
Excluding VOCs Exceeding Csat Values
Benzo(a)anthracene

Raw Statistics	
Number of Valid Samples	182
Number of Unique Samples	106
Minimum	0.11
Maximum	12000
Mean	1277.54401
Median	160
Standard Deviation	2502.97418
Variance	6264879.74
Coefficient of Variation	1.95920779
Skewness	2.51003293

Gamma Statistics	
k hat	0.34144834
k star (bias corrected)	0.33948308
Theta hat	3741.54402
Theta star	3763.2038
nu hat	124.287197
nu star	123.571841
Approx.Chi Square Value (.05)	98.8944769
Adjusted Level of Significance	0.04868132
Adjusted Chi Square Value	98.7195706

Log-transformed Statistics	
Minimum of log data	-2.20727491
Maximum of log data	9.39266193
Mean of log data	5.17537321
Standard Deviation of log data	2.19629208
Variance of log data	4.82369891

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.30489737
Lilliefors 5% Critical Value	0.06567469
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	1584.28823

Gamma Distribution Test	
A-D Test Statistic	9.46277959
A-D 5% Critical Value	0.85885615
K-S Test Statistic	0.17201792
K-S 5% Critical Value	0.07376127
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	1596.33247
Adjusted Gamma UCL	1599.16077

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.15727275
Lilliefors 5% Critical Value	0.06567469
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	3432.62646
95% Chebyshev (MVUE) UCL	4201.78848
97.5% Chebyshev (MVUE) UCL	5202.72463
99% Chebyshev (MVUE) UCL	7168.86988

95% Non-parametric UCLs	
CLT UCL	1582.71829
Adj-CLT UCL (Adjusted for skewness)	1619.60287
Mod-t UCL (Adjusted for skewness)	1590.04148
Jackknife UCL	1584.28823
Standard Bootstrap UCL	1576.90995
Bootstrap-t UCL	1628.33656
Hall's Bootstrap UCL	1632.78341
Percentile Bootstrap UCL	1586.64566
BCA Bootstrap UCL	1636.1605
95% Chebyshev (Mean, Sd) UCL	2086.26269
97.5% Chebyshev (Mean, Sd) UCL	2436.19591
99% Chebyshev (Mean, Sd) UCL	3123.57196

Attachment H2

ProUCL Summary Sheet
Construction Worker Receptor Exposed to Surface Soil
Excluding VOCs Exceeding Csat Values
2-Methylnaphthalene

Raw Statistics	
Number of Valid Samples	182
Number of Unique Samples	84
Minimum	7.6
Maximum	380000
Mean	12930.51978
Median	95.25
Standard Deviation	48373.89795
Variance	2340034002
Coefficient of Variation	3.741063682
Skewness	5.535417545

Gamma Statistics	
k hat	0.179832415
k star (bias corrected)	0.180531148
Theta hat	71903.16474
Theta star	71624.86861
nu hat	65.45899916
nu star	65.713338
Approx.Chi Square Value (.05)	*48.0566441*
Adjusted Level of Significance	0.048681319
Adjusted Chi Square Value	47.93668427

Log-transformed Statistics	
Minimum of log data	2.028148247
Maximum of log data	12.84792653
Mean of log data	5.307437891
Standard Deviation of log data	2.781941593
Variance of log data	7.739199027

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.4193881
Lilliefors 5% Critical Value	0.06567469
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	18858.8324

Gamma Distribution Test	
A-D Test Statistic	24.6391785
A-D 5% Critical Value	0.94899178
K-S Test Statistic	0.2970641
K-S 5% Critical Value	0.07658433
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	17681.3765
Adjusted Gamma UCL	17725.6235

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.17261533
Lilliefors 5% Critical Value	0.06567469
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	22558.5274
95% Chebyshev (MVUE) UCL	24222.0241
97.5% Chebyshev (MVUE) UCL	30908.4031
99% Chebyshev (MVUE) UCL	44042.4998

95% Non-parametric UCLs	
CLT UCL	18828.491
Adj-CLT UCL (Adjusted for skewness)	20400.556
Mod-t UCL (Adjusted for skewness)	19104.0428
Jackknife UCL	18858.8324
Standard Bootstrap UCL	18804.6955
Bootstrap-t UCL	23132.0829
Hall's Bootstrap UCL	22159.5431
Percentile Bootstrap UCL	19418.9841
BCA Bootstrap UCL	20892.5577
95% Chebyshev (Mean, Sd) UCL	28560.2755
97.5% Chebyshev (Mean, Sd) UCL	35323.2833
99% Chebyshev (Mean, Sd) UCL	48607.9025

Attachment H2

ProUCL Summary Sheet
Construction Worker Receptor Exposed to Surface Soil
Excluding VOCs Exceeding Csat Values
1-Methylnaphthalene

Raw Statistics	
Number of Valid Samples	155
Number of Unique Samples	61
Minimum	16
Maximum	230000
Mean	10899.89677
Median	80
Standard Deviation	36736.08831
Variance	1349540184
Coefficient of Variation	3.370315249
Skewness	4.29213855

Gamma Statistics	
k hat	0.176638129
k star (bias corrected)	0.177520401
Theta hat	61707.49691
Theta star	61400.81191
nu hat	54.75781986
nu star	55.03132442
Approx.Chi Square Value (.05)	38.98148229
Adjusted Level of Significance	0.048451613
Adjusted Chi Square Value	38.85514473

Log-transformed Statistics	
Minimum of log data	2.772588722
Maximum of log data	12.34583459
Mean of log data	5.049810281
Standard Deviation of log data	2.732198678
Variance of log data	7.464909618

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.42498165
Lilliefors 5% Critical Value	0.07116523
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	15782.7616

Gamma Distribution Test	
A-D Test Statistic	24.6318758
A-D 5% Critical Value	0.9488835
K-S Test Statistic	0.32943485
K-S 5% Critical Value	0.08439745
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	15387.7103
Adjusted Gamma UCL	15437.7434

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.20228816
Lilliefors 5% Critical Value	0.07116523
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	15996.5056
95% Chebyshev (MVUE) UCL	16548.6543
97.5% Chebyshev (MVUE) UCL	21175.6536
99% Chebyshev (MVUE) UCL	30264.4977

95% Non-parametric UCLs	
CLT UCL	15753.3888
Adj-CLT UCL (Adjusted for skewness)	16840.3533
Mod-t UCL (Adjusted for skewness)	15952.3061
Jackknife UCL	15782.7616
Standard Bootstrap UCL	15712.9317
Bootstrap-t UCL	17715.6343
Hall's Bootstrap UCL	16475.5192
Percentile Bootstrap UCL	15768.2807
BCA Bootstrap UCL	16709.0323
95% Chebyshev (Mean, Sd) UCL	23761.7593
97.5% Chebyshev (Mean, Sd) UCL	29327.0974
99% Chebyshev (Mean, Sd) UCL	40259.1266

Attachment H2

ProUCL Summary Sheet
Construction Worker Receptor Exposed to Surface Soil
Excluding VOCs Exceeding Csat Values
Lead

Raw Statistics	
Number of Valid Samples	207
Number of Unique Samples	149
Minimum	0.5
Maximum	4000
Mean	88.7353865
Median	18
Standard Deviation	310.578035
Variance	96458.7158
Coefficient of Variation	3.50004713
Skewness	10.2804523

Gamma Statistics	
k hat	0.45689771
k star (bias corrected)	0.45349662
Theta hat	194.212806
Theta star	195.669346
nu hat	189.155652
nu star	187.7476
Approx.Chi Square Value (.05)	157.044817
Adjusted Level of Significance	0.04884058
Adjusted Chi Square Value	156.849744

Log-transformed Statistics	
Minimum of log data	-0.69314718
Maximum of log data	8.29404964
Mean of log data	3.07568947
Standard Deviation of log data	1.5857833
Variance of log data	2.51470869

RECOMMENDATION

Data are Non-parametric (0.05)

Use 97.5% Chebyshev (Mean, Sd) UCL

All units are in milligram per kilogram (mg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.38816673
Lilliefors 5% Critical Value	0.06158126
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	124.402686

Gamma Distribution Test	
A-D Test Statistic	10.0236266
A-D 5% Critical Value	0.83138294
K-S Test Statistic	0.16091984
K-S 5% Critical Value	0.06684915
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	106.083449
Adjusted Gamma UCL	106.215384

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.06509663
Lilliefors 5% Critical Value	0.06158126
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	102.58546
95% Chebyshev (MVUE) UCL	127.877825
97.5% Chebyshev (MVUE) UCL	150.690818
99% Chebyshev (MVUE) UCL	195.502527

95% Non-parametric UCLs	
CLT UCL	124.242292
Adj-CLT UCL (Adjusted for skewness)	140.723651
Mod-t UCL (Adjusted for skewness)	126.973445
Jackknife UCL	124.402686
Standard Bootstrap UCL	123.884641
Bootstrap-t UCL	171.06804
Hall's Bootstrap UCL	265.669878
Percentile Bootstrap UCL	128.030411
BCA Bootstrap UCL	144.979541
95% Chebyshev (Mean, Sd) UCL	182.829481
97.5% Chebyshev (Mean, Sd) UCL	223.54407
99% Chebyshev (Mean, Sd) UCL	303.519998

Attachment H2

ProUCL Summary Sheet
Construction Worker Receptor Exposed to Surface Soil
Excluding VOCs Exceeding Csat Values
1,2,4-Trichlorobenzene

Raw Statistics	
Number of Valid Samples	45
Number of Unique Samples	30
Minimum	9.7
Maximum	157000
Mean	9194.61556
Median	50
Standard Deviation	31594.8307
Variance	998233327
Coefficient of Variation	3.43623184
Skewness	3.82564332

Gamma Statistics	
k hat	0.1744733
k star (bias corrected)	0.17765656
Theta hat	52699.271
Theta star	51755.0021
nu hat	15.7025967
nu star	15.9890903
Approx.Chi Square Value (.05)	7.95322239
Adjusted Level of Significance	0.04466667
Adjusted Chi Square Value	7.76489334

Log-transformed Statistics	
Minimum of log data	2.27212589
Maximum of log data	11.9640011
Mean of log data	4.81893821
Standard Deviation of log data	2.63160411
Variance of log data	6.92534019

RECOMMENDATION

Data are Non-parametric (0.05)

Use 99% Chebyshev (Mean, Sd) UCL

All units are in microgram per kilogram (µg/kg)

Normal Distribution Test	
Shapiro-Wilk Test Statisitic	0.33663387
Shapiro-Wilk 5% Critical Value	0.945
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	17108.2947

Gamma Distribution Test	
A-D Test Statistic	8.01909673
A-D 5% Critical Value	0.92163498
K-S Test Statistic	0.37438212
K-S 5% Critical Value	0.14698875
Data do not follow gamma distribution at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	18484.7765
Adjusted Gamma UCL	18933.1046

Lognormal Distribution Test	
Shapiro-Wilk Test Statisitic	0.7864052
Shapiro-Wilk 5% Critical Value	0.945
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	23825.7029
95% Chebyshev (MVUE) UCL	10692.7072
97.5% Chebyshev (MVUE) UCL	14038.5342
99% Chebyshev (MVUE) UCL	20610.7636

95% Non-parametric UCLs	
CLT UCL	16941.6776
Adj-CLT UCL (Adjusted for skewness)	19811.7206
Mod-t UCL (Adjusted for skewness)	17555.9634
Jackknife UCL	17108.2947
Standard Bootstrap UCL	16869.2339
Bootstrap-t UCL	25076.5967
Hall's Bootstrap UCL	16728.5908
Percentile Bootstrap UCL	17218.2667
BCA Bootstrap UCL	21422.1778
95% Chebyshev (Mean, Sd) UCL	29724.5034
97.5% Chebyshev (Mean, Sd) UCL	38607.8022
99% Chebyshev (Mean, Sd) UCL	56057.3227

Attachment H2

ProUCL Summary Sheet
Construction Worker Receptor Exposed to Surface Soil
Excluding VOCs Exceeding Csat Values
Arsenic

Raw Statistics	
Number of Valid Samples	190
Number of Unique Samples	108
Minimum	0.325
Maximum	36
Mean	4.22360526
Median	2.3
Standard Deviation	5.55180566
Variance	30.8225461
Coefficient of Variation	1.31447077
Skewness	2.66360182

Gamma Statistics	
k hat	0.91953022
k star (bias corrected)	0.90852009
Theta hat	4.59322072
Theta star	4.64888481
nu hat	349.421484
nu star	345.237636
Approx.Chi Square Value (.05)	303.173898
Adjusted Level of Significance	0.04873684
Adjusted Chi Square Value	302.875841

Log-transformed Statistics	
Minimum of log data	-1.1239301
Maximum of log data	3.58351894
Mean of log data	0.80660335
Standard Deviation of log data	1.12746075
Variance of log data	1.27116774

RECOMMENDATION

Data are Non-parametric (0.05)

Use 97.5% Chebyshev (Mean, Sd) UCL

All units are in milligram per kilogram (mg/kg)

Normal Distribution Test	
Lilliefors Test Statisitic	0.25553735
Lilliefors 5% Critical Value	0.0642772
Data not normal at 5% significance level	

95% UCL (Assuming Normal Distribution)	
Student's-t UCL	4.88936664

Gamma Distribution Test	
A-D Test Statistic	4.57927176
A-D 5% Critical Value	0.78778434
K-S Test Statistic	0.13761738
K-S 5% Critical Value	0.0683839
Data do not follow gamma distribution	
at 5% significance level	

95% UCLs (Assuming Gamma Distribution)	
Approximate Gamma UCL	4.80960764
Adjusted Gamma UCL	4.81434072

Lognormal Distribution Test	
Lilliefors Test Statisitic	0.10301092
Lilliefors 5% Critical Value	0.0642772
Data not lognormal at 5% significance level	

95% UCLs (Assuming Lognormal Distribution)	
95% H-UCL	5.09038915
95% Chebyshev (MVUE) UCL	6.09745074
97.5% Chebyshev (MVUE) UCL	6.91541843
99% Chebyshev (MVUE) UCL	8.52215757

95% Non-parametric UCLs	
CLT UCL	4.88610348
Adj-CLT UCL (Adjusted for skewness)	4.96926652
Mod-t UCL (Adjusted for skewness)	4.9023384
Jackknife UCL	4.88936664
Standard Bootstrap UCL	4.89108746
Bootstrap-t UCL	5.04634846
Hall's Bootstrap UCL	4.97801405
Percentile Bootstrap UCL	4.91184211
BCA Bootstrap UCL	5.00602632
95% Chebyshev (Mean, Sd) UCL	5.97924036
97.5% Chebyshev (Mean, Sd) UCL	6.73890507
99% Chebyshev (Mean, Sd) UCL	8.2311193

ATTACHMENT H4

Risk Calculations

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Attachment H4

Table 1a
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Incidental Ingestion of Soil Pathway (0-10 feet) – Carcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Ing-Risk} = \frac{(\text{Csoil} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{SIRadj} \times \text{FI})}{\text{ATc}}$$

Equation Units	Ing - Risk unitless	= (	Csoil mg/kg	×	SFo kg-day/mg	×	CF kg/mg	×	EF days/year	×	SIRadj mg-yr/kg-day	×	FI unitless	) ÷ (	ATc days	)
Arsenic	1.19E-05	= (	5.07E+00	×	1.50E+00	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Lead	NA	= (	9.05E+01	×	a	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Thallium	NA	= (	8.17E-01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25550	)
1-Methylnaphthalene	NA	= (	1.50E+02	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
2-Methylnaphthalene	NA	= (	1.44E+02	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Acenaphthene	NA	= (	3.64E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Benzo(a)anthracene	2.81E-05	= (	2.46E+01	×	7.30E-01	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Benzo(a)pyrene	2.23E-04	= (	1.95E+01	×	7.30E+00	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Benzo(b)fluoranthene	2.43E-05	= (	2.13E+01	×	7.30E-01	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Benzo(k)fluoranthene	1.16E-06	= (	1.01E+01	×	7.30E-02	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Chrysene	2.67E-07	= (	2.34E+01	×	7.30E-03	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Dibenzo(a,h)anthracene	3.56E-05	= (	3.12E+00	×	7.30E+00	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Dibenzofuran	NA	= (	9.93E+00	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Fluoranthene	NA	= (	6.36E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Fluorene	NA	= (	4.59E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Indeno(1,2,3-cd)pyrene	6.11E-06	= (	5.34E+00	×	7.30E-01	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Naphthalene	NA	= (	1.86E+02	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Phenanthrene	NA	= (	1.44E+02	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Pyrene	NA	= (	8.56E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
1,2,4-Trichlorobenzene	NA	= (	2.96E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	6.05E+00	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	2.22E+00	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Benzene	1.22E-06	= (	1.41E+01	×	5.50E-02	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Xylenes (total)	NA	= (	1.30E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – Soil Concentration
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
SIRadj – Age-adjusted Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. *Toxicity criteria for lead have not been derived by USEPA.*

Attachment H4

Table 1b
Risk Calculations: Reasonable Maximum Exposure
Residential Child: Incidental Ingestion of Soil Pathway (0-10 feet) – Noncarcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$Ing\text{-}HQ = \frac{(Csoil \times CF \times EF \times EDc \times SIRc \times FI)}{(BWc \times ATn \times RfDo)}$$

Equation	Ing - HQ	= (	Csoil	×	CF	×	EF	×	EDc	×	SIRc	×	FI	) ÷ (	BWc	×	ATn	×	RfDo [b]	)
Units	unitless		mg/kg		kg/mg		days/year		years		mg/day		unitless		kg		days		mg/kg-day	
Arsenic	2.16E-01	= (	5.07E+00	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	3.0E-04	)
Lead	NA	= (	9.05E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	a	)
Thallium	1.31E-02	= (	8.17E-01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	8.0E-04	)
1-Methylnaphthalene	2.74E-02	= (	1.50E+02	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	7.0E-02	)
2-Methylnaphthalene	4.60E-01	= (	1.44E+02	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	4.0E-03	)
Acenaphthene	7.76E-04	= (	3.64E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	6.0E-01	)
Benzo(a)anthracene	NA	= (	2.46E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	= (	1.95E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	= (	2.13E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.01E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	NV	)
Chrysene	NA	= (	2.34E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	3.12E+00	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	NV	)
Dibenzofuran	6.35E-02	= (	9.93E+00	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	2.0E-03	)
Fluoranthene	2.03E-03	= (	6.36E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	4.0E-01	)
Fluorene	1.47E-03	= (	4.59E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	4.0E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (	5.34E+00	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	NV	)
Naphthalene	1.19E-01	= (	1.86E+02	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	2.0E-02	)
Phenanthrene	NA	= (	1.44E+02	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	NV	)
Pyrene	3.65E-03	= (	8.56E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	3.0E-01	)
1,2,4-Trichlorobenzene	3.79E-02	= (	2.96E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	1.0E-02	)
1,2,4-Trimethylbenzene	1.55E-03	= (	6.05E+00	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	5.0E-02	)
1,3,5-Trimethylbenzene	5.66E-05	= (	2.22E+00	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	5.0E-01	)
Benzene	4.52E-02	= (	1.41E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	4.0E-03	)
Xylenes (total)	4.67E-04	= (	1.30E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	3.6E-01	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
EDc – Exposure Duration, child
SIRc – *Soil Ingestion Rate, child*
FI – Fraction Ingested from Contaminated Source
BWc – Body Weight, child
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose (subchronic)
NV – No toxicity value available for this pathway.
NA – *Not Applicable*

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment H4

Table 2a
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Dermal Contact with Soil Pathway (0-10 feet) – Carcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{EV} \times \text{SCRadj} \times \text{ABSd})}{\text{ATc}}$$

Equation Units	Derm - Risk unitless	= (	Csoil mg/kg	×	SFabs kg-day/mg	×	CF kg/mg	×	EF days/year	×	EV events/day	×	SCRadj mg-yr/kg-event	×	ABSd unitless	) ÷ (	ATc days	)
Arsenic	1.18E-06	= (	5.07E+00	×	1.58E+00	×	1E-06	×	350	×	1	×	360	×	3.00E-02	) ÷ (	25,550	)
Lead	NA	= (	9.05E+01	×	a	×	1E-06	×	350	×	1	×	360	×	NA	) ÷ (	25,550	)
Thallium	NA	= (	8.17E-01	×	NV	×	1E-06	×	350	×	1	×	360	×	NA	) ÷ (	25,550	)
1-Methylnaphthalene	NA	= (	1.50E+02	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
2-Methylnaphthalene	NA	= (	1.44E+02	×	NV	×	1E-06	×	350	×	1	×	360	×	1.00E-01	) ÷ (	25,550	)
Acenaphthene	NA	= (	3.64E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Benzo(a)anthracene	1.15E-05	= (	2.46E+01	×	7.30E-01	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Benzo(a)pyrene	9.14E-05	= (	1.95E+01	×	7.30E+00	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Benzo(b)fluoranthene	9.97E-06	= (	2.13E+01	×	7.30E-01	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Benzo(k)fluoranthene	4.74E-07	= (	1.01E+01	×	7.30E-02	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Chrysene	1.10E-07	= (	2.34E+01	×	7.30E-03	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Dibenzo(a,h)anthracene	1.46E-05	= (	3.12E+00	×	7.30E+00	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Dibenzofuran	NA	= (	9.93E+00	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Fluoranthene	NA	= (	6.36E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Fluorene	NA	= (	4.59E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Indeno(1,2,3-cd)pyrene	2.50E-06	= (	5.34E+00	×	7.30E-01	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Naphthalene	NA	= (	1.86E+02	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Phenanthrene	NA	= (	1.44E+02	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Pyrene	NA	= (	8.56E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
1,2,4-Trichlorobenzene	NA	= (	2.96E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	NV	) ÷ (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	6.05E+00	×	NV	×	1E-06	×	350	×	1	×	360	×	NA	) ÷ (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	2.22E+00	×	NV	×	1E-06	×	350	×	1	×	360	×	NA	) ÷ (	25,550	)
Benzene	NA	= (	1.41E+01	×	5.50E-02	×	1E-06	×	350	×	1	×	360	×	NA	) ÷ (	25,550	)
Xylenes (total)	NA	= (	1.30E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	NA	) ÷ (	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csoil – Soil Concentration
SFabs – Absorbed slope factor (SFo ÷ ABSgi)
CF – Unit Conversion Factor
EF – Exposure Frequency
EV – Event Frequency
SCRadj – Age-adjusted Soil Contact Rate
ABSd – Dermal Soil Absorption Factor
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment H4

Table 2b
Risk Calculations: Reasonable Maximum Exposure
Residential Child: Dermal Contact with Soil Pathway (0-10 feet) – Noncarcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{EDc} \times \text{EV} \times \text{SAc} \times \text{AFc} \times \text{ABSd})}{(\text{BWc} \times \text{ATn} \times \text{RfDabs})}$$

Equation / Units	Derm - HQ unitless	= (	Csoil mg/kg	×	CF kg/mg	×	EF days/year	×	EDc years	×	EV events/day	×	SAc cm²	×	AFc mg/cm²-event	×	ABSd unitless	) ÷ (	BWc kg	×	ATn days	×	RfDabs [6] mg/kg-day	)
Arsenic	1.91E-02	= (	5.07E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	3.00E-02	) ÷ (	15	×	2,190	×	2.85E-04	)
Lead	NA	= (	9.05E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	a	)
Thallium	NA	= (	8.17E-01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	8.00E-04	)
1-Methylnaphthalene	9.98E-03	= (	1.50E+02	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	7.00E-02	)
2-Methylnaphthalene	1.29E-01	= (	1.44E+02	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.00E-01	) ÷ (	15	×	2,190	×	4.00E-03	)
Acenaphthene	2.82E-04	= (	3.64E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	6.00E-01	)
Benzo(a)anthracene	NA	= (	2.46E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	= (	1.95E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	= (	2.13E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.01E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Chrysene	NA	= (	2.34E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	3.12E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Dibenzofuran	2.31E-02	= (	9.93E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	2.00E-03	)
Fluoranthene	7.40E-04	= (	6.36E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	4.00E-01	)
Fluorene	5.34E-04	= (	4.59E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	4.00E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (	5.34E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Naphthalene	4.33E-02	= (	1.86E+02	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	2.00E-02	)
Phenanthrene	NA	= (	1.44E+02	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Pyrene	1.33E-03	= (	8.56E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	3.00E-01	)
1,2,4-Trichlorobenzene	NA	= (	2.96E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	NV	) ÷ (	15	×	2,190	×	NV	)
1,2,4-Trimethylbenzene	NA	= (	6.05E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	5.00E-02	)
1,3,5-Trimethylbenzene	NA	= (	2.22E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	5.00E-01	)
Benzene	NA	= (	1.41E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	4.00E-03	)
Xylenes (total)	NA	= (	1.30E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	3.57E-01	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
EDc – Exposure Duration, child
EV – Event Frequency
SAc – Skin Surface Area, child
AFc – Soil-to-skin Adherence Factor, child
ABSd – Dermal Soil Absorption Factor
BWc – Body Weight, child
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo × ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment H4

Table 3a
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Inhalation of Soil-derived Chemicals Pathway (0-10 feet)– Carcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{EF} \times \text{SInhRadj} \times [(1/\text{VF}) + (1/\text{PEF})])}{\text{ATc}}$$

Equation	Inh - Risk	= (	Csoil	×	SFi	×	EF	×	SInhRadj	× [	1	/	VF_{adult}	+	1	/	PEF	]) + (	ATc	)
Units	unitless		mg/kg		kg-day/mg		days/year		m3-yr/kg-day				m^3/kg				m^3/kg		days	
Arsenic	1.72E-09	= (	5.07E+00	×	1.51E+01	×	350	×	10.86	× [	1	/	NA	+	1	/	6.58E+09	]) + (	25,550	)
Lead	NA	= (	9.05E+01	×	a	×	350	×	10.86	× [	1	/	NA	+	1	/	6.58E+09	]) + (	25,550	)
Thallium	NA	= (	8.17E-01	×	NV	×	350	×	10.86	× [	1	/	NA	+	1	/	6.58E+09	]) + (	25,550	)
1-Methylnaphthalene	NA	= (	1.50E+02	×	NV	×	350	×	10.86	× [	1	/	3.28E+04	+	1	/	6.58E+09	]) + (	25,550	)
2-Methylnaphthalene	NA	= (	1.44E+02	×	NV	×	350	×	10.86	× [	1	/	3.11E+04	+	1	/	6.58E+09	]) + (	25,550	)
Acenaphthene	NA	= (	3.64E+01	×	NV	×	350	×	10.86	× [	1	/	6.00E+04	+	1	/	6.58E+09	]) + (	25,550	)
Benzo(a)anthracene	NA	= (	2.46E+01	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Benzo(a)pyrene	1.36E-09	= (	1.95E+01	×	3.08E+00	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Benzo(b)fluoranthene	NA	= (	2.13E+01	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Benzo(k)fluoranthene	NA	= (	1.01E+01	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Chrysene	NA	= (	2.34E+01	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Dibenzo(a,h)anthracene	NA	= (	3.12E+00	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Dibenzofuran	NA	= (	9.93E+00	×	NV	×	350	×	10.86	× [	1	/	4.98E+04	+	1	/	6.58E+09	]) + (	25,550	)
Fluoranthene	NA	= (	6.36E+01	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Fluorene	NA	= (	4.59E+01	×	NV	×	350	×	10.86	× [	1	/	9.16E+04	+	1	/	6.58E+09	]) + (	25,550	)
Indeno(1,2,3-cd)pyrene	NA	= (	5.34E+00	×	NV	×	350	×	10.86	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Naphthalene	NA	= (	1.86E+02	×	NV	×	350	×	10.86	× [	1	/	2.87E+04	+	1	/	6.58E+09	]) + (	25,550	)
Phenanthrene	NA	= (	1.44E+02	×	NV	×	350	×	10.86	× [	1	/	1.46E+05	+	1	/	6.58E+09	]) + (	25,550	)
Pyrene	NA	= (	8.56E+01	×	NV	×	350	×	10.86	× [	1	/	3.05E+05	+	1	/	6.58E+09	]) + (	25,550	)
1,2,4-Trichlorobenzene	NA	= (	2.96E+01	×	NV	×	350	×	10.86	× [	1	/	1.44E+05	+	1	/	6.58E+09	]) + (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	6.05E+00	×	NV	×	350	×	10.86	× [	1	/	5.47E+03	+	1	/	6.58E+09	]) + (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	2.22E+00	×	NV	×	350	×	10.86	× [	1	/	4.52E+03	+	1	/	6.58E+09	]) + (	25,550	)
Benzene	1.80E-05	= (	1.41E+01	×	2.73E-02	×	350	×	10.86	× [	1	/	3.20E+03	+	1	/	6.58E+09	]) + (	25,550	)
Xylenes (total)	NA	= (	1.30E+01	×	NV	×	350	×	10.86	× [	1	/	4.43E+03	+	1	/	6.58E+09	]) + (	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Soil Concentration
SFi – Inhalation Slope Factor
EF – Exposure frequency
SInhRadj – Age-adjusted Soil Inhalation Rate
VF – Volatilization Factor
PEF – Particulate Emission Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment H4

Table 3b
Risk Calculations: Reasonable Maximum Exposure
Residential Child: Inhalation of Soil-derived Pathway (0-10 feet) – Noncarcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{InhRc} \times \text{EF} \times \text{EDc} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BWc} \times \text{ATn} \times \text{RfDi})}$$

Equation	Inh - HQ	=	(	Csoil	×	InhRc	×	EF	×	EDc	×	[	1	/	VF_{child}	+	1	/	PEF	]	÷	(	BWc	×	ATn	×	RfDi (b)	)
Units	unitless			mg/kg		m^3/day		days/year		year					m^3/kg				m^3/kg				kg		days		mg/kg-day	
Arsenic	NA	=	(	5.07E+00	×	10	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Lead	NA	=	(	9.05E+01	×	10	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	a	)
Thallium	NA	=	(	8.17E-01	×	10	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
1-Methylnaphthalene	NA	=	(	1.50E+02	×	10	×	350	×	6	×	[	1	/	1.47E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
2-Methylnaphthalene	NA	=	(	1.44E+02	×	10	×	350	×	6	×	[	1	/	1.39E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Acenaphthene	NA	=	(	3.64E+01	×	10	×	350	×	6	×	[	1	/	2.68E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Benzo(a)anthracene	NA	=	(	2.46E+01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	=	(	1.95E+01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	=	(	2.13E+01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	=	(	1.01E+01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Chrysene	NA	=	(	2.34E+01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	=	(	3.12E+00	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Dibenzofuran	NA	=	(	9.93E+00	×	10	×	350	×	6	×	[	1	/	2.23E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Fluoranthene	NA	=	(	6.36E+01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Fluorene	NA	=	(	4.59E+01	×	10	×	350	×	6	×	[	1	/	4.10E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	=	(	5.34E+00	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Naphthalene	1.08E+01	=	(	1.86E+02	×	10	×	350	×	6	×	[	1	/	1.29E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	8.57E-04	)
Phenanthrene	NA	=	(	1.44E+02	×	10	×	350	×	6	×	[	1	/	6.54E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Pyrene	NA	=	(	8.56E+01	×	10	×	350	×	6	×	[	1	/	1.36E+05	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
1,2,4-Trichlorobenzene	2.59E-01	=	(	2.96E+01	×	10	×	350	×	6	×	[	1	/	6.42E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	1.14E-03	)
1,2,4-Trimethylbenzene	9.24E-01	=	(	6.05E+00	×	10	×	350	×	6	×	[	1	/	2.44E+03	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	1.71E-03	)
1,3,5-Trimethylbenzene	4.12E-02	=	(	2.22E+00	×	10	×	350	×	6	×	[	1	/	2.02E+03	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	1.70E-02	)
Benzene	7.38E-01	=	(	1.41E+01	×	10	×	350	×	6	×	[	1	/	1.43E+03	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	8.57E-03	)
Xylenes (total)	1.47E-01	=	(	1.30E+01	×	10	×	350	×	6	×	[	1	/	1.98E+03	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	2.86E-02	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Csoil – Soil Concentration
InhRc – Inhalation Rate, child
EF – Exposure frequency
EDc – Exposure duration, child
VF – Volatilization Factor
PEF – Particulate Emission Factor
BWc – Body Weight, child
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

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Table 3c
Residential Scenario: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} \times \frac{(3.14 \times D_A \times T)^{1/2}}{(2 \times \rho_b \times D_A)} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} $(g/m^2\text{-}s)/(kg/m^3)$	π	D_A (cm^2/s)	T_{adult} (s)	T_{child} (s)	2	ρb (g/cm^3)	10^{-4} (m^2/cm^2)	VF_{adult} (m^3/kg)
1-Methylnaphthalene	73.32	3.14	1.95E-05	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.28E+04
2-Methylnaphthalene	73.32	3.14	2.17E-05	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.11E+04
Acenaphthene	73.32	3.14	5.82E-06	9.46E+08	1.89E+08	2	1.38	1.00E-04	6.00E+04
Benzo(a)anthracene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Benzo(a)pyrene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Benzo(b)fluoranthene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Benzo(k)fluoranthene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Chrysene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Dibenzo(a,h)anthracene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Dibenzofuran	73.32	3.14	8.46E-06	9.46E+08	1.89E+08	2	1.38	1.00E-04	4.98E+04
Fluoranthene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Fluorene	73.32	3.14	2.50E-06	9.46E+08	1.89E+08	2	1.38	1.00E-04	9.16E+04
Indeno(1,2,3-cd)pyrene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Naphthalene	73.32	3.14	2.54E-05	9.46E+08	1.89E+08	2	1.38	1.00E-04	2.87E+04
Phenanthrene	73.32	3.14	9.79E-07	9.46E+08	1.89E+08	2	1.38	1.00E-04	1.46E+05
Pyrene	73.32	3.14	2.25E-07	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.05E+05
1,2,4-Trichlorobenzene	73.32	3.14	1.02E-06	9.46E+08	1.89E+08	2	1.38	1.00E-04	1.44E+05
1,2,4-Trimethylbenzene	73.32	3.14	7.01E-04	9.46E+08	1.89E+08	2	1.38	1.00E-04	5.47E+03
1,3,5-Trimethylbenzene	73.32	3.14	1.02E-03	9.46E+08	1.89E+08	2	1.38	1.00E-04	4.52E+03
Benzene	73.32	3.14	2.05E-03	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.20E+03
Xylenes (total)	73.32	3.14	1.07E-03	9.46E+08	1.89E+08	2	1.38	1.00E-04	4.43E+03

Notes:

Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

VF_{adult} – Volatilization Factor (m^3/kg) for adults (calculated)

VF_{child} – Volatilization Factor (m^3/kg) for children (calculated)

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source $(g/m^2\text{-}s)/(kg/m^3)$(Value used is for Minneapolis, MN.)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T_{adult} – Exposure interval (s) for adults

T_{Child} – Exposure interval (s) for children

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated; PAHs are not considered volatile chemicals

Attachment H4

Table 3d
Residential Scenario: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical Units	VOC?	θa (Lair /Lsoil)	Di (cm^2/s)	H' unitless	θw (Lwater /Lsoil)	Dw (cm^2/s)	η (Lpore /Lsoil)	ρb (g/cm^3)	ρs (g/cm^3)	Kd (cm^3/g)	D_A (cm^2/s)
1-Methylnaphthalene	Yes	3.29E-01	6.31E-02	1.64E-02	0.15	7.13E-06	4.79E-01	1.38	2.65	3.75E+01	1.95E-05
2-Methylnaphthalene	Yes	3.29E-01	4.80E-02	2.12E-02	0.15	7.84E-06	4.79E-01	1.38	2.65	1.79E+01	2.17E-05
Acenaphthene	Yes	3.29E-01	4.21E-02	7.44E-03	0.15	7.69E-06	4.79E-01	1.38	2.65	3.67E+01	5.82E-06
Benzo(a)anthracene	No	3.29E-01	5.10E-02	4.91E-04	0.15	9.00E-06	4.79E-01	1.38	2.65	1.39E+03	NC
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Benzo(b)fluoranthene	No	3.29E-01	2.26E-02	2.69E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.82E+03	NC
Benzo(k)fluoranthene	No	3.29E-01	2.26E-02	2.39E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Chrysene	No	3.29E-01	2.48E-02	2.14E-04	0.15	6.21E-06	4.79E-01	1.38	2.65	1.42E+03	NC
Dibenzo(a,h)anthracene	No	3.29E-01	2.02E-02	5.03E-06	0.15	5.18E-06	4.79E-01	1.38	2.65	1.57E+04	NC
Dibenzofuran	Yes	3.29E-01	5.51E-02	8.71E-03	0.15	7.04E-06	4.79E-01	1.38	2.65	6.78E+01	8.46E-06
Fluoranthene	No	3.29E-01	3.02E-02	3.62E-04	0.15	6.35E-06	4.79E-01	1.38	2.65	4.25E+02	NC
Fluorene	Yes	3.29E-01	3.63E-02	3.93E-03	0.15	7.88E-06	4.79E-01	1.38	2.65	6.78E+01	2.50E-06
Indeno(1,2,3-cd)pyrene	No	3.29E-01	1.90E-02	1.42E-05	0.15	5.66E-06	4.79E-01	1.38	2.65	1.61E+04	NC
Naphthalene	Yes	3.29E-01	5.90E-02	1.80E-02	0.15	7.50E-06	4.79E-01	1.38	2.65	1.10E+01	2.54E-05
Phenanthrene	Yes	3.29E-01	3.33E-02	1.73E-03	0.15	7.47E-06	4.79E-01	1.38	2.65	1.25E+02	9.79E-07
Pyrene	Yes	3.29E-01	2.72E-02	4.87E-04	0.15	7.24E-06	4.79E-01	1.38	2.65	4.16E+02	2.25E-07
1,2,4-Trichlorobenzene	Yes	3.29E-01	3.00E-02	1.42E-03	0.15	8.23E-06	4.79E-01	1.38	2.65	1.07E+01	1.02E-06
1,2,4-Trimethylbenzene	Yes	3.29E-01	6.44E-02	2.52E-01	0.15	7.92E-06	4.79E-01	1.38	2.65	4.31E+00	7.01E-04
1,3,5-Trimethylbenzene	Yes	3.29E-01	6.02E-02	3.59E-01	0.15	8.67E-06	4.79E-01	1.38	2.65	4.22E+00	1.02E-03
Benzene	Yes	3.29E-01	8.80E-02	2.27E-01	0.15	9.80E-06	4.79E-01	1.38	2.65	9.93E-01	2.05E-03
Xylenes (total)	Yes	3.29E-01	7.14E-02	2.71E-01	0.15	9.34E-06	4.79E-01	1.38	2.65	2.66E+00	1.07E-03

Notes:

D_A – *apparent diffusivity*
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's Law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User'S Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density

Kd – *soil-water partition coefficient, where:*
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm^3/g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)
VOC? – Volatile organic compounds; If no, an apparent diffusivity was not calculated.
NV – no value available
NC – not calculated

Attachment H4

Table 4a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Ingestion of Soil Pathway – Carcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$Ing\text{-}Risk = \frac{(Csoil \times SFo \times CF \times EF \times ED \times SIR \times FI)}{(BW \times ATc)}$$

Equation	Ing - Risk	= (	Csoil	×	SFo	×	CF	×	EF	×	ED	×	SIR	×	FI	) + (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		mg/day		unitless		kg		days	
Inorganics																				
Arsenic	3.39E-07	= (	4.90E+00	×	1.50E+00	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
Lead	NA	= (	8.87E+01	×	a	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
SVOCs																				
1-Methylnaphthalene	NA	= (	1.31E+03	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	1.41E+03	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25550	)
Acenaphthene	NA	= (	4.41E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
Benzo(a)anthracene	6.64E-06	= (	1.97E+02	×	7.30E-01	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
Benzo(a)pyrene	5.82E-05	= (	1.73E+02	×	7.30E+00	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
Benzo(b)fluoranthene	3.43E-06	= (	1.02E+02	×	7.30E-01	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
Benzo(k)fluoranthene	4.00E-07	= (	1.19E+02	×	7.30E-02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
Chyrsene	6.11E-08	= (	1.81E+02	×	7.30E-03	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
Dibenzo(a,h)anthracene	8.82E-06	= (	2.62E+01	×	7.30E+00	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
Dibenzofuran	NA	= (	8.92E+01	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
Fluoranthene	NA	= (	3.29E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
Fluorene	NA	= (	2.82E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	3.15E-06	= (	9.34E+01	×	7.30E-01	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
Naphthalene	NA	= (	1.17E+03	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
Pyrene	NA	= (	4.85E+02	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
VOCs																) + (				
1,2,4-Trichlorobenzene	NA	= (	1.69E+01	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	3.56E+00	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	= (	1.44E+00	×	NV	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)
Benzene	3.61E-08	= (	1.42E+01	×	5.50E-02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – Concentration in soil
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
VOC – Volatile organic compound
SIR – Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
SVOC – Semivolatile organic compound
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment H4

Table 4b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Ingestion of Soil Pathway – Noncarcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Ing - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation	Ing - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	SIR	×	FI	) + (	BW	×	ATn	×	RfDo [a]	)
Units	unitless		mg/kg		kg/mg		days/year		years		mg/day		unitless		kg		days		mg/kg-day	
Inorganics																				
Arsenic	5.3E-02	= (	4.90E+00	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	3.0E-04	)
Lead	NA	= (	8.87E+01	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	a	)
SVOCs																				
1-Methylnaphthalene	6.1E-02	= (	1.31E+03	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	7.0E-02	)
2-Methylnaphthalene	1.1E+00	= (	1.41E+03	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	4.0E-03	)
Acenaphthene	2.4E-03	= (	4.41E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	6.0E-01	)
Benzo(a)anthracene	NA	= (	1.97E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	NV	)
Benzo(a)pyrene	NA	= (	1.73E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.02E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.19E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	NV	)
Chyrsene	NA	= (	1.81E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.62E+01	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	NV	)
Dibenzofuran	1.4E-01	= (	8.92E+01	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	2.0E-03	)
Fluoranthene	2.7E-03	= (	3.29E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	4.0E-01	)
Fluorene	2.3E-03	= (	2.82E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	4.0E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (	9.34E+01	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	NV	)
Naphthalene	1.9E-01	= (	1.17E+03	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	2.0E-02	)
Pyrene	5.2E-03	= (	4.85E+02	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	3.0E-01	)
VOCs																				
1,2,4-Trichlorobenzene	5.4E-03	= (	1.69E+01	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	1.0E-02	)
1,2,4-Trimethylbenzene	2.3E-04	= (	3.56E+00	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	5.0E-02	)
1,3,5-Trimethylbenzene	9.3E-06	= (	1.44E+00	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	5.0E-01	)
Benzene	1.1E-02	= (	1.42E+01	×	1E-06	×	250	×	1	×	330	×	1	) + (	70	×	365	×	4.0E-03	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Concentration in Soil
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
SIR – Soil Ingestion Rate
VOC – Volatile organic compound
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose
NV – *No toxicity value available for this pathway.*
NA – Not Applicable
SVOC – Semivolatile organic compound

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available. Toxicity criteria is presented in Attachment A, Table 1b.

Attachment H4

Table 5a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Dermal Contact with Soil Pathway – Carcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATc})}$$

Equation	Derm - Risk	= (	Csoil	×	SFabs	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless		kg		days	
Inorganics																								
Arsenic	1.88E-08	= (	4.90E+00	×	1.58E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	3.00E-02	) ÷ (	70	×	25,550	)
Lead	NA	= (	8.87E+01	×	a	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
SVOCs																								
1-Methylnaphthalene	NA	= (	1.31E+03	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	1.41E+03	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.00E-01	) ÷ (	70	×	25,550	)
Acenaphthene	NA	= (	4.41E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(a)anthracene	1.52E-06	= (	1.97E+02	×	7.30E-01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	1.33E-05	= (	1.73E+02	×	7.30E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	7.83E-07	= (	1.02E+02	×	7.30E-01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	9.11E-08	= (	1.19E+02	×	7.30E-02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Chyrsene	1.39E-08	= (	1.81E+02	×	7.30E-03	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	2.01E-06	= (	2.62E+01	×	7.30E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	8.92E+01	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	3.29E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	2.82E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	7.18E-07	= (	9.34E+01	×	7.30E-01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	1.17E+03	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	4.86E+02	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) ÷ (	70	×	25,550	)
VOCs																								
1,2,4-Trichlorobenzene	NA	= (	1.69E+01	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	3.56E+00	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	= (	1.44E+00	×	NV	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)
Benzene	NA	= (	1.42E+01	×	5.50E-02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) ÷ (	70	×	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csoil – Concentration in Soil
SFabs – Absorbed slope factor (SFo ÷ ABSgi)
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
VOC – Volatile organic compound
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment H4

Table 5b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Dermal Contact with Soil Pathway – Noncarcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(BW \times ATn \times \text{RfDabs})}$$

Equation	Derm - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) + (	BW	×	ATn	×	RfDabs [b]	)
Units	unitless		mg/kg		kg/mg		days/year		years		events/day		cm^2		mg/cm^2-event		unitless		kg		days		mg/kg-day	
Inorganics																								
Arsenic	2.92E-03	= (	4.90E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	3.00E-02	) + (	70	×	365	×	2.85E-04	)
Lead	NA	= (	8.87E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	a	)
SVOCs																								
1-Methylnaphthalene	1.38E-02	= (	1.31E+03	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	7.00E-02	)
2-Methylnaphthalene	2.00E-01	= (	1.41E+03	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.00E-01	) + (	70	×	365	×	4.00E-03	)
Acenaphthene	5.41E-04	= (	4.41E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	6.00E-01	)
Benzo(a)anthracene	NA	= (	1.97E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Benzo(a)pyrene	NA	= (	1.73E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.02E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.19E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Chyrsene	NA	= (	1.81E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.62E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Dibenzofuran	3.29E-02	= (	8.92E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	2.00E-03	)
Fluoranthene	6.06E-04	= (	3.29E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	4.00E-01	)
Fluorene	5.20E-04	= (	2.82E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	4.00E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (	9.34E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	NV	)
Naphthalene	4.32E-02	= (	1.17E+03	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	2.00E-02	)
Pyrene	1.19E-03	= (	4.85E+02	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	1.30E-01	) + (	70	×	365	×	3.00E-01	)
VOCs																								
1,2,4-Trichlorobenzene	NA	= (	1.69E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NV	) + (	70	×	365	×	NV	)
1,2,4-Trimethylbenzene	NA	= (	3.56E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	5.00E-02	)
1,3,5-Trimethylbenzene	NA	= (	1.44E+00	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	5.00E-01	)
Benzene	NA	= (	1.42E+01	×	1E-06	×	250	×	1	×	1	×	1,930	×	0.3	×	NA	) + (	70	×	365	×	4.00E-03	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Concentration in Soil
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
SSAF – Soil-to-skin Adherence Factor
ABSd – Dermal Soil Absorption Factor
BW – Body Weight
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo ×ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.
VOC – Volatile organic compound
SVOC – Semivolatile organic compound

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available. Toxicity criteria is presented in Attachment A, Table 1b.

Attachment H4

Table 6a
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Inhalation of Soil (Fugitive Emissions and Volatile Compounds) Pathway– Carcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times [(1/\text{VF}) + (1/\text{PEF})])}{(\text{BW} \times \text{ATc})}$$

Equation	Inh - Risk	= (	Csoil	×	SFi	×	IR	×	ET	×	EF	×	ED	× [	1	/	VF	+	1	/	PEF	]) + (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		m³/hour		hours/day		days/year		year				m³/kg				m³/kg		kg		days	
Inorganics																										
Arsenic	9.02E-09	= (	4.90E+00	×	1.51E+01	×	1.5	×	8	×	250	×	1	× [	1	/	NA	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Lead	NA	= (	8.87E+01	×	a	×	1.5	×	8	×	250	×	1	× [	1	/	NA	+	1	/	1.37E+07	]) + (	70	×	25,550	)
SVOCs																										
1-Methylnaphthalene	NA	= (	1.31E+03	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	6.00E+03	+	1	/	1.37E+07	]) + (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	1.41E+03	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	5.68E+03	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Acenaphthene	NA	= (	4.41E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	1.10E+04	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Benzo(a)anthracene	NA	= (	1.97E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Benzo(a)pyrene	6.52E-08	= (	1.73E+02	×	3.08E+00	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Benzo(b)fluoranthene	NA	= (	1.02E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Benzo(k)fluoranthene	NA	= (	1.19E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Chyrsene	NA	= (	1.81E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Dibenzo(a,h)anthracene	NA	= (	2.62E+01	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Dibenzofuran	NA	= (	8.92E+01	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	9.09E+03	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Fluoranthene	NA	= (	3.29E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Fluorene	NA	= (	2.82E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	1.67E+04	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	NA	= (	9.34E+01	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Naphthalene	NA	= (	1.17E+03	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	5.25E+03	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Pyrene	NA	= (	4.85E+02	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	5.57E+04	+	1	/	1.37E+07	]) + (	70	×	25,550	)
VOCs																										
1,2,4-Trichlorobenzene	NA	= (	1.69E+01	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	2.62E+04	+	1	/	1.37E+07	]) + (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	3.56E+00	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	9.98E+02	+	1	/	1.37E+07	]) + (	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	= (	1.44E+00	×	NV	×	1.5	×	8	×	250	×	1	× [	1	/	8.26E+02	+	1	/	1.37E+07	]) + (	70	×	25,550	)
Benzene	1.12E-06	= (	1.42E+01	×	2.73E-02	×	1.5	×	8	×	250	×	1	× [	1	/	5.83E+02	+	1	/	1.37E+07	]) + (	70	×	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Concentration in Soil
SFi – Inhalation Slope Factor
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VOC – Volatile organic compound
VF – Volatilization Factor
PEF – Particulate Emission Factor (See Attachment G)
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
SVOC – Semivolatile organic compound
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment H4

Table 6b
Risk Calculations: Reasonable Maximum Exposure
Construction Worker: Incidental Inhalation of Soil (Fugitive Emissions and Volatile Compounds) Pathway – Carcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BW} \times \text{ATn} \times \text{RfDi})}$$

Equation	Inh - HQ	= (	Csoil	×	IR	×	ET	×	EF	×	ED	× [	1	/	VF	+	1	/	PEF	] ÷ (	BW	×	ATn	×	RfDi [b]	)
Units	unitless		mg/kg		m³/hour		hours/day		days/year		year				m³/kg				m³/kg		kg		days		mg/kg-day	
Inorganics																										
Arsenic	NA	= (	4.90E+00	×	1.5	×	8	×	250	×	1	× [	1	/	NA	+	1	/	1.37E+07	] ÷ (	70	×	365	×	NV	)
Lead	NA	= (	8.87E+01	×	1.5	×	8	×	250	×	1	× [	1	/	NA	+	1	/	1.37E+07	] ÷ (	70	×	365	×	a	)
SVOCs																										
1-Methylnaphthalene	NA	= (	1.31E+03	×	1.5	×	8	×	250	×	1	× [	1	/	6.00E+03	+	1	/	1.37E+07	] ÷ (	70	×	365	×	NV	)
2-Methylnaphthalene	NA	= (	1.41E+03	×	1.5	×	8	×	250	×	1	× [	1	/	5.68E+03	+	1	/	1.37E+07	] ÷ (	70	×	365	×	NV	)
Acenaphthene	NA	= (	4.41E+02	×	1.5	×	8	×	250	×	1	× [	1	/	1.10E+04	+	1	/	1.37E+07	] ÷ (	70	×	365	×	NV	
Benzo(a)anthracene	NA	= (	1.97E+02	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	] ÷ (	70	×	365	×	NV	)
Benzo(a)pyrene	NA	= (	1.73E+02	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	] ÷ (	70	×	365	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.02E+02	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	] ÷ (	70	×	365	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.19E+02	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	] ÷ (	70	×	365	×	NV	
Chyrsene	NA	= (	1.81E+02	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	] ÷ (	70	×	365	×	NV	
Dibenzo(a,h)anthracene	NA	= (	2.62E+01	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	] ÷ (	70	×	365	×	NV	)
Dibenzofuran	NA	= (	8.92E+01	×	1.5	×	8	×	250	×	1	× [	1	/	9.09E+03	+	1	/	1.37E+07	] ÷ (	70	×	365	×	NV	)
Fluoranthene	NA	= (	3.29E+02	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	] ÷ (	70	×	365	×	NV	
Fluorene	NA	= (	2.82E+02	×	1.5	×	8	×	250	×	1	× [	1	/	1.67E+04	+	1	/	1.37E+07	] ÷ (	70	×	365	×	NV	
Indeno(1,2,3-cd)pyrene	NA	= (	9.34E+01	×	1.5	×	8	×	250	×	1	× [	1	/	NC	+	1	/	1.37E+07	] ÷ (	70	×	365	×	NV	)
Naphthalene	3.06E+01	= (	1.17E+03	×	1.5	×	8	×	250	×	1	× [	1	/	5.25E+03	+	1	/	1.37E+07	] ÷ (	70	×	365	×	8.57E-04	)
Pyrene	NA	= (	4.85E+02	×	1.5	×	8	×	250	×	1	× [	1	/	5.57E+04	+	1	/	1.37E+07	] ÷ (	70	×	365	×	NV	
VOCs																										
1,2,4-Trichlorobenzene	6.64E-02	= (	1.69E+01	×	1.5	×	8	×	250	×	1	× [	1	/	2.62E+04	+	1	/	1.37E+07	] ÷ (	70	×	365	×	1.14E-03	)
1,2,4-Trimethylbenzene	2.45E-01	= (	3.56E+00	×	1.5	×	8	×	250	×	1	× [	1	/	9.98E+02	+	1	/	1.37E+07	] ÷ (	70	×	365	×	1.71E-03	)
1,3,5-Trimethylbenzene	1.20E-02	= (	1.44E+00	×	1.5	×	8	×	250	×	1	× [	1	/	8.26E+02	+	1	/	1.37E+07	] ÷ (	70	×	365	×	1.70E-02	)
Benzene	3.34E-01	= (	1.42E+01	×	1.5	×	8	×	250	×	1	× [	1	/	5.83E+02	+	1	/	1.37E+07	] ÷ (	70	×	365	×	8.57E-03	)

Notes:

Inh - Risk – *Inhalation Hazard Quotient*
Csoil – Concentration in Soil
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VF – Volatilization Factor
VOC – Volatile organic compound
PEF – Particulate Emission Factor (See Attachment G)
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
SVOC – Semivolatile organic compound

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. *Toxicity criteria for lead have not* been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available. Toxicity criteria is presented in Attachment A, Table 1b.

Attachment H4

Table 6c
Construction Worker: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} \times \frac{(3.14 \times D_A \times T)^{1/2}}{(2 \times \rho_b \times D_A)} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} $(g/m^2\text{-}s)/(kg/m^3)$	π	D_A (cm^2/s)	T (s)	2	ρb (g/cm^3)	10^{-4} (m^2/cm^2)	VF (m^3/kg)
1-Methylnaphthalene	73.32	3.14	1.94E-05	3.15E+07	2	1.38	1.00E-04	6.00E+03
2-Methylnaphthalene	73.32	3.14	2.17E-05	3.15E+07	2	1.38	1.00E-04	5.68E+03
Acenaphthene	73.32	3.14	5.82E-06	3.15E+07	2	1.38	1.00E-04	1.10E+04
Benzo(a)anthracene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Benzo(a)pyrene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Benzo(b)fluoranthene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Benzo(k)fluoranthene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Chrysene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Dibenzo(a,h)anthracene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Dibenzofuran	73.32	3.14	8.46E-06	3.15E+07	2	1.38	1.00E-04	9.09E+03
Fluoranthene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Fluorene	73.32	3.14	2.50E-06	3.15E+07	2	1.38	1.00E-04	1.67E+04
Indeno(1,2,3-cd)pyrene	73.32	3.14	NC	3.15E+07	2	1.38	1.00E-04	NC
Naphthalene	73.32	3.14	2.54E-05	3.15E+07	2	1.38	1.00E-04	5.25E+03
Pyrene	73.32	3.14	2.25E-07	3.15E+07	2	1.38	1.00E-04	5.57E+04
1,2,4-Trichlorobenzene	73.32	3.14	1.02E-06	3.15E+07	2	1.38	1.00E-04	2.62E+04
1,2,4-Trimethylbenzene	73.32	3.14	7.01E-04	3.15E+07	2	1.38	1.00E-04	9.98E+02
1,3,5-Trimethylbenzene	73.32	3.14	1.02E-03	3.15E+07	2	1.38	1.00E-04	8.26E+02
Benzene	73.32	3.14	2.05E-03	3.15E+07	2	1.38	1.00E-04	5.83E+02

Notes:

Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

VF – Volatilization Factor (m^3/kg) (calculated)

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source $(g/m^2\text{-}s)/(kg/m^2)$(Value used is for Minneapolis, MN.)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T – Exposure interval (s)

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated

Attachment H4

Table 6d
Construction Worker: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical	VOC?	θa	Di	H'	θw	Dw	η	ρb	ρs	Kd	D_A
Units		(Lair /Lsoil)	(cm^2/s)	unitless	(Lwater /Lsoil)	(cm^2/s)	(Lpore /Lsoil)	(g/cm^3)	(g/cm^3)	(cm^3/g)	(cm^2/s)
1-Methylnaphthalene	*Yes*	3.29E-01	6.31E-02	1.64E-02	0.15	7.13E-06	4.79E-01	1.38	2.65	3.75E+01	1.948E-05
2-Methylnaphthalene	*Yes*	*3.29E-01*	*4.80E-02*	*2.12E-02*	*0.15*	*7.84E-06*	*4.79E-01*	*1.38*	*2.65*	*1.79E+01*	*2.166E-05*
Acenaphthene	*Yes*	3.29E-01	4.21E-02	7.44E-03	0.15	7.69E-06	4.79E-01	1.38	2.65	3.67E+01	5.819E-06
Benzo(a)anthracene	No	3.29E-01	5.10E-02	4.91E-04	0.15	9.00E-06	4.79E-01	1.38	2.65	1.39E+03	NC
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Benzo(b)fluoranthene	No	3.29E-01	2.26E-02	2.69E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.82E+03	NC
Benzo(k)fluoranthene	No	3.29E-01	2.26E-02	2.39E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Chrysene	No	3.29E-01	2.48E-02	2.14E-04	0.15	6.21E-06	4.79E-01	1.38	2.65	1.42E+03	NC
Dibenzo(a,h)anthracene	No	*3.29E-01*	*2.02E-02*	*5.03E-06*	*0.15*	*5.18E-06*	*4.79E-01*	*1.38*	*2.65*	*1.57E+04*	NC
Dibenzofuran	*Yes*	3.29E-01	5.51E-02	8.71E-03	0.15	7.04E-06	4.79E-01	1.38	2.65	6.78E+01	8.463E-06
Fluoranthene	No	3.29E-01	3.02E-02	3.62E-04	0.15	6.35E-06	4.79E-01	1.38	2.65	4.25E+02	NC
Fluorene	*Yes*	3.29E-01	3.63E-02	3.93E-03	0.15	7.88E-06	4.79E-01	1.38	2.65	6.78E+01	2.499E-06
Indeno(1,2,3-cd)pyrene	No	3.29E-01	1.90E-02	1.42E-05	0.15	5.66E-06	4.79E-01	1.38	2.65	1.61E+04	NC
Naphthalene	*Yes*	3.29E-01	5.90E-02	1.80E-02	0.15	7.50E-06	4.79E-01	1.38	2.65	1.10E+01	2.537E-05
Pyrene	*Yes*	3.29E-01	2.72E-02	4.87E-04	0.15	7.24E-06	4.79E-01	1.38	2.65	4.16E+02	2.254E-07
1,2,4-Trichlorobenzene	NV	3.29E-01	3.00E-02	1.42E-03	0.15	8.23E-06	4.79E-01	1.38	2.65	1.07E+01	1.02E-06
1,2,4-Trimethylbenzene	*Yes*	3.29E-01	6.44E-02	2.52E-01	0.15	7.92E-06	4.79E-01	1.38	2.65	4.31E+00	7.01E-04
1,3,5-Trimethylbenzene	*Yes*	3.29E-01	6.02E-02	3.59E-01	0.15	8.67E-06	4.79E-01	1.38	2.65	4.22E+00	1.02E-03
Benzene	*Yes*	3.29E-01	8.80E-02	2.27E-01	0.15	9.80E-06	4.79E-01	1.38	2.65	9.93E-01	2.05E-03

Notes:

D_A – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's Law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User'S Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density
Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm^3/g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)
VOC? – Volatile organic compounds; If no an apparent diffusivity was not calculated.
NV – no value available
NC – not calculated

Attachment H4

Table 7a
Risk Calculations: Central Tendency Evaluation
Residential Adult and Child (0-10 feet): Incidental Ingestion of Soil Pathway – Carcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$Ing\text{-}Risk = \frac{(Csoil \times SFo \times CF \times EF \times ED \times SIRadj \times FI)}{ATc}$$

Equation / Units	Ing - Risk unitless	=	Csoil mg/kg	×	SFo kg-day/mg	×	CF kg/mg	×	EF days/year	×	SIRadj mg-yr/kg-day	×	FI unitless	) + (	ATc days	)
Arsenic	4.10E-06	= (	4.30E+00	×	1.50E+00	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Lead	NA	= (	9.05E+01	×	a	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Thallium	NA	= (	7.83E-01	×	NV	×	1E-06	×	350	×	46.43	×	1	) + (	25550	)
1-Methylnaphthalene	NA	= (	7.53E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
2-Methylnaphthalene	NA	= (	8.05E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Acenaphthene	NA	= (	2.18E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Benzo(a)anthracene	6.79E-06	= (	1.46E+01	×	7.30E-01	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Benzo(a)pyrene	5.70E-05	= (	1.23E+01	×	7.30E+00	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Benzo(b)fluoranthene	6.05E-06	= (	1.30E+01	×	7.30E-01	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Benzo(k)fluoranthene	2.95E-07	= (	6.35E+00	×	7.30E-02	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Chrysene	6.51E-08	= (	1.40E+01	×	7.30E-03	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Dibenzo(a,h)anthracene	9.42E-06	= (	2.03E+00	×	7.30E+00	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Dibenzofuran	NA	= (	4.67E+00	×	NV	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Fluoranthene	NA	= (	3.67E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Fluorene	NA	= (	2.54E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Indeno(1,2,3-cd)pyrene	1.59E-06	= (	3.44E+00	×	7.30E-01	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Naphthalene	NA	= (	1.21E+02	×	NV	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Phenanthrene	NA	= (	7.94E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Pyrene	NA	= (	4.92E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
1,2,4-Trichlorobenzene	NA	= (	1.54E+01	×	NV	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	3.77E+00	×	NV	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	1.46E+00	×	NV	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Benzene	2.94E-07	= (	8.40E+00	×	5.50E-02	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)
Xylenes (total)	NA	= (	5.88E+00	×	NV	×	1E-06	×	350	×	46.43	×	1	) + (	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – Soil Concentration
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
SIRadj – Age-adjusted Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment H4

Table 7b
Risk Calculations: Central Tendency Evaluation
Residential Child (0-10 feet): Incidental Ingestion of Soil Pathway – Noncarcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$Ing\text{-}HQ = \frac{(Csoil \times CF \times EF \times EDc \times SIRc \times FI)}{(BWc \times ATn \times RfDo)}$$

Equation	Ing - HQ	= (	Csoil	×	CF	×	EF	×	EDc	×	SIRc	×	FI	) ÷ (	BWc	×	ATn	×	RfDo [b]	)
Units	unitless		mg/kg		kg/mg		days/year		years		mg/day		unitless		kg		days		mg/kg-day	
Arsenic	9.2E-02	= (	4.30E+00	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	3.0E-04	)
Lead	NA	= (	9.05E+01	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	a	)
Thallium	6.26E-02	= (	7.83E-01	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	8.0E-05	)
1-Methylnaphthalene	6.88E-03	= (	7.53E+01	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	7.0E-02	)
2-Methylnaphthalene	1.29E-01	= (	8.05E+01	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	4.0E-03	)
Acenaphthene	2.32E-03	= (	2.18E+01	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	6.0E-02	)
Benzo(a)anthracene	NA	= (	1.46E+01	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	= (	1.23E+01	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.30E+01	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	= (	6.35E+00	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	NV	)
Chrysene	NA	= (	1.40E+01	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.03E+00	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	NV	)
Dibenzofuran	1.49E-02	= (	4.67E+00	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	2.0E-03	)
Fluoranthene	5.87E-03	= (	3.67E+01	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	4.0E-02	)
Fluorene	4.05E-03	= (	2.54E+01	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	4.0E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	3.44E+00	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	NV	)
Naphthalene	1.55E-02	= (	1.21E+02	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	5.0E-02	)
Phenanthrene	NA	= (	7.94E+01	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	NV	)
Pyrene	1.05E-03	= (	4.92E+01	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	3.0E-01	)
1,2,4-Trichlorobenzene	9.87E-03	= (	1.54E+01	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	1.0E-02	)
1,2,4-Trimethylbenzene	4.82E-04	= (	3.77E+00	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	5.0E-02	)
1,3,5-Trimethylbenzene	1.87E-04	= (	1.46E+00	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	5.0E-02	)
Benzene	1.34E-02	= (	8.40E+00	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	4.0E-03	)
Xylenes (total)	4.70E-04	= (	5.88E+00	×	1E-06	×	350	×	6	×	100	×	1	) ÷ (	15	×	2,190	×	8.0E-02	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
EDc – Exposure Duration, child
SIRc – Soil Ingestion Rate, child
FI – Fraction Ingested from Contaminated Source
BWc – Body Weight, child
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – *Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead.* Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment H4

Table 8a
Risk Calculations: Central Tendency Evaluation
Residential Adult and Child (0-10 feet): Dermal Contact with Soil Pathway – Carcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{EV} \times \text{SCRadj} \times \text{ABSd})}{\text{ATc}}$$

Equation / Units	Derm - Risk unitless	= (	Csoil mg/kg	×	SFabs kg-day/mg	×	CF kg/mg	×	EF days/year	×	EV events/day	×	SCRadj mg-yr/kg-event	×	ABSd unitless	) ÷ (	ATc days	)
Arsenic	1.45E-07	= (	4.30E+00	×	1.58E+00	×	1E-06	×	350	×	1	×	52.1	×	3.00E-02	) ÷ (	25,550	)
Lead	NA	= (	9.05E+01	×	a	×	1E-06	×	350	×	1	×	52.1	×	NA	) ÷ (	25,550	)
Thallium	NA	= (	7.83E-01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	NA	) ÷ (	25,550	)
1-Methylnaphthalene	NA	= (	7.53E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
2-Methylnaphthalene	NA	= (	8.05E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.00E-01	) ÷ (	25,550	)
Acenaphthene	NA	= (	2.18E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Benzo(a)anthracene	9.91E-07	= (	1.46E+01	×	7.30E-01	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Benzo(a)pyrene	8.31E-06	= (	1.23E+01	×	7.30E+00	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Benzo(b)fluoranthene	8.83E-07	= (	1.30E+01	×	7.30E-01	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Benzo(k)fluoranthene	4.31E-08	= (	6.35E+00	×	7.30E-02	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Chrysene	9.50E-09	= (	1.40E+01	×	7.30E-03	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Dibenzo(a,h)anthracene	1.37E-06	= (	2.03E+00	×	7.30E+00	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Dibenzofuran	NA	= (	4.67E+00	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Fluoranthene	NA	= (	3.67E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Fluorene	NA	= (	2.54E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Indeno(1,2,3-cd)pyrene	2.33E-07	= (	3.44E+00	×	7.30E-01	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Naphthalene	NA	= (	1.21E+02	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Phenanthrene	NA	= (	7.94E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
Pyrene	NA	= (	4.92E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	1.30E-01	) ÷ (	25,550	)
1,2,4-Trichlorobenzene	NA	= (	1.54E+01	×	NV	×	1E-06	×	350	×	1	×	52.1	×	NV	) ÷ (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	3.77E+00	×	NV	×	1E-06	×	350	×	1	×	52.1	×	NA	) ÷ (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	1.46E+00	×	NV	×	1E-06	×	350	×	1	×	52.1	×	NA	) ÷ (	25,550	)
Benzene	NA	= (	8.40E+00	×	5.50E-02	×	1E-06	×	350	×	1	×	52.1	×	NA	) ÷ (	25,550	)
Xylenes (total)	NA	= (	5.88E+00	×	NV	×	1E-06	×	350	×	1	×	52.1	×	NA	) ÷ (	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csoil – Soil Concentration
SFabs – Absorbed slope factor (SFo + ABSgi)
CF – Unit Conversion Factor
EF – Exposure Frequency
EV – Event Frequency
SCRadj – Age-adjusted Soil Contact Rate
ABSd – Dermal Soil Absorption Factor
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment H4

Table 8b
Risk Calculations: Central Tendency Evaluation
Residential Child (0-10 feet): Dermal Contact with Soil Pathway – Noncarcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{EDc} \times \text{EV} \times \text{SAc} \times \text{AFc} \times \text{ABSd})}{(\text{BWc} \times \text{ATn} \times \text{RfDabs})}$$

Equation / Units	Derm - HQ unitless	= (	Csoil mg/kg	×	CF kg/mg	×	EF days/year	×	EDc years	×	EV events/day	×	SAc cm²	×	AFc mg/cm²-event	×	ABSd unitless	) ÷ (	BWc kg	×	ATn days	×	RfDabs [b] mg/kg-day	)
Arsenic	3.24E-03	= (	4.30E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	3.00E-02	) ÷ (	15	×	2,190	×	2.85E-04	)
Lead	NA	= (	9.05E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	NA	) ÷ (	15	×	2,190	×	a	)
Thallium	NA	= (	7.83E-01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	NA	) ÷ (	15	×	2,190	×	8.00E-05	)
1-Methylnaphthalene	1.00E-03	= (	7.53E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	7.00E-02	)
2-Methylnaphthalene	1.44E-02	= (	8.05E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.00E-01	) ÷ (	15	×	2,190	×	4.00E-03	)
Acenaphthene	3.38E-04	= (	2.18E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	6.00E-02	)
Benzo(a)anthracene	NA	= (	1.46E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	= (	1.23E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.30E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	= (	6.35E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Chrysene	NA	= (	1.40E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.03E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Dibenzofuran	2.17E-03	= (	4.67E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	2.00E-03	)
Fluoranthene	8.55E-04	= (	3.67E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	4.00E-02	)
Fluorene	5.90E-04	= (	2.54E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	3.44E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Naphthalene	2.26E-03	= (	1.21E+02	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	5.00E-02	)
Phenanthrene	NA	= (	7.94E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Pyrene	1.53E-04	= (	4.92E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	1.30E-01	) ÷ (	15	×	2,190	×	3.00E-01	)
1,2,4-Trichlorobenzene	NA	= (	1.54E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	NV	) ÷ (	15	×	2,190	×	NV	)
1,2,4-Trimethylbenzene	NA	= (	3.77E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	NA	) ÷ (	15	×	2,190	×	5.00E-02	)
1,3,5-Trimethylbenzene	NA	= (	1.46E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	NA	) ÷ (	15	×	2,190	×	5.00E-02	)
Benzene	NA	= (	8.40E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	NA	) ÷ (	15	×	2,190	×	4.00E-03	)
Xylenes (total)	NA	= (	5.88E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.04	×	NA	) ÷ (	15	×	2,190	×	8.00E-02	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
EDc – Exposure Duration, child
EV – Event Frequency
SAc – Skin Surface Area, child
AFc – Soil-to-skin Adherence Factor, child
ABSd – Dermal Soil Absorption Factor
BWc – Body Weight, child
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo × ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment H4

Table 9a
Risk Calculations: Central Tendency Evaluation
Residential Adult and Child (0-10 feet): Inhalation of Soil-derived Chemicals Pathway– Carcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{EF} \times \text{SInhRadj} \times [(1/\text{VF}) + (1/\text{PEF})])}{\text{ATc}}$$

Equation	Inh - Risk	= (	Csoil	×	SFi	×	EF	×	SInhRadj	× [	1	/	VF_{adult}	+	1	/	PEF	]) + (	ATc	)
Units	unitless		mg/kg		kg-day/mg		days/year		m3-yr/kg-day				m^3/kg				m^3/kg		days	
Arsenic	NA	= (	4.30E+00	×	1.51E+01	×	350	×	4.58	× [	1	/	NA	+	1	/	6.58E+09	]) + (	25,550	)
Lead	NA	= (	9.05E+01	×	a	×	350	×	4.58	× [	1	/	NA	+	1	/	6.58E+09	]) + (	25,550	)
Thallium	NA	= (	7.83E-01	×	NV	×	350	×	4.58	× [	1	/	NA	+	1	/	6.58E+09	]) + (	25,550	)
1-Methylnaphthalene	NA	= (	7.53E+01	×	NV	×	350	×	4.58	× [	1	/	5.41E+04	+	1	/	6.58E+09	]) + (	25,550	)
2-Methylnaphthalene	NA	= (	8.05E+01	×	NV	×	350	×	4.58	× [	1	/	3.77E+04	+	1	/	6.58E+09	]) + (	25,550	)
Acenaphthene	NA	= (	2.18E+01	×	NV	×	350	×	4.58	× [	1	/	9.73E+04	+	1	/	6.58E+09	]) + (	25,550	)
Benzo(a)anthracene	NA	= (	1.46E+01	×	NV	×	350	×	4.58	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Benzo(a)pyrene	3.61E-10	= (	1.23E+01	×	3.08E+00	×	350	×	4.58	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Benzo(b)fluoranthene	NA	= (	1.30E+01	×	NV	×	350	×	4.58	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Benzo(k)fluoranthene	NA	= (	6.35E+00	×	NV	×	350	×	4.58	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Chrysene	NA	= (	1.40E+01	×	NV	×	350	×	4.58	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Dibenzo(a,h)anthracene	NA	= (	2.03E+00	×	NV	×	350	×	4.58	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Dibenzofuran	NA	= (	4.67E+00	×	NV	×	350	×	4.58	× [	1	/	1.07E+05	+	1	/	6.58E+09	]) + (	25,550	)
Fluoranthene	NA	= (	3.67E+01	×	NV	×	350	×	4.58	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Fluorene	NA	= (	2.54E+01	×	NV	×	350	×	4.58	× [	1	/	1.95E+05	+	1	/	6.58E+09	]) + (	25,550	)
Indeno(1,2,3-cd)pyrene	NA	= (	3.44E+00	×	NV	×	350	×	4.58	× [	1	/	NC	+	1	/	6.58E+09	]) + (	25,550	)
Naphthalene	NA	= (	1.21E+02	×	NV	×	350	×	4.58	× [	1	/	2.91E+04	+	1	/	6.58E+09	]) + (	25,550	)
Phenanthrene	NA	= (	7.94E+01	×	NV	×	350	×	4.58	× [	1	/	4.16E+05	+	1	/	6.58E+09	]) + (	25,550	)
Pyrene	NA	= (	4.92E+01	×	NV	×	350	×	4.58	× [	1	/	1.56E+06	+	1	/	6.58E+09	]) + (	25,550	)
1,2,4-Trichlorobenzene	NA	= (	1.54E+01	×	NV	×	350	×	4.58	× [	1	/	2.23E+04	+	1	/	6.58E+09	]) + (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	3.77E+00	×	NV	×	350	×	4.58	× [	1	/	4.71E+03	+	1	/	6.58E+09	]) + (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	1.46E+00	×	NV	×	350	×	4.58	× [	1	/	4.06E+03	+	1	/	6.58E+09	]) + (	25,550	)
Benzene	1.01E-15	= (	8.40E+00	×	2.73E-02	×	350	×	4.58	× [	1	/	2.16E+03	+	1	/	6.58E+09	]) + (	25,550	)
Xylenes (total)	NA	= (	5.88E+00	×	NV	×	350	×	4.58	× [	1	/	3.43E+03	+	1	/	6.58E+09	]) + (	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Soil Concentration
SFi – Inhalation Slope Factor
EF – Exposure frequency
SInhRadj – Age-adjusted Soil Inhalation Rate
VF_{adult} – Volatilization Factor (adults) - calculated
PEF – Particulate Emission Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment H4

Table 9b
Risk Calculations: Central Tendency Evaluation
Residential Child (0-10 feet): Inhalation of Soil-derived Pathway – Noncarcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{InhRc} \times \text{EF} \times \text{EDc} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BWc} \times \text{ATn} \times \text{RfDi})}$$

Equation / Units	Inh - HQ unitless	=	(	Csoil mg/kg	×	InhRc m³/day	×	EF days/year	×	EDc year	×	[	1	/	VF_{child} m³/kg	+	1	/	PEF m³/kg	]	÷	(	BWc kg	×	ATn days	×	RfDi [b] mg/kg-day	)
Arsenic	NA	=	(	4.30E+00	×	7.2	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Lead	NA	=	(	9.05E+01	×	7.2	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	a	)
Thallium	NA	=	(	7.83E-01	×	7.2	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
1-Methylnaphthalene	NA	=	(	7.53E+01	×	7.2	×	350	×	6	×	[	1	/	4.42E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
2-Methylnaphthalene	NA	=	(	8.05E+01	×	7.2	×	350	×	6	×	[	1	/	3.08E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Acenaphthene	NA	=	(	2.18E+01	×	7.2	×	350	×	6	×	[	1	/	7.94E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Benzo(a)anthracene	NA	=	(	1.46E+01	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	=	(	1.23E+01	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	=	(	1.30E+01	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	=	(	6.35E+00	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Chrysene	NA	=	(	1.40E+01	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	=	(	2.03E+00	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Dibenzofuran	NA	=	(	4.67E+00	×	7.2	×	350	×	6	×	[	1	/	8.71E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Fluoranthene	NA	=	(	3.67E+01	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Fluorene	NA	=	(	2.54E+01	×	7.2	×	350	×	6	×	[	1	/	1.60E+05	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	=	(	3.44E+00	×	7.2	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Naphthalene	2.74E+00	=	(	1.21E+02	×	7.2	×	350	×	6	×	[	1	/	2.37E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	8.57E-04	)
Phenanthrene	NA	=	(	7.94E+01	×	7.2	×	350	×	6	×	[	1	/	3.40E+05	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Pyrene	NA	=	(	4.92E+01	×	7.2	×	350	×	6	×	[	1	/	1.27E+06	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
1,2,4-Trichlorobenzene	3.42E-01	=	(	1.54E+01	×	7.2	×	350	×	6	×	[	1	/	1.82E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	1.14E-03	)
1,2,4-Trimethylbenzene	2.64E-01	=	(	3.77E+00	×	7.2	×	350	×	6	×	[	1	/	3.85E+03	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	1.71E-03	)
1,3,5-Trimethylbenzene	1.19E-01	=	(	1.46E+00	×	7.2	×	350	×	6	×	[	1	/	3.31E+03	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	1.71E-03	)
Benzene	2.56E-01	=	(	8.40E+00	×	7.2	×	350	×	6	×	[	1	/	1.76E+03	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	8.57E-03	)
Xylenes (total)	3.38E-02	=	(	5.88E+00	×	7.2	×	350	×	6	×	[	1	/	2.80E+03	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	2.86E-02	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Csoil – Soil Concentration
InhRc – Inhalation Rate, child
EF – Exposure frequency
EDc – Exposure duration, child
VF_{child} – Volatilization Factor (child) - calculated
PEF – Particulate Emission Factor
BWc – Body Weight, child
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – *Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead.* Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment H4

Table 9c
Residential Scenario: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} x \frac{(3.14 \times D_A \times T)^{1/2}}{(2 \times \rho_b \times D_A)} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} $(g/m^2\text{-}s)/(kg/m^3)$	π	D_A (cm^2/s)	T_{adult} (s)	T_{child} (s)	2	ρb (g/cm^3)	10^{-4} (m^2/cm^2)	VFadult (m^3/kg)	VFchild (m^3/kg)
1-Methylnaphthalene	73.32	3.14	2.15E-06	2.84E+08	1.89E+08	2	1.38	1.00E-04	5.41E+04	4.42E+04
2-Methylnaphthalene	73.32	3.14	4.42E-06	2.84E+08	1.89E+08	2	1.38	1.00E-04	3.77E+04	3.08E+04
Acenaphthene	73.32	3.14	6.65E-07	2.84E+08	1.89E+08	2	1.38	1.00E-04	9.73E+04	7.94E+04
Benzo(a)anthracene	73.32	3.14	NC	2.84E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Benzo(a)pyrene	73.32	3.14	NC	2.84E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Benzo(b)fluoranthene	73.32	3.14	NC	2.84E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Benzo(k)fluoranthene	73.32	3.14	NC	2.84E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Chrysene	73.32	3.14	NC	2.84E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Dibenzo(a,h)anthracene	73.32	3.14	NC	2.84E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Dibenzofuran	73.32	3.14	5.52E-07	2.84E+08	1.89E+08	2	1.38	1.00E-04	1.07E+05	8.71E+04
Fluoranthene	73.32	3.14	NC	2.84E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Fluorene	73.32	3.14	1.65E-07	2.84E+08	1.89E+08	2	1.38	1.00E-04	1.95E+05	1.60E+05
Indeno(1,2,3-cd)pyrene	73.32	3.14	NC	2.84E+08	1.89E+08	2	1.38	1.00E-04	NC	NC
Naphthalene	73.32	3.14	7.45E-06	2.84E+08	1.89E+08	2	1.38	1.00E-04	2.91E+04	2.37E+04
Phenanthrene	73.32	3.14	3.63E-08	2.84E+08	1.89E+08	2	1.38	1.00E-04	4.16E+05	3.40E+05
Pyrene	73.32	3.14	2.58E-09	2.84E+08	1.89E+08	2	1.38	1.00E-04	1.56E+06	1.27E+06
1,2,3-Trimethylbenzene	73.32	3.14	1.91E-04	2.84E+08	1.89E+08	2	1.38	1.00E-04	5.74E+03	4.69E+03
1,2,4-Trichlorobenzene	73.32	3.14	1.26E-05	2.84E+08	1.89E+08	2	1.38	1.00E-04	2.23E+04	1.82E+04
1,2,4-Trimethylbenzene	73.32	3.14	2.83E-04	2.84E+08	1.89E+08	2	1.38	1.00E-04	4.71E+03	3.85E+03
1,3,5-Trimethylbenzene	73.32	3.14	3.82E-04	2.84E+08	1.89E+08	2	1.38	1.00E-04	4.06E+03	3.31E+03
Benzene	73.32	3.14	1.35E-03	2.84E+08	1.89E+08	2	1.38	1.00E-04	2.16E+03	1.76E+03
Xylenes (total)	73.32	3.14	5.33E-04	2.84E+08	1.89E+08	2	1.38	1.00E-04	3.43E+03	2.80E+03

Notes:

Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

VF_{adult} – Volatilization Factor (adults) - calculated

VF_{child} – Volatilization Factor (child) - calculated

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source $(g/m^2\text{-}s)/(kg/m^3)$(Value used is for Minneapolis, MN.)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T_{adult} – Exposure interval for adults (s)

T_{child} – Exposure interval for child (s)

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated; PAHs are not considered volatile chemicals

Attachment H4

Table 9d
Residential Scenario: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical Units	VOC?	θa (Lair /Lsoil)	Di (cm^2/s)	H' unitless	θw (Lwater /Lsoil)	Dw (cm^2/s)	η (Lpore /Lsoil)	ρb (g/cm^3)	ρs (g/cm^3)	Kd (cm^3/g)	D_A (cm^2/s)
1-Methylnaphthalene	Yes	3.29E-01	6.31E-02	1.64E-02	0.15	7.13E-06	4.79E-01	1.38	2.65	3.75E+01	2.15E-06
2-Methylnaphthalene	Yes	3.29E-01	4.80E-02	2.12E-02	0.15	7.84E-06	4.79E-01	1.38	2.65	1.79E+01	4.42E-06
Acenaphthene	Yes	3.29E-01	4.21E-02	7.44E-03	0.15	7.69E-06	4.79E-01	1.38	2.65	3.67E+01	6.65E-07
Benzo(a)anthracene	No	3.29E-01	5.10E-02	4.91E-04	0.15	9.00E-06	4.79E-01	1.38	2.65	1.39E+03	NC
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Benzo(b)fluoranthene	No	3.29E-01	2.26E-02	2.69E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.82E+03	NC
Benzo(k)fluoranthene	No	3.29E-01	2.26E-02	2.39E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Chrysene	No	3.29E-01	2.48E-02	2.14E-04	0.15	6.21E-06	4.79E-01	1.38	2.65	1.42E+03	NC
Dibenzo(a,h)anthracene	No	3.29E-01	2.02E-02	5.03E-06	0.15	5.18E-06	4.79E-01	1.38	2.65	1.57E+04	NC
Dibenzofuran	Yes	3.29E-01	5.51E-02	8.71E-03	0.15	7.04E-06	4.79E-01	1.38	2.65	6.78E+01	5.52E-07
Fluoranthene	No	3.29E-01	3.02E-02	3.62E-04	0.15	6.35E-06	4.79E-01	1.38	2.65	4.25E+02	NC
Fluorene	Yes	3.29E-01	3.63E-02	3.93E-03	0.15	7.88E-06	4.79E-01	1.38	2.65	6.78E+01	1.65E-07
Indeno(1,2,3-cd)pyrene	No	3.29E-01	1.90E-02	1.42E-05	0.15	5.66E-06	4.79E-01	1.38	2.65	1.61E+04	NC
Naphthalene	Yes	3.29E-01	5.90E-02	1.80E-02	0.15	7.50E-06	4.79E-01	1.38	2.65	1.10E+01	7.45E-06
Phenanthrene	Yes	3.29E-01	3.33E-02	1.73E-03	0.15	7.47E-06	4.79E-01	1.38	2.65	1.25E+02	3.63E-08
Pyrene	Yes	3.29E-01	2.72E-02	4.87E-04	0.15	7.24E-06	4.79E-01	1.38	2.65	4.16E+02	2.58E-09
1,2,3-Trimethylbenzene	NV	3.29E-01	6.77E-02	1.33E-01	0.15	7.41E-06	4.79E-01	1.38	2.65	3.53E+00	1.91E-04
1,2,4-Trichlorobenzene	Yes	3.29E-01	3.00E-02	5.82E-02	0.15	8.23E-06	4.79E-01	1.38	2.65	1.07E+01	1.26E-05
1,2,4-Trimethylbenzene	Yes	3.29E-01	6.44E-02	2.52E-01	0.15	7.92E-06	4.79E-01	1.38	2.65	4.31E+00	2.83E-04
1,3,5-Trimethylbenzene	Yes	3.29E-01	6.02E-02	3.59E-01	0.15	8.67E-06	4.79E-01	1.38	2.65	4.22E+00	3.82E-04
Benzene	Yes	3.29E-01	8.80E-02	2.27E-01	0.15	9.80E-06	4.79E-01	1.38	2.65	9.93E-01	1.35E-03
Xylenes (total)	Yes	3.29E-01	7.14E-02	2.71E-01	0.15	9.34E-06	4.79E-01	1.38	2.65	2.66E+00	5.33E-04

Notes:

D_A – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User'S Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density

Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm^3 /g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)
VOC? – Volatile organic compounds; If no, an apparent diffusivity was not calculated.
NV – no value available
NC – not calculated

Attachment H4

Table 10a
Risk Calculations: Central Tendency Evaluation
Construction Worker: Incidental Ingestion of Soil Pathway – Carcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Ing-Risk} = \frac{(\text{Csoil} \times \text{SFo} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{SIR} \times \text{FI})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	= (	Csoil	×	SFo	×	CF	×	EF	×	ED	×	SIR	×	FI	) ÷ (	BW	×	ATc	)
Units	unitless		mg/kg		kg-day/mg		kg/mg		days/year		years		mg/day		unitless		kg		days	
Inorganics																				
Arsenic	7.76E-08	= (	4.22E+00	×	1.50E+00	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Lead	NA	= (	8.87E+01	×	a	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
SVOCs																				
1-Methylnaphthalene	NA	= (	8.99E+02	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	9.65E+02	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25550	)
Acenaphthene	NA	= (	3.17E+02	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Benzo(a)anthracene	1.31E-06	= (	1.46E+02	×	7.30E-01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	1.13E-05	= (	1.27E+02	×	7.30E+00	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	6.86E-07	= (	7.68E+01	×	7.30E-01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	7.79E-08	= (	8.72E+01	×	7.30E-02	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Chrysene	1.20E-08	= (	1.35E+02	×	7.30E-03	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	1.74E-06	= (	1.94E+01	×	7.30E+00	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	6.31E+01	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	2.45E+02	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	2.07E+02	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	6.12E-07	= (	6.84E+01	×	7.30E-01	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	8.01E+02	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	3.60E+02	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
VOCs																				
1,2,4-Trichlorobenzene	NA	= (	9.19E+00	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	2.23E+00	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	= (	9.74E-01	×	NV	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)
Benzene	5.33E-09	= (	7.91E+00	×	5.50E-02	×	1E-06	×	219	×	1	×	100	×	1	) ÷ (	70	×	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – Concentration in soil
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
ED – Exposure Duration
VOC – Volatile organic compound
SIR – Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
SVOC – Semivolatile organic compound
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment H4

Table 10b
Risk Calculations: Central Tendency Evaluation
Construction Worker: Incidental Ingestion of Soil Pathway – Noncarcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$Ing\text{-}HQ = \frac{(Csoil \times CF \times EF \times ED \times SIR \times FI)}{(BW \times ATn \times RfDo)}$$

Equation	*Ing - HQ*	= (	*Csoil*	×	*CF*	×	*EF*	×	*ED*	×	*SIR*	×	*FI*	) + (	*BW*	×	*ATn*	×	*RfDo* [6]	)
Units	**unitless**		**mg/kg**		**kg/mg**		**days/year**		**years**		**mg/day**		**unitless**		**kg**		**days**		**mg/kg-day**	
Inorganics																				
Arsenic	1.2E-02	= (	4.22E+00	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	3.0E-04	)
Lead	NA	= (	8.87E+01	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	a	)
SVOCs																				
1-Methylnaphthalene	1.1E-02	= (	8.99E+02	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	7.0E-02	)
2-Methylnaphthalene	2.1E-01	= (	9.65E+02	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	4.0E-03	)
Acenaphthene	4.5E-04	= (	3.17E+02	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	6.0E-01	)
Benzo(a)anthracene	NA	= (	1.46E+02	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	NV	)
Benzo(a)pyrene	NA	= (	1.27E+02	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	NV	)
Benzo(b)fluoranthene	NA	= (	7.68E+01	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	NV	)
Benzo(k)fluoranthene	NA	= (	8.72E+01	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	NV	)
Chrysene	NA	= (	1.35E+02	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.94E+01	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	NV	)
Dibenzofuran	2.7E-02	= (	6.31E+01	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	2.0E-03	)
Fluoranthene	5.3E-04	= (	2.45E+02	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	4.0E-01	)
Fluorene	4.4E-04	= (	2.07E+02	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	4.0E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (	6.84E+01	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	NV	)
Naphthalene	3.4E-02	= (	8.01E+02	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	2.0E-02	)
Pyrene	1.0E-03	= (	3.60E+02	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	3.0E-01	)
VOCs																				
1,2,4-Trichlorobenzene	7.9E-04	= (	9.19E+00	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	1.0E-02	)
1,2,4-Trimethylbenzene	3.8E-05	= (	2.23E+00	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	5.0E-02	)
1,3,5-Trimethylbenzene	1.7E-06	= (	9.74E-01	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	5.0E-01	)
Benzene	1.7E-03	= (	7.91E+00	×	1E-06	×	219	×	1	×	100	×	1	) + (	70	×	365	×	4.0E-03	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Concentration in Soil
CF – *Unit Conversion Factor*
EF – Exposure Frequency
ED – Exposure Duration
SIR – Soil Ingestion Rate
VOC – Volatile organic compound
FI – Fraction Ingested from Contaminated Source
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral reference dose
NV – No toxicity value available for this pathway
NA – Not Applicable
SVOC – Semivolatile organic compound

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available. Toxicity criteria is presented in Attachment A, Table 1b.

Attachment H4

Table 11a
Risk Calculations: Central Tendency Evaluation
Construction Worker: Incidental Dermal Contact with Soil Pathway – Carcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATc})}$$

Equation / Units	Derm - Risk unitless	= (	Csoil mg/kg	×	SFabs kg-day/mg	×	CF kg/mg	×	EF days/year	×	ED years	×	EV events/day	×	SA cm²	×	SSAF mg/cm²-event	×	ABSd unitless	) ÷ (	BW kg	×	ATc days	)
Inorganics																								
Arsenic	4.73E-09	= (	4.22E+00	×	1.58E+00	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	3.00E-02	) ÷ (	70	×	25,550	)
Lead	NA	= (	8.87E+01	×	*a*	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	25,550	)
SVOCs																								
1-Methylnaphthalene	NA	= (	8.99E+02	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	9.65E+02	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.00E-01	) ÷ (	70	×	25,550	)
Acenaphthene	NA	= (	3.17E+02	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(a)anthracene	3.28E-07	= (	1.46E+02	×	7.30E-01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	2.64E-06	= (	1.27E+02	×	7.30E+00	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	1.72E-07	= (	7.68E+01	×	7.30E-01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	1.96E-08	= (	8.72E+01	×	7.30E-02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Chrysene	3.02E-09	= (	1.35E+02	×	7.30E-03	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	4.36E-07	= (	1.94E+01	×	7.30E+00	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	6.31E+01	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	2.45E+02	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	2.07E+02	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.53E-07	= (	6.84E+01	×	7.30E-01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	8.01E+02	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	3.60E+02	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	25,550	)
VOCs																								
1,2,4-Trichlorobenzene	NA	= (	9.19E+00	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	2.23E+00	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	= (	9.74E-01	×	NV	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	25,550	)
Benzene	NA	= (	7.91E+00	×	5.50E-02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csoil – Concentration in Soil
SFabs – Absorbed slope factor (SFo ÷ ABSgi)
CF – Conversion factor
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
VOC – Volatile organic compound
SA – Skin Surface Area
SSAF – Soil-to-skin Adherence Factor
ABSd – Dermal Soil Absorption Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.
SVOC – Semivolatile organic compound
a – *Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead.* Toxicity criteria for lead have not been derived by USEPA.

Attachment H4

Table 11b
Risk Calculations: Central Tendency Evaluation
Construction Worker: Incidental Dermal Contact with Soil Pathway – Noncarcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{EF} \times \text{EF} \times \text{ED} \times \text{EV} \times \text{SA} \times \text{SSAF} \times \text{ABSd})}{(\text{BW} \times \text{ATn} \times \text{RfDabs})}$$

Equation	Derm - HQ	= (	Csoil	×	CF	×	EF	×	ED	×	EV	×	SA	×	SSAF	×	ABSd	) ÷ (	BW	×	ATn	×	RfDabs [b]	)
Units	unitless		mg/kg		kg/mg		days/year		years		events/day		cm²		mg/cm²-event		unitless		kg		days		mg/kg-day	
Inorganics																								
Arsenic	7.35E-04	(	4.22E+00	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	3.00E-02	) ÷ (	70	×	365	×	2.85E-04	)
Lead	NA	= (	8.87E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	365	×	NV	)
SVOCs																								
1-Methylnaphthalene	2.76E-03	= (	8.99E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	365	×	7.00E-02	)
2-Methylnaphthalene	3.99E-02	= (	9.65E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.00E-01	) ÷ (	70	×	365	×	4.00E-03	)
Acenaphthene	1.14E-04	= (	3.17E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	365	×	6.00E-01	)
Benzo(a)anthracene	NA	= (	1.46E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	365	×	NV	)
Benzo(a)pyrene	NA	= (	1.27E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	365	×	NV	)
Benzo(b)fluoranthene	NA	= (	7.68E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	365	×	NV	)
Benzo(k)fluoranthene	NA	= (	8.72E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	365	×	NV	)
Chrysene	NA	= (	1.35E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	365	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.94E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	365	×	NV	)
Dibenzofuran	6.78E-03	= (	6.31E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	365	×	2.00E-03	)
Fluoranthene	1.32E-04	= (	2.45E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	365	×	4.00E-01	)
Fluorene	1.11E-04	= (	2.07E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	365	×	4.00E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (	6.84E+01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	365	×	NV	)
Naphthalene	8.61E-03	= (	8.01E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	365	×	2.00E-02	)
Pyrene	2.58E-04	= (	3.60E+02	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	1.30E-01	) ÷ (	70	×	365	×	3.00E-01	)
VOCs																								
1,2,4-Trichlorobenzene	NA	= (	9.19E+00	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NV	) ÷ (	70	×	365	×	NV	)
1,2,4-Trimethylbenzene	NA	= (	2.23E+00	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	365	×	5.00E-02	)
1,3,5-Trimethylbenzene	NA	= (	9.74E-01	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	365	×	5.00E-01	)
Benzene	NA	= (	7.91E+00	×	1E-06	×	219	×	1	×	1	×	1,930	×	0.1	×	NA	) ÷ (	70	×	365	×	4.00E-03	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Concentration in Soil
EF – Exposure Frequency
ED – Exposure Duration
EV – Event Frequency
SA – Skin Surface Area
SSAF – Soil-to-skin Adherence Factor
VOC – Volatile organic compound
ABSd – Dermal Soil Absorption Factor
BW – Body Weight
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo ×ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.
SVOC – Semivolatile organic compound
CF – Unit Conversion Factor

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead.
Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.
Toxicity criteria is presented in Attachment A, Table 1b.

Attachment H4

Table 12a
Risk Calculations: Central Tendency Evaluation
Construction Worker: Incidental Soil-Derived Chemicals Pathway– Carcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times [(1/\text{VF}) + (1/\text{PEF})])}{(\text{BW} \times \text{ATc})}$$

Equation / Units	Inh - Risk unitless	=	Csoil mg/kg	×	SFi kg-day/mg	×	IR m³/hour	×	ET hours/day	×	EF days/year	×	ED year	×	[	1	/	VF m³/kg	+	1	/	PEF m³/kg	]	)	÷	(	BW kg	×	ATc days	)
Inorganics																														
Arsenic	5.91E-09	=	4.22E+00	×	1.51E+01	×	1.3	×	8	×	219	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Lead	NA	=	8.87E+01	×	a	×	1.3	×	8	×	219	×	1	×	[	1	/	NA	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
SVOCs																														
1-Methylnaphthalene	NA	=	8.99E+02	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	1.18E+04	+	1	/	1.37E+07	]	)	÷	(	70	×	25550	)
2-Methylnaphthalene	NA	=	9.65E+02	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	1.12E+04	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Acenaphthene	NA	=	3.17E+02	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	2.56E+04	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Benzo(a)anthracene	NA	=	1.46E+02	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Benzo(a)pyrene	3.63E-08	=	1.27E+02	×	3.08E+00	×	1.3	×	8	×	219	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Benzo(b)fluoranthene	NA	=	7.68E+01	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Benzo(k)fluoranthene	NA	=	8.72E+01	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Chrysene	NA	=	1.35E+02	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Dibenzo(a,h)anthracene	NA	=	1.94E+01	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Dibenzofuran	NA	=	6.31E+01	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	1.79E+04	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Fluoranthene	NA	=	2.45E+02	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Fluorene	NA	=	2.07E+02	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	3.30E+04	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	NA	=	6.84E+01	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	NC	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Naphthalene	NA	=	8.01E+02	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	1.04E+04	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Pyrene	NA	=	3.60E+02	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	1.10E+05	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
VOCs																														
1,2,4-Trichlorobenzene	NA	=	9.19E+00	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	5.18E+04	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	=	2.23E+00	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	1.97E+03	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
1,3,5-Trimethylbenzene	NA	=	9.74E-01	×	NV	×	1.3	×	8	×	219	×	1	×	[	1	/	1.63E+03	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)
Benzene	2.39E-07	=	7.91E+00	×	2.73E-02	×	1.3	×	8	×	219	×	1	×	[	1	/	1.15E+03	+	1	/	1.37E+07	]	)	÷	(	70	×	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Concentration in Soil
SFi – Inhalation Slope Factor
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VOC – Volatile organic compound
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.
VF – Volatilization Factor
PEF – Particulate Emission Factor (See Attachment G)
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
SVOC – Semivolatile organic compound

Attachment H4

Table 12b
Risk Calculations: Central Tendency Evaluation
Construction Worker: Incidental Inhalation of Soil-Derived Chemicals Pathway – Noncarcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{IR} \times \text{ET} \times \text{EF} \times \text{ED} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BW} \times \text{ATn} \times \text{RfDi})}$$

Equation / Units	Inh - HQ unitless	= (	Csoil mg/kg	×	IR m³/hour	×	ET hours/day	×	EF days/year	×	ED year	× [	1	/	VF m³/kg	+	1	/	PEF m³/kg	]	+ (	BW kg	×	ATn days	×	RfDi [b] mg/kg-day	)
Inorganics																											
Arsenic	NA	= (	4.22	×	1.3	×	8	×	219	×	1	× [	1	/	NA	+	1	/	1.37E+07	]	+ (	70	×	365	×	NV	)
Lead	NA	= (	88.74	×	1.3	×	8	×	219	×	1	× [	1	/	NA	+	1	/	1.37E+07	]	+ (	70	×	365	×	NV	)
SVOCs																											
1-Methylnaphthalene	NA	= (	899.28	×	1.3	×	8	×	219	×	1	× [	1	/	1.18E+04	+	1	/	1.37E+07	]	+ (	70	×	365	×	NV	)
2-Methylnaphthalene	NA	= (	965.35	×	1.3	×	8	×	219	×	1	× [	1	/	1.12E+04	+	1	/	1.37E+07	]	+ (	70	×	365	×	NV	)
Acenaphthene	NA	= (	317.16	×	1.3	×	8	×	219	×	1	× [	1	/	2.56E+04	+	1	/	1.37E+07	]	+ (	70	×	365	×	NV	)
Benzo(a)anthracene	NA	= (	146.29	×	1.3	×	8	×	219	×	1	× [	1	/	NC	+	1	/	1.37E+07	]	+ (	70	×	365	×	NV	)
Benzo(a)pyrene	NA	= (	126.85	×	1.3	×	8	×	219	×	1	× [	1	/	NC	+	1	/	1.37E+07	]	+ (	70	×	365	×	NV	)
Benzo(b)fluoranthene	NA	= (	76.78	×	1.3	×	8	×	219	×	1	× [	1	/	NC	+	1	/	1.37E+07	]	+ (	70	×	365	×	NV	)
Benzo(k)fluoranthene	NA	= (	87.17	×	1.3	×	8	×	219	×	1	× [	1	/	NC	+	1	/	1.37E+07	]	+ (	70	×	365	×	NV	)
Chrysene	NA	= (	134.76	×	1.3	×	8	×	219	×	1	× [	1	/	NC	+	1	/	1.37E+07	]	+ (	70	×	365	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	19.43	×	1.3	×	8	×	219	×	1	× [	1	/	NC	+	1	/	1.37E+07	]	+ (	70	×	365	×	NV	)
Dibenzofuran	NA	= (	63.08	×	1.3	×	8	×	219	×	1	× [	1	/	1.79E+04	+	1	/	1.37E+07	]	+ (	70	×	365	×	NV	)
Fluoranthene	NA	= (	245.24	×	1.3	×	8	×	219	×	1	× [	1	/	NC	+	1	/	1.37E+07	]	+ (	70	×	365	×	NV	)
Fluorene	NA	= (	206.67	×	1.3	×	8	×	219	×	1	× [	1	/	3.30E+04	+	1	/	1.37E+07	]	+ (	70	×	365	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	= (	68.43	×	1.3	×	8	×	219	×	1	× [	1	/	NC	+	1	/	1.37E+07	]	+ (	70	×	365	×	NV	)
Naphthalene	8.04E+00	= (	800.64	×	1.3	×	8	×	219	×	1	× [	1	/	1.04E+04	+	1	/	1.37E+07	]	+ (	70	×	365	×	8.57E-04	)
Pyrene	NA	= (	360.14	×	1.3	×	8	×	219	×	1	× [	1	/	1.10E+05	+	1	/	1.37E+07	]	+ (	70	×	365	×	NV	)
VOCs																											
1,2,4-*Trichlorobenzene*	1.59E-02	= (	9.19	×	1.3	×	8	×	219	×	1	× [	1	/	5.18E+04	+	1	/	1.37E+07	]	+ (	70	×	365	×	1.00E-03	)
1,2,4-Trimethylbenzene	5.90E-02	= (	2.23	×	1.3	×	8	×	219	×	1	× [	1	/	1.97E+03	+	1	/	1.37E+07	]	+ (	70	×	365	×	1.71E-03	)
1,3,5-Trimethylbenzene	3.13E-03	= (	0.97	×	1.3	×	8	×	219	×	1	× [	1	/	1.63E+03	+	1	/	1.37E+07	]	+ (	70	×	365	×	1.70E-02	)
Benzene	7.15E-02	= (	7.91	×	1.3	×	8	×	219	×	1	× [	1	/	1.15E+03	+	1	/	1.37E+07	]	+ (	70	×	365	×	8.57E-03	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Csoil – *Concentration in Soil*
IR – Inhalation Rate
ET – Exposure Time
EF – Exposure frequency
ED – Exposure duration
VF – Volatilization Factor
VOC – Volatile organic compound
PEF – Particulate Emission Factor (See Attachment G)
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
SVOC – Semivolatile organic compound

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available. Toxicity criteria is presented in Attachment A, Table 1b.

Attachment H4

Table 12c
Construction Worker: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} x \frac{(3.14 \times D_A \times T)^{1/2}}{(2 \times \rho_b \times D_A)} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} $(g/m^2\text{-}s)/(kg/m^3)$	π	D_A (cm^2/s)	T (s)	2	ρb (g/cm^3)	10^{-4} (m^2/cm^2)	VF (m^3/kg)
1-Methylnaphthalene	73.32	3.14	1.94E-05	3.15E+07	2	0.7	1.00E-04	1.18E+04
2-Methylnaphthalene	73.32	3.14	2.16E-05	3.15E+07	2	0.7	1.00E-04	1.12E+04
Acenaphthene	73.32	3.14	5.80E-06	3.15E+07	2	0.7	1.00E-04	2.16E+04
Benzo(a)anthracene	73.32	3.14	NC	3.15E+07	2	0.7	1.00E-04	NC
Benzo(a)pyrene	73.32	3.14	NC	3.15E+07	2	0.7	1.00E-04	NC
Benzo(b)fluoranthene	73.32	3.14	NC	3.15E+07	2	0.7	1.00E-04	NC
Benzo(k)fluoranthene	73.32	3.14	NC	3.15E+07	2	0.7	1.00E-04	NC
Chrysene	73.32	3.14	NC	3.15E+07	2	0.7	1.00E-04	NC
Dibenzo(a,h)anthracene	73.32	3.14	NC	3.15E+07	2	0.7	1.00E-04	NC
Dibenzofuran	73.32	3.14	8.43E-06	3.15E+07	2	0.7	1.00E-04	1.79E+04
Fluoranthene	73.32	3.14	NC	3.15E+07	2	0.7	1.00E-04	NC
Fluorene	73.32	3.14	2.49E-06	3.15E+07	2	0.7	1.00E-04	3.30E+04
Indeno(1,2,3-cd)pyrene	73.32	3.14	NC	3.15E+07	2	0.7	1.00E-04	NC
Naphthalene	73.32	3.14	2.53E-05	3.15E+07	2	0.7	1.00E-04	1.04E+04
Pyrene	73.32	3.14	2.24E-07	3.15E+07	2	0.7	1.00E-04	1.10E+05
1,2,4-Trichlorobenzene	73.32	3.14	1.01E-06	3.15E+07	2	0.7	1.00E-04	5.18E+04
1,2,3-Trimethylbenzene	73.32	3.14	3.84E-04	3.15E+07	2	0.7	1.00E-04	2.66E+03
1,2,4-Trimethylbenzene	73.32	3.14	6.99E-04	3.15E+07	2	0.7	1.00E-04	1.97E+03
1,3,5-Trimethylbenzene	73.32	3.14	1.02E-03	3.15E+07	2	0.7	1.00E-04	1.63E+03
Benzene	73.32	3.14	2.05E-03	3.15E+07	2	0.7	1.00E-04	1.15E+03

Notes:

Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

VF – Volatilization Factor (m^3/kg) (calculated)

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source $(g/m^2\text{-}s)/(kg/m^3)$(Value used is for Minneapolis, MN.)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T – Exposure interval (s)

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated

Attachment H4

Table 12d
Construction Worker: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical Units	VOC?	θa (Lair /Lsoil)	Di (cm^2/s)	H' unitless	θw (Lwater /Lsoil)	Dw (cm^2/s)	η (Lpore /Lsoil)	ρb (g/cm^3)	ρs (g/cm^3)	Kd (cm^3/g)	D_A (cm^2/s)
1-Methylnaphthalene	Yes	3.29E-01	6.31E-02	1.64E-02	0.15	7.13E-06	4.79E-01	1.38	2.65	3.75E+01	1.94E-05
2-Methylnaphthalene	Yes	3.29E-01	4.80E-02	2.12E-02	0.15	7.84E-06	4.79E-01	1.38	2.65	1.79E+01	2.16E-05
Acenaphthene	Yes	3.29E-01	4.21E-02	7.44E-03	0.15	7.69E-06	4.79E-01	1.38	2.65	3.67E+01	5.80E-06
Benzo(a)anthracene	No	3.29E-01	5.10E-02	4.91E-04	0.15	9.00E-06	4.79E-01	1.38	2.65	1.39E+03	NC
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Benzo(b)fluoranthene	No	3.29E-01	2.26E-02	2.69E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.82E+03	NC
Benzo(k)fluoranthene	No	3.29E-01	2.26E-02	2.39E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Chrysene	No	3.29E-01	2.48E-02	2.14E-04	0.15	6.21E-06	4.79E-01	1.38	2.65	1.42E+03	NC
Dibenzo(a,h)anthracene	No	3.29E-01	2.02E-02	5.03E-06	0.15	5.18E-06	4.79E-01	1.38	2.65	1.57E+04	NC
Dibenzofuran	Yes	3.29E-01	5.51E-02	8.71E-03	0.15	7.04E-06	4.79E-01	1.38	2.65	6.78E+01	8.43E-06
Fluoranthene	No	3.29E-01	3.02E-02	3.62E-04	0.15	6.35E-06	4.79E-01	1.38	2.65	4.25E+02	NC
Fluorene	Yes	3.29E-01	3.63E-02	3.93E-03	0.15	7.88E-06	4.79E-01	1.38	2.65	6.78E+01	2.49E-06
Indeno(1,2,3-cd)pyrene	No	3.29E-01	1.90E-02	1.42E-05	0.15	5.66E-06	4.79E-01	1.38	2.65	1.61E+04	NC
Naphthalene	Yes	3.29E-01	5.90E-02	1.80E-02	0.15	7.50E-06	4.79E-01	1.38	2.65	1.10E+01	2.53E-05
Pyrene	Yes	3.29E-01	2.72E-02	4.87E-04	0.15	7.24E-06	4.79E-01	1.38	2.65	4.16E+02	2.24E-07
1,2,4-Trichlorobenzene	NV	3.29E-01	3.00E-02	1.42E-03	0.15	8.23E-06	4.79E-01	1.38	2.65	1.07E+01	1.01E-06
1,2,3-Trimethylbenzene	NV	3.29E-01	6.77E-02	1.33E-01	0.15	7.41E-06	4.79E-01	1.38	2.65	3.53E+00	3.84E-04
1,2,4-Trimethylbenzene	Yes	3.29E-01	6.44E-02	2.52E-01	0.15	7.92E-06	4.79E-01	1.38	2.65	4.31E+00	6.99E-04
1,3,5-Trimethylbenzene	Yes	3.29E-01	6.02E-02	3.59E-01	0.15	8.67E-06	4.79E-01	1.38	2.65	4.22E+00	1.02E-03
Benzene	Yes	3.29E-01	8.80E-02	2.27E-01	0.15	9.80E-06	4.79E-01	1.38	2.65	9.93E-01	2.05E-03

Notes:

D_A – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User'S Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density
Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm^3/g)
foc – *fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)*
VOC? – Volatile organic compounds; If no an apparent diffusivity was not calculated.
NV – no value available
NC – not calculated

Attachment H4

Table 13a
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Incidental Ingestion of Soil Pathway (0-10 feet) – Carcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$Ing\text{-}Risk = \frac{(Csoil \times SFo \times CF \times EF \times SIRadj \times FI)}{ATc}$$

Equation / Units	*Ing - Risk* unitless	= (	*Csoil* mg/kg	×	SFo kg-day/mg	×	CF kg/mg	×	EF days/year	×	SIRadj mg-yr/kg-day	×	FI unitless	) ÷ (	ATc days	)
Arsenic	8.78E-06	= (	3.74E+00	×	1.50E+00	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Lead	NA	= (	1.76E+02	×	a	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
1-Methylnaphthalene	NA	= (	1.66E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Benzo(a)anthracene	1.55E-05	= (	1.36E+01	×	7.30E-01	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Benzo(a)pyrene	1.84E-04	= (	1.61E+01	×	7.30E+00	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Benzo(b)fluoranthene	1.54E-05	= (	1.35E+01	×	7.30E-01	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Benzo(k)fluoranthene	4.83E-07	= (	4.23E+00	×	7.30E-02	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Dibenzo(a,h)anthracene	8.70E-06	= (	7.61E-01	×	7.30E+00	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Fluoranthene	NA	= (	2.65E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Indeno(1,2,3-cd)pyrene	3.88E-06	= (	3.39E+00	×	7.30E-01	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Naphthalene	NA	= (	6.46E+00	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Pyrene	NA	= (	4.70E+01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	1.32E+00	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	4.86E-01	×	NV	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)
Benzene	1.67E-07	= (	1.95E+00	×	5.50E-02	×	1E-06	×	350	×	114.28	×	1	) ÷ (	25,550	)

Notes:

Ing - Risk – Ingestion risk
Csoil – Soil Concentration
SFo – Oral Slope Factor
CF – Unit Conversion Factor
EF – Exposure Frequency
SIRadj – Age-adjusted Soil Ingestion Rate
FI – Fraction Ingested from Contaminated Source
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment H4

Table 13b
Risk Calculations: Reasonable Maximum Exposure
Residential Child: Incidental Ingestion of Soil Pathway (0-10 feet) – Noncarcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$Ing\text{-}HQ = \frac{(Csoil \times CF \times EF \times EDc \times SIRc \times FI)}{(BWc \times ATn \times RfDo)}$$

Equation / Units	Ing - HQ unitless	= (	Csoil mg/kg	×	CF kg/mg	×	EF days/year	×	EDc years	×	SIRc mg/day	×	FI unitless	) ÷ (	BWc kg	×	ATn days	×	RfDo [b] mg/kg-day	)
Arsenic	1.59E-01	= (	3.74E+00	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	3.0E-04	)
Lead	NA	= (	1.76E+02	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	a	)
1-Methylnaphthalene	3.03E-03	= (	1.66E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	7.0E-02	)
Benzo(a)anthracene	NA	= (	1.36E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	= (	1.61E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.35E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	= (	4.23E+00	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	7.61E-01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	NV	)
Fluoranthene	8.46E-04	= (	2.65E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	4.0E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (	3.39E+00	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	NV	)
Naphthalene	4.13E-03	= (	6.46E+00	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	2.0E-02	)
Pyrene	2.00E-03	= (	4.70E+01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	3.0E-01	)
1,2,4-Trimethylbenzene	3.38E-04	= (	1.32E+00	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	5.0E-02	)
1,3,5-Trimethylbenzene	1.24E-05	= (	4.86E-01	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	5.0E-01	)
Benzene	6.22E-03	= (	1.95E+00	×	1E-06	×	350	×	6	×	200	×	1	) ÷ (	15	×	2,190	×	4.0E-03	)

Notes:

Ing - HQ – Ingestion Hazard
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
EDc – Exposure Duration, child
SIRc – Soil Ingestion Rate, child
FI – Fraction Ingested from Contaminated Source
BWc – Body Weight, child
ATn – *Averaging Time for Noncarcinogens*
RfDo – Oral reference dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment H4

Table 14a
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Dermal Contact with Soil Pathway (0-10 feet) – Carcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Derm - Risk} = \frac{(\text{Csoil} \times \text{SFabs} \times \text{CF} \times \text{EF} \times \text{EV} \times \text{SCRadj} \times \text{ABSd})}{\text{ATc}}$$

Equation / Units	Derm - Risk unitless	= (	Csoil mg/kg	×	SFabs kg-day/mg	×	CF kg/mg	×	EF days/year	×	EV events/day	×	SCRadj mg-yr/kg-event	×	ABSd unitless	) ÷ (	ATc days	)
Arsenic	8.74E-07	= (	3.74E+00	×	1.58E+00	×	1E-06	×	350	×	1	×	360	×	3.00E-02	) ÷ (	25,550	)
Lead	NA	= (	1.76E+02	×	a	×	1E-06	×	350	×	1	×	360	×	NA	) ÷ (	25,550	)
1-Methylnaphthalene	NA	= (	1.66E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Benzo(a)anthracene	6.36E-06	= (	1.36E+01	×	7.30E-01	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Benzo(a)pyrene	7.55E-05	= (	1.61E+01	×	7.30E+00	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Benzo(b)fluoranthene	6.31E-06	= (	1.35E+01	×	7.30E-01	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Benzo(k)fluoranthene	1.98E-07	= (	4.23E+00	×	7.30E-02	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Dibenzo(a,h)anthracene	3.57E-06	= (	7.61E-01	×	7.30E+00	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Fluoranthene	NA	= (	2.65E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Indeno(1,2,3-cd)pyrene	1.59E-06	= (	3.39E+00	×	7.30E-01	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Naphthalene	NA	= (	6.46E+00	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
Pyrene	NA	= (	4.70E+01	×	NV	×	1E-06	×	350	×	1	×	360	×	1.30E-01	) ÷ (	25,550	)
1,2,4-Trimethylbenzene	NA	= (	1.32E+00	×	NV	×	1E-06	×	350	×	1	×	360	×	NA	) ÷ (	25,550	)
1,3,5-Trimethylbenzene	NA	= (	4.86E-01	×	NV	×	1E-06	×	350	×	1	×	360	×	NA	) ÷ (	25,550	)
Benzene	NA	= (	1.95E+00	×	5.50E-02	×	1E-06	×	350	×	1	×	360	×	NA	) ÷ (	25,550	)

Notes:

Derm - Risk – Dermal Risk
Csoil – Soil Concentration
SFabs – Absorbed slope factor (SFo ÷ ABSgi)
CF – Unit Conversion Factor
EF – Exposure Frequency
EV – Event Frequency
SCRadj – Age-adjusted Soil Contact Rate
ABSd – Dermal Soil Absorption Factor
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment H4

Table 14b
Risk Calculations: Reasonable Maximum Exposure
Residential Child: Dermal Contact with Soil Pathway (0-10 feet) – Noncarcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Derm - HQ} = \frac{(\text{Csoil} \times \text{CF} \times \text{EF} \times \text{EDc} \times \text{EV} \times \text{SAc} \times \text{AFc} \times \text{ABSd})}{(\text{BWc} \times \text{ATn} \times \text{RfDabs})}$$

Equation / Units	Derm - HQ unitless	= (	Csoil mg/kg	×	CF kg/mg	×	EF days/year	×	EDc years	×	EV events/day	×	SAc cm²	×	AFc mg/cm²-event	×	ABSd unitless	) ÷ (	BWc kg	×	ATn days	×	RfDabs [b] mg/kg-day	)
Arsenic	1.41E-02	= (	3.74E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	3.00E-02	) ÷ (	15	×	2,190	×	2.85E-04	)
Lead	NA	= (	1.76E+02	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	a	)
1-Methylnaphthalene	1.10E-03	= (	1.66E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	7.00E-02	)
Benzo(a)anthracene	NA	= (	1.36E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	= (	1.61E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.35E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	= (	4.23E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	7.61E-01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Fluoranthene	3.08E-04	= (	2.65E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	4.00E-01	)
Indeno(1,2,3-cd)pyrene	NA	= (	3.39E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	NV	)
Naphthalene	1.50E-03	= (	6.46E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	2.00E-02	)
Pyrene	7.29E-04	= (	4.70E+01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	1.30E-01	) ÷ (	15	×	2,190	×	3.00E-01	)
1,2,4-Trimethylbenzene	NA	= (	1.32E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	5.00E-02	)
1,3,5-Trimethylbenzene	NA	= (	4.86E-01	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	5.00E-01	)
Benzene	NA	= (	1.95E+00	×	1E-06	×	350	×	6	×	1	×	2,800	×	0.2	×	NA	) ÷ (	15	×	2,190	×	4.00E-03	)

Notes:

Derm - HQ – Dermal Hazard Quotient
Csoil – Soil Concentration
CF – Unit Conversion Factor
EF – Exposure Frequency
EDc – Exposure Duration, child
EV – Event Frequency
SAc – Skin Surface Area, child
AFc – Soil-to-skin Adherence Factor, child
ABSd – Dermal Soil Absorption Factor
BWc – Body Weight, child
ATn – Averaging Time for noncarcinogens
RfDabs – Absorbed reference dose (RfDo × ABSgi)
NA – Not Applicable
NV – No toxicity value available for this pathway.

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment H4

Table 15a
Risk Calculations: Reasonable Maximum Exposure
Residential Adult and Child: Inhalation of Soil-derived Chemicals Pathway (0-10 feet)– Carcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Inh - Risk} = \frac{(\text{Csoil} \times \text{SFi} \times \text{EF} \times \text{SInhRadj} \times [(1/\text{VF}) + (1/\text{PEF})])}{\text{ATc}}$$

Equation	Inh - Risk	=	(	Csoil	×	SFi	×	EF	×	SInhRadj	×	[	1	/	VF_{adult}	+	1	/	PEF	]	)	÷	(	ATc	)
Units	unitless			mg/kg		kg-day/mg		days/year		m3-yr/kg-day					m^3/kg				m^3/kg					days	
Arsenic	1.27E-09	=	(	3.74E+00	×	1.51E+01	×	350	×	10.86	×	[	1	/	NA	+	1	/	6.58E+09	]	)	÷	(	25,550	)
Lead	NA	=	(	1.76E+02	×	a	×	350	×	10.86	×	[	1	/	NA	+	1	/	6.58E+09	]	)	÷	(	25,550	)
1-Methylnaphthalene	NA	=	(	1.66E+01	×	NV	×	350	×	10.86	×	[	1	/	3.28E+04	+	1	/	6.58E+09	]	)	÷	(	25,550	)
Benzo(a)anthracene	NA	=	(	1.36E+01	×	NV	×	350	×	10.86	×	[	1	/	NC	+	1	/	6.58E+09	]	)	÷	(	25,550	)
Benzo(a)pyrene	1.12E-09	=	(	1.61E+01	×	3.08E+00	×	350	×	10.86	×	[	1	/	NC	+	1	/	6.58E+09	]	)	÷	(	25,550	)
Benzo(b)fluoranthene	NA	=	(	1.35E+01	×	NV	×	350	×	10.86	×	[	1	/	NC	+	1	/	6.58E+09	]	)	÷	(	25,550	)
Benzo(k)fluoranthene	NA	=	(	4.23E+00	×	NV	×	350	×	10.86	×	[	1	/	NC	+	1	/	6.58E+09	]	)	÷	(	25,550	)
Dibenzo(a,h)anthracene	NA	=	(	7.61E-01	×	NV	×	350	×	10.86	×	[	1	/	NC	+	1	/	6.58E+09	]	)	÷	(	25,550	)
Fluoranthene	NA	=	(	2.65E+01	×	NV	×	350	×	10.86	×	[	1	/	NC	+	1	/	6.58E+09	]	)	÷	(	25,550	)
Indeno(1,2,3-cd)pyrene	NA	=	(	3.39E+00	×	NV	×	350	×	10.86	×	[	1	/	NC	+	1	/	6.58E+09	]	)	÷	(	25,550	)
Naphthalene	NA	=	(	6.46E+00	×	NV	×	350	×	10.86	×	[	1	/	2.87E+04	+	1	/	6.58E+09	]	)	÷	(	25,550	)
Pyrene	NA	=	(	4.70E+01	×	NV	×	350	×	10.86	×	[	1	/	3.05E+05	+	1	/	6.58E+09	]	)	÷	(	25,550	)
1,2,4-Trimethylbenzene	NA	=	(	1.32E+00	×	NV	×	350	×	10.86	×	[	1	/	5.47E+03	+	1	/	6.58E+09	]	)	÷	(	25,550	)
1,3,5-Trimethylbenzene	NA	=	(	4.86E-01	×	NV	×	350	×	10.86	×	[	1	/	4.52E+03	+	1	/	6.58E+09	]	)	÷	(	25,550	)
Benzene	2.47E-06	=	(	1.95E+00	×	2.73E-02	×	350	×	10.86	×	[	1	/	3.20E+03	+	1	/	6.58E+09	]	)	÷	(	25,550	)

Notes:

Inh - Risk – Inhalation Risk
Csoil – Soil Concentration
SFi – Inhalation Slope Factor
EF – Exposure frequency
SInhRadj – Age-adjusted Soil Inhalation Rate
VF – Volatilization Factor
PEF – Particulate Emission Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NV – No toxicity value available for this pathway.
NA – Not Applicable
NC – Not Calculated
a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

Attachment H4

Table 15b
Risk Calculations: Reasonable Maximum Exposure
Residential Child: Inhalation of Soil-derived Pathway (0-10 feet) – Noncarcinogenic Effects
Excluding VOCs Exceeding Csat Values

$$\text{Inh - HQ} = \frac{(\text{Csoil} \times \text{InhRc} \times \text{EF} \times \text{EDc} \times ([1/\text{VF}] + [1/\text{PEF}]))}{(\text{BWc} \times \text{ATn} \times \text{RfDi})}$$

Equation	Inh - HQ	=	(	Csoil	×	InhRc	×	EF	×	EDc	×	[	1	/	VF_{child}	+	1	/	PEF	]	÷	(	BWc	×	ATn	×	RfDi (b)	)
Units	unitless			mg/kg		m^3/day		days/year		year					m^3/kg				m^3/kg				kg		days		mg/kg-day	
Arsenic	NA	=	(	3.74E+00	×	10	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Lead	NA	=	(	1.76E+02	×	10	×	350	×	6	×	[	1	/	NA	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	a	)
1-Methylnaphthalene	NA	=	(	1.66E+01	×	10	×	350	×	6	×	[	1	/	1.47E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Benzo(a)anthracene	NA	=	(	1.36E+01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Benzo(a)pyrene	NA	=	(	1.61E+01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Benzo(b)fluoranthene	NA	=	(	1.35E+01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Benzo(k)fluoranthene	NA	=	(	4.23E+00	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Dibenzo(a,h)anthracene	NA	=	(	7.61E-01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Fluoranthene	NA	=	(	2.65E+01	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Indeno(1,2,3-cd)pyrene	NA	=	(	3.39E+00	×	10	×	350	×	6	×	[	1	/	NC	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
Naphthalene	3.75E-01	=	(	6.46E+00	×	10	×	350	×	6	×	[	1	/	1.29E+04	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	8.57E-04	)
Pyrene	NA	=	(	4.70E+01	×	10	×	350	×	6	×	[	1	/	1.36E+05	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	NV	)
1,2,4-Trimethylbenzene	2.02E-01	=	(	1.32E+00	×	10	×	350	×	6	×	[	1	/	2.44E+03	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	1.71E-03	)
1,3,5-Trimethylbenzene	9.02E-03	=	(	4.86E-01	×	10	×	350	×	6	×	[	1	/	2.02E+03	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	1.70E-02	)
Benzene	1.02E-01	=	(	1.95E+00	×	10	×	350	×	6	×	[	1	/	1.43E+03	+	1	/	6.58E+09	]	÷	(	15	×	2,190	×	8.57E-03	)

Notes:

Inh - Risk – Inhalation Hazard Quotient
Csoil – Soil Concentration
InhRc – Inhalation Rate, child
EF – Exposure frequency
EDc – Exposure duration, child
VF – Volatilization Factor
PEF – Particulate Emission Factor
BWc – Body Weight, child
ATn – Averaging Time for Noncarcinogens
RfDi – Inhalation Reference Dose (subchronic)
NV – No toxicity value available for this pathway.
NA – Not Applicable

a – Quantifying risk following exposure involves many uncertainties, some of which may be unique to lead. Toxicity criteria for lead have not been derived by USEPA.

b – Subchronic toxicity values were used for each individual chemical, chronic toxicity values were used if subchronic values were not available.

Attachment H4

Table 15c
Residential Scenario: Volatilization Factor Calculations

Equation:

$$VF = \frac{Q}{C_{VF}} \times \frac{(3.14 \times D_A \times T)^{1/2}}{(2 \times \rho_b \times D_A)} \times 10^{-4} \frac{m^2}{cm^2}$$

Chemical	Q/C_{VF} $(g/m^2\text{-}s)/(kg/m^3)$	π	D_A (cm^2/s)	T_{adult} (s)	T_{child} (s)	2	ρb (g/cm^3)	10^{-4} (m^2/cm^2)	VF_{adult} (m^3/kg)
1-Methylnaphthalene	73.32	3.14	1.95E-05	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.28E+04
Benzo(a)anthracene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Benzo(a)pyrene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Benzo(b)fluoranthene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Benzo(k)fluoranthene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Dibenzo(a,h)anthracene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Fluoranthene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Indeno(1,2,3-cd)pyrene	73.32	3.14	NC	9.46E+08	1.89E+08	2	1.38	1.00E-04	NC
Naphthalene	73.32	3.14	2.54E-05	9.46E+08	1.89E+08	2	1.38	1.00E-04	2.87E+04
Pyrene	73.32	3.14	2.25E-07	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.05E+05
1,2,4-Trimethylbenzene	73.32	3.14	7.01E-04	9.46E+08	1.89E+08	2	1.38	1.00E-04	5.47E+03
1,3,5-Trimethylbenzene	73.32	3.14	1.02E-03	9.46E+08	1.89E+08	2	1.38	1.00E-04	4.52E+03
Benzene	73.32	3.14	2.05E-03	9.46E+08	1.89E+08	2	1.38	1.00E-04	3.20E+03

Notes:

Default values are as presented in Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (USEPA 2002).

VF_{adult} – Volatilization Factor (m^3/kg) for adults (calculated)

VF_{child} – Volatilization Factor (m^3/kg) for children (calculated)

Q/C_{VF} – Inverse of mean concentration at the center of 1 acre square source $(g/m^2\text{-}s)/(kg/m^3)$(Value used is for Minneapolis, MN.)

π – pi (3.14)

D_A – Apparent Diffusivity (cm^2/s)

T_{adult} – Exposure interval (s) for adults

T_{Child} – Exposure interval (s) for children

ρ_b – Dry soil bulk density (g/cm^3) (site-specific value)

NC – Not calculated; PAHs are not considered volatile chemicals

Attachment H4

Table 15d
Residential Scenario: Apparent Diffusivity Calculations

Equation:

$$D_A = \frac{\left(\theta_a^{3.33} \times D_i \times H'\right) + \left(\theta_w^{3.33} \times D_w\right)}{\eta^2} \times \frac{1}{\left(\rho_b \times K_d\right) + \theta_w + \left(\theta_a \times H'\right)}$$

Chemical Units	VOC?	θa (Lair /Lsoil)	Di (cm^2/s)	H' unitless	θw (Lwater /Lsoil)	Dw (cm^2/s)	η (Lpore /Lsoil)	ρb (g/cm^3)	ρs (g/cm^3)	Kd (cm^3/g)	D_A (cm^2/s)
1-Methylnaphthalene	Yes	3.29E-01	6.31E-02	1.64E-02	0.15	7.13E-06	4.79E-01	1.38	2.65	3.75E+01	1.95E-05
Benzo(a)anthracene	No	3.29E-01	5.10E-02	4.91E-04	0.15	9.00E-06	4.79E-01	1.38	2.65	1.39E+03	NC
Benzo(a)pyrene	No	3.29E-01	4.30E-02	4.63E-05	0.15	9.00E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Benzo(b)fluoranthene	No	3.29E-01	2.26E-02	2.69E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.82E+03	NC
Benzo(k)fluoranthene	No	3.29E-01	2.26E-02	2.39E-05	0.15	5.56E-06	4.79E-01	1.38	2.65	4.72E+03	NC
Dibenzo(a,h)anthracene	No	3.29E-01	2.02E-02	5.03E-06	0.15	5.18E-06	4.79E-01	1.38	2.65	1.57E+04	NC
Fluoranthene	No	3.29E-01	3.02E-02	3.62E-04	0.15	6.35E-06	4.79E-01	1.38	2.65	4.25E+02	NC
Indeno(1,2,3-cd)pyrene	No	3.29E-01	1.90E-02	1.42E-05	0.15	5.66E-06	4.79E-01	1.38	2.65	1.61E+04	NC
Naphthalene	Yes	3.29E-01	5.90E-02	1.80E-02	0.15	7.50E-06	4.79E-01	1.38	2.65	1.10E+01	2.54E-05
Pyrene	Yes	3.29E-01	2.72E-02	4.87E-04	0.15	7.24E-06	4.79E-01	1.38	2.65	4.16E+02	2.25E-07
1,2,4-Trimethylbenzene	Yes	3.29E-01	6.44E-02	2.52E-01	0.15	7.92E-06	4.79E-01	1.38	2.65	4.31E+00	7.01E-04
1,3,5-Trimethylbenzene	Yes	3.29E-01	6.02E-02	3.59E-01	0.15	8.67E-06	4.79E-01	1.38	2.65	4.22E+00	1.02E-03
Benzene	Yes	3.29E-01	8.80E-02	2.27E-01	0.15	9.80E-06	4.79E-01	1.38	2.65	9.93E-01	2.05E-03

Notes:

D_A – apparent diffusivity
θa – air-filled soil porosity
Di – diffusivity in air
H' – dimensionless Henry's Law constant
θw – water-filled soil porosity
Dw – diffusivity in water
η – total soil porosity
ρb – dry soil bulk density based on soil type of silty clay. Value obtained from *User'S Guide For Evaluating Subsurface Vapor Intrusion Into Buildings* (USEPA, 2003).
ρs – soil particle density

Kd – soil-water partition coefficient, where:
Kd = Koc × foc
Koc – soil organic carbon partition coefficient (cm^3 /g)
foc – fraction organic carbon in soil (g/g) (A default value of 0.006 g/g was used.)
VOC? – Volatile organic compounds; If no, an apparent diffusivity was not calculated.
NV – no value available
NC – not calculated

Attachment I

Evaluation of Exposures to Oily Materials in Groundwater & Oil Slicks in Surface Water

Attachment I1

Calculation of Site Oily Materials in Groundwater & Oil Slicks in Surface Water using DNAPL Concentrations

Attachment I1
Table 1
Exposure Parameters – Adult Swimmer and Wader

Exposure Pathway	Parameter	Description	Exposure Parameters			
			CTE	Source	RME	Source
Incidental Surface Water Ingestion	$WIR_{swimming}$	Surface Water Ingestion Rate (L/hour)	0.01	(a)	0.05	(b)
	WIR_{wading}	Surface Water Ingestion Rate (L/hour)	0.01	(a)	0.01	(a)
	EF	Exposure Frequency (events/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	9	(e)	30	(e)
	ET	Exposure Time (hours/event)	1 (swimming) 2 (wading)	(f)	1 (swimming) 2 (wading)	(f)
	BW	Body Weight (kg)	70	(g)	70	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	3,285	(l)	10,950	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Dermal Contact with Surface Water	$SA_{swimming}$	Skin Surface Area Exposed (cm^2)	18,000	(k)	18,000	(k)
	SA_{wading}	Skin Surface Area Exposed (cm^2)	9,000	(k)	9,000	(k)
	EF	Exposure Frequency (days/yr)	6	(c)	12	(d)
	ED	Exposure Duration (years)	9	(e)	30	(e)
	EV	Event Frequency (events/day)	1		1	
	ET	Exposure Time (hours/event)	1 (swimming) 2 (wading)	(f)	1 (swimming) 2 (wading)	(f)
	BW	Body Weight (kg)	70	(g)	70	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	3,285	(l)	10,950	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Incidental Sediment Ingestion	SIR	Sediment Ingestion Rate (mg/day)	(m)		(m)	
	CF	Conversion Factor (kg/mg)	1E-06	--	1E-06	--
	EF	Exposure Frequency (days/yr)	6	(c)	12	(d)
	ED	Exposure Duration (years)	9	(e)	30	(e)
	FI	Fraction Ingested from Contaminated Source (unitless)	1		1	
	BW	Body Weight (kg)	70	(g)	70	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	3,285	(l)	10,950	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Dermal Contact with Sediment	SA	Skin Surface Area Exposed (cm^2)	4,499	(n)	5,672	(n)
	SSAF	Soil-to-Skin Adherence Factor (mg/cm^2)	0.5	(o)	1	(o)
	CF	Conversion Factor (kg/mg)	1E-06	--	1E-06	--
	EF	Exposure Frequency (days/yr)	6	(c)	12	(d)
	ED	Exposure Duration (years)	9	(e)	30	(e)
	EV	Event Frequency (events/day)	1		1	
	BW	Body Weight (kg)	70	(g)	70	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	3,285	(l)	10,950	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)

Notes:

CTE - Central Tendency Evaluation

RME - Reasonable Maximum Exposure.

(a) US EPA, 1989. Risk Assessment Guidance for Superfund, Volume I (RAGS, Part A). Value is one-fifth of that assumed to occur during a swimming event.

(b) US EPA, 1989. RAGS Part A. Value for a swimming event.

(c) One event per month for the 6 warmest months of the year.

(d) Two events per month for the 6 warmest months of the year.

(e) The default values for a residential adult, assuming the individual resides in the same residence for 9 (average) or 30 years (upperbound).

(f) US EPA, 1997. Exposure Factors Handbook, Table 1-2. Recommended values for exposure frequency of 1event per month and exposure time of 1 hours per event for swimming. The exposure time of 2 hours per event for wading is based on the estimated time spent on outdoor activities.

(g) US EPA, 1997. Exposure Factors Handbook. Body weight is the average of adult males and females

(h) 70 year lifetime is used to be consistent with the development of cancer slope factors.

(i) US EPA, 1991. Standard Default Exposure Factors. Value for adult.

(j) US EPA, 1989. RAGS, Part A.

(k) Value represents recommended skin surface area (100% for swimmers and 50% for waders).

(l) US EPA, 1989. RAGS, Part A. Averaging Time for noncarcinogens is equal to ED (year) × 365 days/year.

(m) Calculated using the equation: Sediment Ingestion Rate (mg/day) = Surface water ingestion rate (ml/day) × total solids (mg/ml).

(n) The RME skin surface area represents the sum of the surface area for forearms, hands, lower legs and feet. The CTE skin surface area represents the sum of the skin surface area for hands, lower legs and feet.

(o) *US EPA, 1997. Exposure Factors Handbook, (Table ??). Using loadings for the hands, arms, and legs for the irrigation worker, a* weighted soil-to-skin adherence factor of 2.0 mg/cm^2 was calculated. One-half this value (1.0 mg/cm^2) used as RME assuming some washoff; 0.5 mg/cm^2 used for CTE.

Attachment I1

Table 2
Risk Calculations
Adult Swimmer: Incidental Ingestion of Surface Water Pathway – Carcinogenic Effects
NSP Ashland

$$\text{Ing-Risk} = \frac{(\text{Cwater} \times \text{WIRswimming} \times \text{EF} \times \text{ED} \times \text{ET} \times \text{SFo})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	= (	Cwater	×	WIRswimming	×	EF	×	ED	×	ET	×	SFo	) ÷ (	BW	×	ATc	)
Units	unitless		mg/L		L/hour		events/year		years		hours/event		kg-day/mg		kg		days	
Cyanides	NA	= (	2.40E-05	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Iron	NA	= (	2.20E-04	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	1.20E-02	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
2,4 Dimethylphenol	NA	= (	4.80E-03	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	3.20E-03	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Anthracene	NA	= (	1.20E-03	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	2.94E-08	= (	4.00E-04	×	0.05	×	12	×	30	×	1	×	7.30E+00	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	2.64E-09	= (	3.60E-04	×	0.05	×	12	×	30	×	1	×	7.30E-01	) ÷ (	70	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	1.80E-04	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	8.08E-11	= (	1.10E-04	×	0.05	×	12	×	30	×	1	×	7.30E-02	) ÷ (	70	×	25,550	)
Chrysene	2.87E-11	= (	3.91E-04	×	0.05	×	12	×	30	×	1	×	7.30E-03	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	8.08E-09	= (	1.10E-04	×	0.05	×	12	×	30	×	1	×	7.30E+00	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	3.50E-04	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	1.20E-03	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	1.20E-03	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.18E-09	= (	1.60E-04	×	0.05	×	12	×	30	×	1	×	7.30E-01	) ÷ (	70	×	25,550	)
m & p-Cresols	NA	= (	6.20E-03	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	2.60E-02	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
o-Cresol	NA	= (	4.20E-03	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Phenanthrene	NA	= (	2.60E-03	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Phenol	NA	= (	1.20E-03	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	2.00E-03	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	5.00E-04	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)

Attachment I1

Table 2
Risk Calculations
Adult Swimmer: Incidental Ingestion of Surface Water Pathway – Carcinogenic Effects
NSP Ashland

$$\text{Ing-Risk} = \frac{(\text{Cwater} \times \text{WIRswimming} \times \text{EF} \times \text{ED} \times \text{ET} \times \text{SFo})}{(\text{BW} \times \text{ATc})}$$

Equation Units		Ing - Risk unitless	= (	Cwater mg/L	×	WIRswimming L/hour	×	EF events/year	×	ED years	×	ET hours/event	×	SFo kg-day/mg	) ÷ (	BW kg	×	ATc days	)
Benzene		2.44E-08	= (	4.40E-02	×	0.05	×	12	×	30	×	1	×	5.50E-02	) ÷ (	70	×	25,550	)
Ethylbenzene		NA	= (	5.50E-04	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
m & p-Xylenes		NA	= (	3.20E-03	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Toluene		NA	= (	1.90E-02	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
	Total CR	***6.58E-08***																	

Notes:

Ing-Risk – Carcinogenic Risk Water Ingestion Pathway
Cwater – DNAPL Concentration in Water
WIR – Water Ingestion Rate
EF – Exposure Frequency
ED – Exposure Duration
SFo – Oral Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 3
Risk Calculations
Adult Swimmer: Incidental Ingestion of Surface Water Pathway – Noncarcinogenic Effects
NSP Ashland

$$\text{Inh-HQ} = \frac{(\text{Cwater} \times \text{WIRswimming} \times \text{EF} \times \text{ED} \times \text{ET})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation Units	Ing - HQ unitless	= (	Cwater mg/L	×	WIRswimming L/hour	×	EF days/year	×	ED years	×	ET hours/event	) ÷ (	BW kg	×	ATn days	×	RfDo mg/kg-day	)
Cyanides	2.82E-08	= (	2.40E-05	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	2.00E-02	)
Iron	1.72E-08	= (	2.20E-04	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	3.00E-01	)
2-Methylnaphthalene	7.05E-05	= (	1.20E-02	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	4.00E-03	)
2,4 Dimethylphenol	5.64E-05	= (	4.80E-03	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	2.00E-03	)
Acenaphthylene	NA	= (	3.20E-03	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Anthracene	9.39E-08	= (	1.20E-03	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	4.00E-04	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Benzo(b)fluoranthene	NA	= (	3.60E-04	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Benzo(g,h,i)perylene	NA	= (	1.80E-04	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.10E-04	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Chrysene	NA	= (	3.91E-04	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.10E-04	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Dibenzofuran	4.11E-06	= (	3.50E-04	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	2.00E-03	)
Fluoranthene	7.05E-07	= (	1.20E-03	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	4.00E-02	)
Fluorene	7.05E-07	= (	1.20E-03	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.60E-04	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
m & p-Cresols	NA	= (	6.20E-03	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Naphthalene	3.05E-05	= (	2.60E-02	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	2.00E-02	)
o-Cresol	1.97E-06	= (	4.20E-03	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	5.00E-02	)
Phenanthrene	NA	= (	2.60E-03	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Phenol	9.39E-08	= (	1.20E-03	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	3.00E-01	)
Pyrene	1.57E-06	= (	2.00E-03	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	3.00E-02	)
1,2,4-Trimethylbenzene	2.35E-07	= (	5.00E-04	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	5.00E-02	)

Attachment I1

Table 3
Risk Calculations
Adult Swimmer: Incidental Ingestion of Surface Water Pathway – Noncarcinogenic Effects
NSP Ashland

$$\text{Inh-HQ} = \frac{(\text{Cwater} \times \text{WIRswimming} \times \text{EF} \times \text{ED} \times \text{ET})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation	Ing - HQ	= (	Cwater	×	WIRswimming	×	EF	×	ED	×	ET	) ÷ (	BW	×	ATn	×	RfDo	)
Units	unitless		mg/L		L/hour		days/year		years		hours/event		kg		days		mg/kg-day	
Benzene	2.58E-04	= (	4.40E-02	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	4.00E-03	)
Ethylbenzene	1.29E-07	= (	5.50E-04	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	1.00E-01	)
m & p-Xylenes	NA	= (	3.20E-03	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Toluene	5.58E-06	= (	1.90E-02	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	8.00E-02	)
Total HI	***4.31E-04***																	

Notes:

Ing-HQ – Water Ingestion Pathway Hazard Quotient
Cwater – DNAPL Concentration in Water
WIR – Water Ingestion Rate
EF – Exposure Frequency
ED – Exposure Duration
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 4a
Risk Calculations
Adult Swimmer: Dermal Contact with Surface Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SAswimming \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	2.40E-08	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Iron	NA	= (	2.20E-07	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	1.42E-03	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
2,4 Dimethylphenol	NA	= (	3.12E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	5.25E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Anthracene	NA	= (	3.16E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	5.89E-02	= (	2.23E-03	×	1	×	30	×	12	×	18,000	×	7.30E+00	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	5.41E-03	= (	2.04E-03	×	1	×	30	×	12	×	18,000	×	7.30E-01	) ÷ (	70	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	2.28E-03	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	1.62E-04	= (	6.14E-04	×	1	×	30	×	12	×	18,000	×	7.30E-02	) ÷ (	70	×	25,550	)
Chrysene	3.20E-05	= (	1.21E-03	×	1	×	30	×	12	×	18,000	×	7.30E-03	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	2.75E-02	= (	1.04E-03	×	1	×	30	×	12	×	18,000	×	7.30E+00	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	4.96E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	8.20E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	1.84E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	2.69E-03	= (	1.02E-03	×	1	×	30	×	12	×	18,000	×	7.30E-01	) ÷ (	70	×	25,550	)
m & p-Cresols	NA	= (	2.96E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	1.51E-03	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
o-Cresol	NA	= (	2.00E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Phenanthrene	NA	= (	8.92E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Phenol	NA	= (	1.83E-06	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	1.32E-03	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	7.45E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)

Attachment I1

Table 4a
Risk Calculations
Adult Swimmer: Dermal Contact with Surface Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SAswimming \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	×	SFabs	) ÷ (	BW	×	ATc	)
Units	**unitless**		**mg/cm²-event**		**events/day**		**years**		**days/year**		**cm²**		**kg-day/mg**		**kg**		**days**	
Benzene	8.10E-05	= (	4.07E-04	×	1	×	30	×	12	×	18,000	×	5.50E-02	) ÷ (	70	×	25,550	)
Ethylbenzene	NA	= (	2.52E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
m & p-Xylenes	NA	= (	2.16E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Toluene	NA	= (	5.53E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Total CR	***9.47E-02***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (Calculated using DNAPL concentration)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 4b
Risk Calculations
Adult Swimmer: Dermal Contact with Surface Water (Non-Linear High Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = 1\text{-exp}\left(-\frac{(DA_{event} \times EV \times ED \times EF \times SAswimming \times SFabs)}{(BW \times ATc)}\right)$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	2.40E-08	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Iron	NA	= (	2.20E-07	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	1.42E-03	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
2,4 Dimethylphenol	NA	= (	3.12E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	5.25E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Anthracene	NA	= (	3.16E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	5.72E-02	= (	2.23E-03	×	1	×	30	×	12	×	18,000	×	7.30E+00	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	5.39E-03	= (	2.04E-03	×	1	×	30	×	12	×	18,000	×	7.30E-01	) ÷ (	70	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	2.28E-03	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	1.62E-04	= (	6.14E-04	×	1	×	30	×	12	×	18,000	×	7.30E-02	) ÷ (	70	×	25,550	)
Chrysene	3.20E-05	= (	1.21E-03	×	1	×	30	×	12	×	18,000	×	7.30E-03	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	2.71E-02	= (	1.04E-03	×	1	×	30	×	12	×	18,000	×	7.30E+00	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	4.96E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	8.20E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	1.84E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	2.68E-03	= (	1.02E-03	×	1	×	30	×	12	×	18,000	×	7.30E-01	) ÷ (	70	×	25,550	)
m & p-Cresols	NA	= (	2.96E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	1.51E-03	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
o-Cresol	NA	= (	2.00E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Phenanthrene	NA	= (	8.92E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Phenol	NA	= (	1.83E-06	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	1.32E-03	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	7.45E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Benzene	8.10E-05	= (	4.07E-04	×	1	×	30	×	12	×	18,000	×	5.50E-02	) ÷ (	70	×	25,550	)

Attachment I1

Table 4b
Risk Calculations
Adult Swimmer: Dermal Contact with Surface Water (Non-Linear High Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = 1\text{-exp}\left(-\frac{(DA_{event} \times EV \times ED \times EF \times SAswimming \times SFabs)}{(BW \times ATc)}\right)$$

Equation / Units	Derm-Risk = unitless		DA_{event} mg/cm²-event	×	EV events/day	×	ED years	×	EF days/year	×	SAswimming cm²	×	SFabs kg-day/mg	) ÷ (	BW kg	×	ATc days	)
Ethylbenzene	NA	= (	2.52E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
m & p-Xylenes	NA	= (	2.16E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Toluene	NA	= (	5.53E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Total CR	***9.26E-02***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (Calculated using DNAPL concentration)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 5
Risk Calculations
Adult Swimmer: Dermal Contact with Surface Water – Noncarcinogenic Effects
NSP Ashland

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SAswimming)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
Cyanides	1.01E-05	= (	2.40E-08	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	2.00E-02	)
Iron	NA	= (	2.20E-07	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
2-Methylnaphthalene	3.00E+00	= (	1.42E-03	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	4.00E-03	)
2,4 Dimethylphenol	1.32E-01	= (	3.12E-05	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	2.00E-03	)
Acenaphthylene	NA	= (	5.25E-04	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Anthracene	8.90E-03	= (	3.16E-04	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	2.23E-03	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Benzo(b)fluoranthene	NA	= (	2.04E-03	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Benzo(g,h,i)perylene	NA	= (	2.28E-03	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Benzo(k)fluoranthene	NA	= (	6.14E-04	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Chrysene	NA	= (	1.21E-03	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.04E-03	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Dibenzofuran	2.10E-01	= (	4.96E-05	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	2.00E-03	)
Fluoranthene	1.73E-01	= (	8.20E-04	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	4.00E-02	)
Fluorene	3.89E-02	= (	1.84E-04	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.02E-03	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
m & p-Cresols	NA	= (	2.96E-05	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Naphthalene	6.38E-01	= (	1.51E-03	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	2.00E-02	)
o-Cresol	3.39E-03	= (	2.00E-05	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	5.00E-02	)
Phenanthrene	NA	= (	8.92E-04	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Phenol	5.16E-05	= (	1.83E-06	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	3.00E-01	)
Pyrene	3.71E-01	= (	1.32E-03	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	3.00E-02	)

Attachment I1

Table 5
Risk Calculations
Adult Swimmer: Dermal Contact with Surface Water – Noncarcinogenic Effects
NSP Ashland

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SAswimming)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	*unitless*		*mg/cm²-event*		*events/day*		*years*		*days/year*		*cm²*		*kg*		*days*		*mg/kg-day*	
1,2,4-Trimethylbenzene	1.26E-02	= (	7.45E-05	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	5.00E-02	)
Benzene	8.59E-01	= (	4.07E-04	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	4.00E-03	)
Ethylbenzene	2.13E-03	= (	2.52E-05	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	1.00E-01	)
m & p-Xylenes	NA	= (	2.16E-04	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Toluene	5.84E-02	= (	5.53E-04	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	8.00E-02	)
Total HI	***5.50E+00***																	

Notes:

Derm-HQ – Dermal Contact with Water Pathway Hazard Quotient
DA_{event} – Absorbed Dose per Event (Calculated using DNAPL concentration)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDabs – Absorbed Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1
Table 6a
Adult Swimmer Risk Summary (Linear Low Dose)
Reasonable Maximum Exposure

	Carcinogenic Risk							Target Organs	Noncarcinogenic Hazard						
Equation	CR	=	Ingestion	+	Dermal	+	Inhalation		HQ	=	Ingestion	+	Dermal	+	Inhalation
Units	unitless		unitless		unitless		unitless		unitless		unitless		unitless		unitless
Cyanides	NA	=	NA	+	NA	+	NA	*Thyroid, Systemic*	1.02E-05	=	2.82E-08	+	1.01E-05	+	NA
Iron	NA	=	NA	+	NA	+	NA		NA	=	1.72E-08	+	NA	+	NA
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA	*Respiratory*	3.00E+00	=	7.05E-05	+	3.00E+00	+	NA
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA	*Systemic*	1.32E-01	=	5.64E-05	+	1.32E-01	+	NA
Acenaphthylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Anthracene	NA	=	NA	+	NA	+	NA	*NOAEL*	8.90E-03	=	9.39E-08	+	8.90E-03	+	NA
Benzo(a)pyrene	5.89E-02	=	2.94E-08	+	5.89E-02	+	NA		NA	=	NA	+	NA	+	NA
Benzo(b)fluoranthene	5.41E-03	=	2.64E-09	+	5.41E-03	+	NA		NA	=	NA	+	NA	+	NA
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Benzo(k)fluoranthene	1.62E-04	=	8.08E-11	+	1.62E-04	+	NA		NA	=	NA	+	NA	+	NA
Chrysene	3.20E-05	=	2.87E-11	+	3.20E-05	+	NA		NA	=	NA	+	NA	+	NA
Dibenzo(a,h)anthracene	2.75E-02	=	8.08E-09	+	2.75E-02	+	NA		NA	=	NA	+	NA	+	NA
Dibenzofuran	NA	=	NA	+	NA	+	NA	*Systemic*	2.10E-01	=	4.11E-06	+	2.10E-01	+	NA
Fluoranthene	NA	=	NA	+	NA	+	NA	*Systemic, Circulatory*	1.73E-01	=	7.05E-07	+	1.73E-01	+	NA
Fluorene	NA	=	NA	+	NA	+	NA	*Circulatory*	3.89E-02	=	7.05E-07	+	3.89E-02	+	NA
Indeno(1,2,3-cd)pyrene	2.69E-03	=	1.18E-09	+	2.69E-03	+	NA		NA	=	NA	+	NA	+	NA
m & p-Cresols	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Naphthalene	NA	=	NA	+	NA	+	NA	*Respiratory, Systemic*	6.38E-01	=	3.05E-05	+	6.38E-01	+	NA
o-Cresol	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	3.39E-03	=	1.97E-06	+	3.39E-03	+	NA
Phenanthrene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Phenol	NA	=	NA	+	NA	+	NA	*Adrenal*	5.17E-05	=	9.39E-08	+	5.16E-05	+	NA
Pyrene	NA	=	NA	+	NA	+	NA	*Systemic*	3.71E-01	=	1.57E-06	+	3.71E-01	+	NA
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	1.26E-02	=	2.35E-07	+	1.26E-02	+	NA
Benzene	8.10E-05	=	2.44E-08	+	8.10E-05	+	NA	*Circulatory*	8.59E-01	=	2.58E-04	+	8.59E-01	+	NA
Ethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, Teratology*	2.13E-03	=	1.29E-07	+	2.13E-03	+	NA
m & p-Xylenes	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	NA	=	NA	+	NA	+	NA
Toluene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	5.84E-02	=	5.58E-06	+	5.84E-02	+	NA
Soil CR	***9E-02***	=	7E-08	+	***9E-02***	+	NA	**Soil HI**	***6***	=	0.0004	+	***6***	+	NA

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Target Organ HI	
Respiratory	
Circulatory	
Systemic	
Adrenal	
CNS	
Teratology	
Skin	

Attachment I1
Table 6b
Adult Swimmer Risk Summary (Non-linear High Dose)
Reasonable Maximum Exposure

	Carcinogenic Risk							Target Organs	Noncarcinogenic Hazard						
Equation	CR	=	Ingestion	+	Dermal	+	Inhalation		HQ	=	Ingestion	+	Dermal	+	Inhalation
Units	unitless		unitless		unitless		unitless		unitless		unitless		unitless		unitless
					0										
Cyanides	NA	=	NA	+	NA	+	NA	*Thyroid, Systemic*	1.02E-05	=	2.82E-08	+	1.01E-05	+	NA
Iron	NA	=	NA	+	NA	+	NA		NA	=	1.72E-08	+	NA	+	NA
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA	*Respiratory*	***3.00E+00***	=	7.05E-05	+	3.00E+00	+	NA
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA	*Systemic*	1.32E-01	=	5.64E-05	+	1.32E-01	+	NA
Acenaphthylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Anthracene	NA	=	NA	+	NA	+	NA	*NOAEL*	8.90E-03	=	9.39E-08	+	8.90E-03	+	NA
Benzo(a)pyrene	***5.72E-02***	=	2.94E-08	+	5.72E-02	+	NA		NA	=	NA	+	NA	+	NA
Benzo(b)fluoranthene	***5.39E-03***	=	2.64E-09	+	5.39E-03	+	NA		NA	=	NA	+	NA	+	NA
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Benzo(k)fluoranthene	***1.62E-04***	=	8.08E-11	+	1.62E-04	+	NA		NA	=	NA	+	NA	+	NA
Chrysene	***3.20E-05***	=	2.87E-11	+	3.20E-05	+	NA		NA	=	NA	+	NA	+	NA
Dibenzo(a,h)anthracene	***2.71E-02***	=	8.08E-09	+	2.71E-02	+	NA		NA	=	NA	+	NA	+	NA
Dibenzofuran	NA	=	NA	+	NA	+	NA	*Systemic*	2.10E-01	=	4.11E-06	+	2.10E-01	+	NA
Fluoranthene	NA	=	NA	+	NA	+	NA	*Systemic, Circulatory*	1.73E-01	=	7.05E-07	+	1.73E-01	+	NA
Fluorene	NA	=	NA	+	NA	+	NA	*Circulatory*	3.89E-02	=	7.05E-07	+	3.89E-02	+	NA
Indeno(1,2,3-cd)pyrene	***2.68E-03***	=	1.18E-09	+	2.68E-03	+	NA		NA	=	NA	+	NA	+	NA
m & p-Cresols	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Naphthalene	NA	=	NA	+	NA	+	NA	*Respiratory, Systemic*	6.38E-01	=	3.05E-05	+	6.38E-01	+	NA
o-Cresol	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	3.39E-03	=	1.97E-06	+	3.39E-03	+	NA
Phenanthrene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Phenol	NA	=	NA	+	NA	+	NA	*Adrenal*	5.17E-05	=	9.39E-08	+	5.16E-05	+	NA
Pyrene	NA	=	NA	+	NA	+	NA	*Systemic*	3.71E-01	=	1.57E-06	+	3.71E-01	+	NA
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	1.26E-02	=	2.35E-07	+	1.26E-02	+	NA
Benzene	***8.10E-05***	=	2.44E-08	+	8.10E-05	+	NA	*Circulatory*	8.59E-01	=	2.58E-04	+	8.59E-01	+	NA
Ethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, Teratology*	2.13E-03	=	1.29E-07	+	2.13E-03	+	NA
m & p-Xylenes	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	NA	=	NA	+	NA	+	NA
Toluene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	5.84E-02	=	5.58E-06	+	5.84E-02	+	NA
Soil CR	***9E-02***	=	7E-08	+	***9E-02***	+	NA	**Soil HI**	***6***	=	0.0004	+	***6***	+	NA

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Target Organ HI	
Respiratory	4
Circulatory	1
Systemic	1
Adrenal	5.E-05
CNS	7.E-02
Teratology	2.E-03

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Table 7
Exposure Parameters – Adolescent Swimmer and Wader

Exposure Pathway	Parameter	Description	Exposure Parameters			
			CTE	Source	RME	Source
Incidental Surface Water Ingestion	$WIR_{swimming}$	Surface Water Ingestion Rate (L/hour)	0.01	(a)	0.05	(b)
	WIR_{wading}	Surface Water Ingestion Rate (L/hour)	0.01	(a)	0.01	(a)
	EF	Exposure Frequency (events/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	12	(e)	12	(e)
	ET	Exposure Time (hours/event)	1 (swimming) 2 (wading)	(f)	1 (swimming) 2 (wading)	(f)
	BW	Body Weight (kg)	47	(g)	47	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	4,380	(l)	4,380	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Dermal Contact with Surface Water	$SA_{swimming}$	Skin Surface Area Exposed (cm^2)	13,533	(k)	13,533	(k)
	SA_{wading}	Skin Surface Area Exposed (cm^2)	6,767	(k)	6,767	(k)
	EF	Exposure Frequency (days/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	12	(e)	12	(e)
	EV	Event Frequency (events/day)	1		1	
	ET	Exposure Time (hours/event)	1 (swimming) 2 (wading)	(f)	1 (swimming) 2 (wading)	(f)
	BW	Body Weight (kg)	47	(g)	47	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	4,380	(l)	4,380	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Incidental Sediment Ingestion	SIR	Sediment Ingestion Rate (mg/hour)	5.60E-02	(m)	2.80E-01	(m)
	CF	Conversion Factor (kg/mg)	1E-06	--	1E-06	--
	EF	Exposure Frequency (days/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	12	(e)	12	(e)
	FI	Fraction Ingested from Contaminated Source (unitless)	1		1	
	BW	Body Weight (kg)	47	(g)	47	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	4,380	(l)	4,380	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Dermal Contact with Sediment	SA	Skin Surface Area Exposed (cm^2)	3,259	(n)	4,046	(n)
	SSAF	Soil-to-Skin Adherence Factor (mg/cm^2)	0.5	(o)	1	(o)
	CF	Conversion Factor (kg/mg)	1E-06	--	1E-06	--
	EF	Exposure Frequency (days/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	12	(e)	12	(e)
	EV	Event Frequency (events/day)	1		1	
	BW	Body Weight (kg)	47	(g)	47	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	4,380	(l)	4,380	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)

Notes:
CTE - Central Tendency Evaluation
RME - Reasonable Maximum Exposure.

(a) US EPA, 1989. Risk Assessment Guidance for Superfund, Volume I (RAGS, Part A). Value is one-fifth of that assumed to occur during a swimming event.
(b) US EPA, 1989. RAGS Part A. Value for a swimming event.
(c) One event per month for the 6 warmest months of the year.
(d) Two events per month for the 6 warmest months of the year.
(e) The default values for a residential adult, assuming the individual resides in the same residence for 9 (average) or 30 years (upperbound).
(f) US EPA, 1997. Exposure Factors Handbook, Table 1-2. Recommended values for exposure frequency of 1event per month and exposure time of 1 hours per event for swimming. The exposure time of 2 hours per event for wading is based on the estimated time spent on outdoor activities.
(g) US EPA, 1997. Exposure Factors Handbook. Body weight is the average of adult males and females
(h) 70 year lifetime is used to be consistent with the development of cancer slope factors.
(i) US EPA, 1991. Standard Default Exposure Factors. Value for adult.
(j) US EPA, 1989. RAGS, Part A.
(k) Value represents recommended skin surface area (100% for swimmers and 50% for waders).
(l) US EPA, 1989. RAGS, Part A. Averaging Time for noncarcinogens is equal to ED (year) × 365 days/year.
(m) Calculated using the equation: Sediment Ingestion Rate (mg/hour) = Surface water ingestion rate (ml/hour) × total solids (mg/ml). The average total suspended solids is 0.0056 mg/mL.
(n) The RME skin surface area represents the sum of the surface area for forearms, hands, lower legs and feet. The CTE skin surface area represents the sum of the skin surface area for hands, lower legs and feet.
(o) US EPA, 1997. Exposure Factors Handbook, (Table ??). Using loadings for the hands, arms, and legs for the irrigation worker, a weighted soil-to-skin adherence factor of 2.0 mg/cm^2 was calculated. One-half this value (1.0 mg/cm^2) used as RME assuming some

Attachment I1

Table 8
Risk Calculations
Adolescent Swimmer: Incidental Ingestion of Surface Water Pathway – Carcinogenic Effects
NSP Ashland

$$\text{Ing-Risk} = \frac{(\text{Cwater} \times \text{WIRswimming} \times \text{EF} \times \text{ED} \times \text{ET} \times \text{SFo})}{(\text{BW} \times \text{ATc})}$$

Equation Units	Ing - Risk unitless	= (	Cwater mg/L	×	WIRswimming L/hour	×	EF events/year	×	ED years	×	ET hours/event	×	SFo kg-day/mg	) ÷ (	BW kg	×	ATc days	)
Cyanides	NA	= (	2.40E-05	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Iron	NA	= (	2.20E-04	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
2-Methylnaphthalene	NA	= (	1.20E-02	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
2,4 Dimethylphenol	NA	= (	4.80E-03	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Acenaphthylene	NA	= (	3.20E-03	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Anthracene	NA	= (	1.20E-03	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Benzo(a)pyrene	1.75E-08	= (	4.00E-04	×	0.05	×	12	×	12	×	1	×	7.30E+00	) ÷ (	47	×	25,550	)
Benzo(b)fluoranthene	1.58E-09	= (	3.60E-04	×	0.05	×	12	×	12	×	1	×	7.30E-01	) ÷ (	47	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	1.80E-04	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Benzo(k)fluoranthene	4.81E-11	= (	1.10E-04	×	0.05	×	12	×	12	×	1	×	7.30E-02	) ÷ (	47	×	25,550	)
Chrysene	1.71E-11	= (	3.91E-04	×	0.05	×	12	×	12	×	1	×	7.30E-03	) ÷ (	47	×	25,550	)
Dibenzo(a,h)anthracene	4.81E-09	= (	1.10E-04	×	0.05	×	12	×	12	×	1	×	7.30E+00	) ÷ (	47	×	25,550	)
Dibenzofuran	NA	= (	3.50E-04	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Fluoranthene	NA	= (	1.20E-03	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Fluorene	NA	= (	1.20E-03	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	7.00E-10	= (	1.60E-04	×	0.05	×	12	×	12	×	1	×	7.30E-01	) ÷ (	47	×	25,550	)
m & p-Cresols	NA	= (	6.20E-03	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Naphthalene	NA	= (	2.60E-02	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
o-Cresol	NA	= (	4.20E-03	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Phenanthrene	NA	= (	2.60E-03	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Phenol	NA	= (	1.20E-03	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Pyrene	NA	= (	2.00E-03	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	5.00E-04	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)

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Table 8
Risk Calculations
Adolescent Swimmer: Incidental Ingestion of Surface Water Pathway – Carcinogenic Effects
NSP Ashland

$$\text{Ing-Risk} = \frac{(\text{Cwater} \times \text{WIRswimming} \times \text{EF} \times \text{ED} \times \text{ET} \times \text{SFo})}{(\text{BW} \times \text{ATc})}$$

Equation Units		Ing - Risk unitless	= (	Cwater mg/L	×	WIRswimming L/hour	×	EF events/year	×	ED years	×	ET hours/event	×	SFo kg-day/mg	) ÷ (	BW kg	×	ATc days	)
Benzene		1.45E-08	= (	4.40E-02	×	0.05	×	12	×	12	×	1	×	5.50E-02	) ÷ (	47	×	25,550	)
Ethylbenzene		NA	= (	5.50E-04	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
m & p-Xylenes		NA	= (	3.20E-03	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Toluene		NA	= (	1.90E-02	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
	Total CR	***3.92E-08***																	

Notes:

Ing-Risk – Carcinogenic Risk Water Ingestion Pathway
Cwater – DNAPL Concentration in Water
WIR – Water Ingestion Rate
EF – Exposure Frequency
ED – Exposure Duration
SFo – Oral Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 9
Risk Calculations
Adolescent Swimmer: Incidental Ingestion of Surface Water Pathway – Noncarcinogenic Effects
NSP Ashland

$$\text{Inh-HQ} = \frac{(\text{Cwater} \times \text{WIRswimming} \times \text{EF} \times \text{ED} \times \text{ET})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation Units	Ing - HQ unitless	=	Cwater mg/L	×	WIRswimming L/hour	×	EF days/year	×	ED years	×	ET hours/event	) ÷ (	BW kg	×	ATn days	×	RfDo mg/kg-day	)
Cyanides	4.20E-08	= (	2.40E-05	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	2.00E-02	)
Iron	2.56E-08	= (	2.20E-04	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	3.00E-01	)
2-Methylnaphthalene	1.05E-04	= (	1.20E-02	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	4.00E-03	)
2,4 Dimethylphenol	8.39E-05	= (	4.80E-03	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	2.00E-03	)
Acenaphthylene	NA	= (	3.20E-03	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Anthracene	1.40E-07	= (	1.20E-03	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	4.00E-04	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Benzo(b)fluoranthene	NA	= (	3.60E-04	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Benzo(g,h,i)perylene	NA	= (	1.80E-04	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.10E-04	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Chrysene	NA	= (	3.91E-04	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.10E-04	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Dibenzofuran	6.12E-06	= (	3.50E-04	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	2.00E-03	)
Fluoranthene	1.05E-06	= (	1.20E-03	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	4.00E-02	)
Fluorene	1.05E-06	= (	1.20E-03	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.60E-04	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
m & p-Cresols	NA	= (	6.20E-03	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Naphthalene	4.55E-05	= (	2.60E-02	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	2.00E-02	)
o-Cresol	2.94E-06	= (	4.20E-03	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	5.00E-02	)
Phenanthrene	NA	= (	2.60E-03	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Phenol	1.40E-07	= (	1.20E-03	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	3.00E-01	)
Pyrene	2.33E-06	= (	2.00E-03	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	3.00E-02	)
1,2,4-Trimethylbenzene	3.50E-07	= (	5.00E-04	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	5.00E-02	)

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Table 9
Risk Calculations
Adolescent Swimmer: Incidental Ingestion of Surface Water Pathway – Noncarcinogenic Effects
NSP Ashland

$$\text{Inh-HQ} = \frac{(\text{Cwater} \times \text{WIRswimming} \times \text{EF} \times \text{ED} \times \text{ET})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation Units	Ing - HQ unitless	= (	Cwater mg/L	×	WIRswimming L/hour	×	EF days/year	×	ED years	×	ET hours/event	) ÷ (	BW kg	×	ATn days	×	RfDo mg/kg-day	)
Benzene	3.85E-04	= (	4.40E-02	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	4.00E-03	)
Ethylbenzene	1.92E-07	= (	5.50E-04	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	1.00E-01	)
m & p-Xylenes	NA	= (	3.20E-03	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Toluene	8.31E-06	= (	1.90E-02	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	8.00E-02	)
Total HI	***6.42E-04***																	

Notes:

Ing-HQ – Water Ingestion Pathway Hazard Quotient
Cwater – DNAPL Concentration in Water
WIR – Water Ingestion Rate
EF – Exposure Frequency
ED – Exposure Duration
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 10a
Risk Calculations
Adolescent Swimmer: Dermal Contact with Surface Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SAswimming \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	2.40E-08	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Iron	NA	= (	2.20E-07	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
2-Methylnaphthalene	NA	= (	1.42E-03	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
2,4 Dimethylphenol	NA	= (	3.12E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Acenaphthylene	NA	= (	5.25E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Anthracene	NA	= (	3.16E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Benzo(a)pyrene	2.64E-02	= (	2.23E-03	×	1	×	12	×	12	×	13,533	×	7.30E+00	) ÷ (	47	×	25,550	)
Benzo(b)fluoranthene	2.42E-03	= (	2.04E-03	×	1	×	12	×	12	×	13,533	×	7.30E-01	) ÷ (	47	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	2.28E-03	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Benzo(k)fluoranthene	7.27E-05	= (	6.14E-04	×	1	×	12	×	12	×	13,533	×	7.30E-02	) ÷ (	47	×	25,550	)
Chrysene	1.43E-05	= (	1.21E-03	×	1	×	12	×	12	×	13,533	×	7.30E-03	) ÷ (	47	×	25,550	)
Dibenzo(a,h)anthracene	1.23E-02	= (	1.04E-03	×	1	×	12	×	12	×	13,533	×	7.30E+00	) ÷ (	47	×	25,550	)
Dibenzofuran	NA	= (	4.96E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Fluoranthene	NA	= (	8.20E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Fluorene	NA	= (	1.84E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.20E-03	= (	1.02E-03	×	1	×	12	×	12	×	13,533	×	7.30E-01	) ÷ (	47	×	25,550	)
m & p-Cresols	NA	= (	2.96E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Naphthalene	NA	= (	1.51E-03	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
o-Cresol	NA	= (	2.00E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Phenanthrene	NA	= (	8.92E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Phenol	NA	= (	1.83E-06	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Pyrene	NA	= (	1.32E-03	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	7.45E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)

Attachment I1

Table 10a
Risk Calculations
Adolescent Swimmer: Dermal Contact with Surface Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SAswimming \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Benzene	3.63E-05	= (	4.07E-04	×	1	×	12	×	12	×	13,533	×	5.50E-02	) ÷ (	47	×	25,550	)
Ethylbenzene	NA	= (	2.52E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
m & p-Xylenes	NA	= (	2.16E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Toluene	NA	= (	5.53E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Total CR	***4.24E-02***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (Calculated using DNAPL concentration)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 10b
Risk Calculations
Adolescent Swimmer: Dermal Contact with Surface Water (Non-Linear High Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = 1\text{-exp}\left(-\frac{(DA_{event} \times EV \times ED \times EF \times SAswimming \times SFabs)}{(BW \times ATc)}\right)$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	2.40E-08	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Iron	NA	= (	2.20E-07	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
2-Methylnaphthalene	NA	= (	1.42E-03	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
2,4 Dimethylphenol	NA	= (	3.12E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Acenaphthylene	NA	= (	5.25E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Anthracene	NA	= (	3.16E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Benzo(a)pyrene	2.60E-02	= (	2.23E-03	×	1	×	12	×	12	×	13,533	×	7.30E+00	) ÷ (	47	×	25,550	)
Benzo(b)fluoranthene	2.42E-03	= (	2.04E-03	×	1	×	12	×	12	×	13,533	×	7.30E-01	) ÷ (	47	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	2.28E-03	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Benzo(k)fluoranthene	7.27E-05	= (	6.14E-04	×	1	×	12	×	12	×	13,533	×	7.30E-02	) ÷ (	47	×	25,550	)
Chrysene	1.43E-05	= (	1.21E-03	×	1	×	12	×	12	×	13,533	×	7.30E-03	) ÷ (	47	×	25,550	)
Dibenzo(a,h)anthracene	1.22E-02	= (	1.04E-03	×	1	×	12	×	12	×	13,533	×	7.30E+00	) ÷ (	47	×	25,550	)
Dibenzofuran	NA	= (	4.96E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Fluoranthene	NA	= (	8.20E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Fluorene	NA	= (	1.84E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.20E-03	= (	1.02E-03	×	1	×	12	×	12	×	13,533	×	7.30E-01	) ÷ (	47	×	25,550	)
m & p-Cresols	NA	= (	2.96E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Naphthalene	NA	= (	1.51E-03	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
o-Cresol	NA	= (	2.00E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Phenanthrene	NA	= (	8.92E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Phenol	NA	= (	1.83E-06	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Pyrene	NA	= (	1.32E-03	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	7.45E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Benzene	3.63E-05	= (	4.07E-04	×	1	×	12	×	12	×	13,533	×	5.50E-02	) ÷ (	47	×	25,550	)

Attachment I1

Table 10b
Risk Calculations
Adolescent Swimmer: Dermal Contact with Surface Water (Non-Linear High Dose) – *Carcinogenic Effects*
NSP Ashland

$$\text{Derm-Risk} = 1\text{-exp}\left(-\frac{(DA_{event} \times EV \times ED \times EF \times SAswimming \times SFabs)}{(BW \times ATc)}\right)$$

Equation																		
Units	**Derm-Risk**	= (	**DA_{event}**	×	**EV**	×	**ED**	×	**EF**	×	**SAswimming**	×	**SFabs**	) ÷ (	**BW**	×	**ATc**	)
	unitless		**mg/cm²-event**		**events/day**		**years**		**days/year**		**cm²**		**kg-day/mg**		**kg**		**days**	
Ethylbenzene	NA	= (	2.52E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
m & p-Xylenes	NA	= (	2.16E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Toluene	NA	= (	5.53E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Total CR	***4.20E-02***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (Calculated using DNAPL concentration)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 11
Risk Calculations
Adolescent Swimmer: Dermal Contact with Surface Water – Noncarcinogenic Effects
NSP Ashland

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SAswimming)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
Cyanides	1.14E-05	= (	2.40E-08	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	2.00E-02	)
Iron	NA	= (	2.20E-07	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
2-Methylnaphthalene	3.36E+00	= (	1.42E-03	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	4.00E-03	)
2,4 Dimethylphenol	1.48E-01	= (	3.12E-05	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	2.00E-03	)
Acenaphthylene	NA	= (	5.25E-04	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Anthracene	9.97E-03	= (	3.16E-04	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	2.23E-03	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Benzo(b)fluoranthene	NA	= (	2.04E-03	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Benzo(g,h,i)perylene	NA	= (	2.28E-03	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Benzo(k)fluoranthene	NA	= (	6.14E-04	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Chrysene	NA	= (	1.21E-03	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.04E-03	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Dibenzofuran	2.35E-01	= (	4.96E-05	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	2.00E-03	)
Fluoranthene	1.94E-01	= (	8.20E-04	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	4.00E-02	)
Fluorene	4.35E-02	= (	1.84E-04	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.02E-03	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
m & p-Cresols	NA	= (	2.96E-05	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Naphthalene	7.15E-01	= (	1.51E-03	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	2.00E-02	)
o-Cresol	3.79E-03	= (	2.00E-05	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	5.00E-02	)
Phenanthrene	NA	= (	8.92E-04	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Phenol	5.77E-05	= (	1.83E-06	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	3.00E-01	)
Pyrene	4.15E-01	= (	1.32E-03	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	3.00E-02	)

Attachment I1

Table 11
Risk Calculations
Adolescent Swimmer: Dermal Contact with Surface Water – Noncarcinogenic Effects
NSP Ashland

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SAswimming)}{(BW \times ATn \times RfDabs)}$$

Equation	*Derm-Risk*	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	**unitless**		**mg/cm²-event**		**events/day**		**years**		**days/year**		**cm²**		**kg**		**days**		**mg/kg-day**	
1,2,4-Trimethylbenzene	1.41E-02	= (	7.45E-05	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	5.00E-02	)
Benzene	9.62E-01	= (	4.07E-04	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	4.00E-03	)
Ethylbenzene	2.39E-03	= (	2.52E-05	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	1.00E-01	)
m & p-Xylenes	NA	= (	2.16E-04	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Toluene	6.54E-02	= (	5.53E-04	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	8.00E-02	)
Total HI	***6.16E+00***																	

Notes:

Derm-HQ – Dermal Contact with Water Pathway Hazard Quotient
DA_{event} – Absorbed Dose per Event (Calculated using DNAPL concentration)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDabs – Absorbed Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 12a
Adolescent Swimmer Risk Summary (Linear Low Dose)
Reasonable Maximum Exposure

	Carcinogenic Risk							Target Organs	Noncarcinogenic Hazard						
Equation	CR	=	Ingestion	+	Dermal	+	Inhalation		HQ	=	Ingestion	+	Dermal	+	Inhalation
Units	unitless		unitless		unitless		unitless		unitless		unitless		unitless		unitless
Cyanides	NA	=	NA	+	NA	+	NA	*Thyroid, Systemic*	1.14E-05	=	4.20E-08	+	1.14E-05	+	NA
Iron	NA	=	NA	+	NA	+	NA		NA	=	2.56E-08	+	NA	+	NA
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA	*Respiratory*	3.36E+00	=	1.05E-04	+	3.36E+00	+	NA
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA	*Systemic*	1.48E-01	=	8.39E-05	+	1.48E-01	+	NA
Acenaphthylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Anthracene	NA	=	NA	+	NA	+	NA	*NOAEL*	9.97E-03	=	1.40E-07	+	9.97E-03	+	NA
Benzo(a)pyrene	2.64E-02	=	1.75E-08	+	2.64E-02	+	NA		NA	=	NA	+	NA	+	NA
Benzo(b)fluoranthene	2.42E-03	=	1.58E-09	+	2.42E-03	+	NA		NA	=	NA	+	NA	+	NA
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Benzo(k)fluoranthene	7.27E-05	=	4.81E-11	+	7.27E-05	+	NA		NA	=	NA	+	NA	+	NA
Chrysene	1.43E-05	=	1.71E-11	+	1.43E-05	+	NA		NA	=	NA	+	NA	+	NA
Dibenzo(a,h)anthracene	1.23E-02	=	4.81E-09	+	1.23E-02	+	NA		NA	=	NA	+	NA	+	NA
Dibenzofuran	NA	=	NA	+	NA	+	NA	*Systemic*	2.35E-01	=	6.12E-06	+	2.35E-01	+	NA
Fluoranthene	NA	=	NA	+	NA	+	NA	*Systemic, Circulatory*	1.94E-01	=	1.05E-06	+	1.94E-01	+	NA
Fluorene	NA	=	NA	+	NA	+	NA	*Circulatory*	4.35E-02	=	1.05E-06	+	4.35E-02	+	NA
Indeno(1,2,3-cd)pyrene	1.20E-03	=	7.00E-10	+	1.20E-03	+	NA		NA	=	NA	+	NA	+	NA
m & p-Cresols	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Naphthalene	NA	=	NA	+	NA	+	NA	*Respiratory, Systemic*	7.15E-01	=	4.55E-05	+	7.15E-01	+	NA
o-Cresol	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	3.80E-03	=	2.94E-06	+	3.79E-03	+	NA
Phenanthrene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Phenol	NA	=	NA	+	NA	+	NA	*Adrenal*	5.79E-05	=	1.40E-07	+	5.77E-05	+	NA
Pyrene	NA	=	NA	+	NA	+	NA	*Systemic*	4.15E-01	=	2.33E-06	+	4.15E-01	+	NA
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	1.41E-02	=	3.50E-07	+	1.41E-02	+	NA
Benzene	3.63E-05	=	1.45E-08	+	3.63E-05	+	NA	*Circulatory*	9.63E-01	=	3.85E-04	+	9.62E-01	+	NA
Ethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, Teratology*	2.39E-03	=	1.92E-07	+	2.39E-03	+	NA
m & p-Xylenes	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	NA	=	NA	+	NA	+	NA
Toluene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	6.54E-02	=	8.31E-06	+	6.54E-02	+	NA
Soil CR	***4E-02***	=	NA	+	***4E-02***	+	NA	**Soil HI**	***6***	=	NA	+	***6***	+	NA

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Target Organ HI

Respiratory	4
Circulatory	1
Systemic	1
Adrenal	6.E-05
CNS	8.E-02
Teratology	2.E-03

Attachment I1
Table 12b
Adolescent Swimmer Risk Summary (Non-linear Low Dose)
Reasonable Maximum Exposure

	Carcinogenic Risk								Target Organs	Noncarcinogenic Hazard							
Equation	CR	=	Ingestion	+	Dermal	+	Inhalation			HQ	=	Ingestion	+	Dermal	+	Inhalation	
Units	unitless		unitless		unitless		unitless			unitless		unitless		unitless		unitless	
					0												
Cyanides	NA	=	NA	+	NA	+	NA		*Thyroid, Systemic*	1.14E-05	=	4.20E-08	+	1.14E-05	+	NA	
Iron	NA	=	NA	+	NA	+	NA			NA	=	2.56E-08	+	NA	+	NA	
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA		*Respiratory*	***3.36E+00***	=	1.05E-04	+	3.36E+00	+	NA	
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA		*Systemic*	1.48E-01	=	8.39E-05	+	1.48E-01	+	NA	
Acenaphthylene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Anthracene	NA	=	NA	+	NA	+	NA		*NOAEL*	9.97E-03	=	1.40E-07	+	9.97E-03	+	NA	
Benzo(a)pyrene	***2.60E-02***	=	1.75E-08	+	2.60E-02	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(b)fluoranthene	***2.42E-03***	=	1.58E-09	+	2.42E-03	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(k)fluoranthene	***7.27E-05***	=	4.81E-11	+	7.27E-05	+	NA			NA	=	NA	+	NA	+	NA	
Chrysene	***1.43E-05***	=	1.71E-11	+	1.43E-05	+	NA			NA	=	NA	+	NA	+	NA	
Dibenzo(a,h)anthracene	***1.22E-02***	=	4.81E-09	+	1.22E-02	+	NA			NA	=	NA	+	NA	+	NA	
Dibenzofuran	NA	=	NA	+	NA	+	NA		*Systemic*	2.35E-01	=	6.12E-06	+	2.35E-01	+	NA	
Fluoranthene	NA	=	NA	+	NA	+	NA		*Systemic, Circulatory*	1.94E-01	=	1.05E-06	+	1.94E-01	+	NA	
Fluorene	NA	=	NA	+	NA	+	NA		*Circulatory*	4.35E-02	=	1.05E-06	+	4.35E-02	+	NA	
Indeno(1,2,3-cd)pyrene	***1.20E-03***	=	7.00E-10	+	1.20E-03	+	NA			NA	=	NA	+	NA	+	NA	
m & p-Cresols	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Naphthalene	NA	=	NA	+	NA	+	NA		*Respiratory, Systemic*	7.15E-01	=	4.55E-05	+	7.15E-01	+	NA	
o-Cresol	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	3.80E-03	=	2.94E-06	+	3.79E-03	+	NA	
Phenanthrene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Phenol	NA	=	NA	+	NA	+	NA		*Adrenal*	5.79E-05	=	1.40E-07	+	5.77E-05	+	NA	
Pyrene	NA	=	NA	+	NA	+	NA		*Systemic*	4.15E-01	=	2.33E-06	+	4.15E-01	+	NA	
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	1.41E-02	=	3.50E-07	+	1.41E-02	+	NA	
Benzene	***3.63E-05***	=	1.45E-08	+	3.63E-05	+	NA		*Circulatory*	9.63E-01	=	3.85E-04	+	9.62E-01	+	NA	
Ethylbenzene	NA	=	NA	+	NA	+	NA		*Systemic, Teratology*	2.39E-03	=	1.92E-07	+	*2.39E-03*	+	NA	
m & p-Xylenes	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	NA	=	NA	+	NA	+	NA	
Toluene	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	6.54E-02	=	8.31E-06	+	6.54E-02	+	NA	
Soil CR	***4E-02***	=	4E-08	+	***4E-02***	+	NA		**Soil HI**	***6***	=	6.4E-04	+	***6***	+	NA	

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Target Organ HI	
Respiratory	4
Circulatory	1
Systemic	1
Adrenal	6.E-05
CNS	8.E-02
Teratology	2.E-03

Attachment I1
Table 13
Exposure Parameters – Adult Swimmer and Wader

Exposure Pathway	Parameter	Description	Exposure Parameters			
			CTE	Source	RME	Source
Incidental Surface Water Ingestion	$WIR_{swimming}$	Surface Water Ingestion Rate (L/hour)	0.01	(a)	0.05	(b)
	WIR_{wading}	Surface Water Ingestion Rate (L/hour)	0.01	(a)	0.01	(a)
	EF	Exposure Frequency (events/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	9	(e)	30	(e)
	ET	Exposure Time (hours/event)	1 (swimming) 2 (wading)	(f)	1 (swimming) 2 (wading)	(f)
	BW	Body Weight (kg)	70	(g)	70	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	3,285	(l)	10,950	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Dermal Contact with Surface Water	$SA_{swimming}$	Skin Surface Area Exposed (cm^2)	18,000	(k)	18,000	(k)
	SA_{wading}	Skin Surface Area Exposed (cm^2)	9,000	(k)	9,000	(k)
	EF	Exposure Frequency (days/yr)	6	(c)	12	(d)
	ED	Exposure Duration (years)	9	(e)	30	(e)
	EV	Event Frequency (events/day)	1		1	
	ET	Exposure Time (hours/event)	1 (swimming) 2 (wading)	(f)	1 (swimming) 2 (wading)	(f)
	BW	Body Weight (kg)	70	(g)	70	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	3,285	(l)	10,950	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Incidental Sediment Ingestion	SIR	Sediment Ingestion Rate (mg/day)	(m)		(m)	
	CF	Conversion Factor (kg/mg)	1E-06	--	1E-06	--
	EF	Exposure Frequency (days/yr)	6	(c)	12	(d)
	ED	Exposure Duration (years)	9	(e)	30	(e)
	FI	Fraction Ingested from Contaminated Source (unitless)	1		1	
	BW	Body Weight (kg)	70	(g)	70	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	3,285	(l)	10,950	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Dermal Contact with Sediment	SA	Skin Surface Area Exposed (cm^2)	4,499	(n)	5,672	(n)
	SSAF	Soil-to-Skin Adherence Factor (mg/cm^2)	0.5	(o)	1	(o)
	CF	Conversion Factor (kg/mg)	1E-06	--	1E-06	--
	EF	Exposure Frequency (days/yr)	6	(c)	12	(d)
	ED	Exposure Duration (years)	9	(e)	30	(e)
	EV	Event Frequency (events/day)	1		1	
	BW	Body Weight (kg)	70	(g)	70	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	3,285	(l)	10,950	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)

Notes:

CTE - Central Tendency Evaluation

RME - Reasonable Maximum Exposure.

(a) US EPA, 1989. Risk Assessment Guidance for Superfund, Volume I (RAGS, Part A). Value is one-fifth of that assumed to occur during a swimming event.

(b) US EPA, 1989. RAGS Part A. Value for a swimming event.

(c) One event per month for the 6 warmest months of the year.

(d) Two events per month for the 6 warmest months of the year.

(e) The default values for a residential adult, assuming the individual resides in the same residence for 9 (average) or 30 years (upperbound).

(f) US EPA, 1997. Exposure Factors Handbook, Table 1-2. Recommended values for exposure frequency of 1event per month and exposure time of 1 hours per event for swimming. The exposure time of 2 hours per event for wading is based on the estimated time spent on outdoor activities.

(g) US EPA, 1997. Exposure Factors Handbook. Body weight is the average of adult males and females

(h) 70 year lifetime is used to be consistent with the development of cancer slope factors.

(i) US EPA, 1991. Standard Default Exposure Factors. Value for adult.

(j) US EPA, 1989. RAGS, Part A.

(k) Value represents recommended skin surface area (100% for swimmers and 50% for waders).

(l) US EPA, 1989. RAGS, Part A. Averaging Time for noncarcinogens is equal to ED (year) × 365 days/year.

(m) Calculated using the equation: Sediment Ingestion Rate (mg/day) = Surface water ingestion rate (ml/day) × total solids (mg/ml).

(n) The RME skin surface area represents the sum of the surface area for forearms, hands, lower legs and feet. The CTE skin surface area represents the sum of the skin surface area for hands, lower legs and feet.

(o) US EPA, 1997. Exposure Factors Handbook, (Table ??). Using loadings for the hands, arms, and legs for the irrigation worker, a weighted soil-to-skin adherence factor of 2.0 mg/cm^2 was calculated. One-half this value (1.0 mg/cm^2) used as RME assuming some washoff; 0.5 mg/cm^2 used for CTE.

Attachment I1

Table 14
Risk Calculations
Adult Wader: Incidental Ingestion of Surface Water Pathway – Carcinogenic Effects
NSP Ashland

$$\text{Ing-Risk} = \frac{(\text{Cwater} \times \text{WIRwader} \times \text{EF} \times \text{ED} \times \text{ET} \times \text{SFo})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	= (	Cwater	×	WIRwader	×	EF	×	ED	×	ET	×	SFo	) ÷ (	BW	×	ATc	)
Units	unitless		mg/L		L/hour		events/year		years		hours/event		kg-day/mg		kg		days	
Cyanides	NA	= (	2.40E-05	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Iron	NA	= (	2.20E-04	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	1.20E-02	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
2,4 Dimethylphenol	NA	= (	4.80E-03	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	3.20E-03	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Anthracene	NA	= (	1.20E-03	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	1.18E-08	= (	4.00E-04	×	0.01	×	12	×	30	×	2	×	7.30E+00	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	1.06E-09	= (	3.60E-04	×	0.01	×	12	×	30	×	2	×	7.30E-01	) ÷ (	70	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	1.80E-04	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	3.23E-11	= (	1.10E-04	×	0.01	×	12	×	30	×	2	×	7.30E-02	) ÷ (	70	×	25,550	)
Chrysene	1.15E-11	= (	3.91E-04	×	0.01	×	12	×	30	×	2	×	7.30E-03	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	3.23E-09	= (	1.10E-04	×	0.01	×	12	×	30	×	2	×	7.30E+00	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	3.50E-04	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	1.20E-03	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	1.20E-03	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	4.70E-10	= (	1.60E-04	×	0.01	×	12	×	30	×	2	×	7.30E-01	) ÷ (	70	×	25,550	)
m & p-Cresols	NA	= (	6.20E-03	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	2.60E-02	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
o-Cresol	NA	= (	4.20E-03	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Phenanthrene	NA	= (	2.60E-03	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Phenol	NA	= (	1.20E-03	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	2.00E-03	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	5.00E-04	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)

Attachment I1

Table 14
Risk Calculations
Adult Wader: Incidental Ingestion of Surface Water Pathway – Carcinogenic Effects
NSP Ashland

$$\text{Ing-Risk} = \frac{(\text{Cwater} \times \text{WIRwader} \times \text{EF} \times \text{ED} \times \text{ET} \times \text{SFo})}{(\text{BW} \times \text{ATc})}$$

Equation		Ing - Risk	= (	Cwater	×	WIRwader	×	EF	×	ED	×	ET	×	SFo	) ÷ (	BW	×	ATc	)
Units		unitless		mg/L		L/hour		events/year		years		hours/event		kg-day/mg		kg		days	
Benzene		9.74E-09	= (	4.40E-02	×	0.01	×	12	×	30	×	2	×	5.50E-02	) ÷ (	70	×	25,550	)
Ethylbenzene		NA	= (	5.50E-04	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
m & p-Xylenes		NA	= (	3.20E-03	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Toluene		NA	= (	1.90E-02	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
	Total CR	***2.63E-08***																	

Notes:

Ing-Risk – Carcinogenic Risk Water Ingestion Pathway
Cwater – DNAPL Concentration in Water
WIR – Water Ingestion Rate
EF – Exposure Frequency
ED – Exposure Duration
SFo – Oral Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 15
Risk Calculations
Adult Wader: Incidental Ingestion of Surface Water Pathway – Noncarcinogenic Effects
NSP Ashland

$$\text{Inh-HQ} = \frac{(\text{Cwater} \times \text{WIRwader} \times \text{EF} \times \text{ED} \times \text{ET})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation Units	Ing - HQ unitless	= (	Cwater mg/L	×	WIRwader L/hour	×	EF days/year	×	ED years	×	ET hours/event	) ÷ (	BW kg	×	ATn days	×	RfDo mg/kg-day	)
Cyanides	1.13E-08	= (	2.40E-05	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	2.00E-02	)
Iron	6.89E-09	= (	2.20E-04	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	3.00E-01	)
2-Methylnaphthalene	2.82E-05	= (	1.20E-02	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	4.00E-03	)
2,4 Dimethylphenol	2.25E-05	= (	4.80E-03	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	2.00E-03	)
Acenaphthylene	NA	= (	3.20E-03	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Anthracene	3.76E-08	= (	1.20E-03	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	4.00E-04	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Benzo(b)fluoranthene	NA	= (	3.60E-04	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Benzo(g,h,i)perylene	NA	= (	1.80E-04	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.10E-04	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Chrysene	NA	= (	3.91E-04	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.10E-04	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Dibenzofuran	1.64E-06	= (	3.50E-04	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	2.00E-03	)
Fluoranthene	2.82E-07	= (	1.20E-03	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	4.00E-02	)
Fluorene	2.82E-07	= (	1.20E-03	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.60E-04	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
m & p-Cresols	NA	= (	6.20E-03	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Naphthalene	1.22E-05	= (	2.60E-02	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	2.00E-02	)
o-Cresol	7.89E-07	= (	4.20E-03	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	5.00E-02	)
Phenanthrene	NA	= (	2.60E-03	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Phenol	3.76E-08	= (	1.20E-03	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	3.00E-01	)
Pyrene	6.26E-07	= (	2.00E-03	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	3.00E-02	)
1,2,4-Trimethylbenzene	9.39E-08	= (	5.00E-04	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	5.00E-02	)

Attachment I1

Table 15
Risk Calculations
Adult Wader: Incidental Ingestion of Surface Water Pathway – Noncarcinogenic Effects
NSP Ashland

$$\text{Inh-HQ} = \frac{(\text{Cwater} \times \text{WIRwader} \times \text{EF} \times \text{ED} \times \text{ET})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation Units		Ing - HQ unitless	= (	Cwater mg/L	×	WIRwader L/hour	×	EF days/year	×	ED years	×	ET hours/event	) ÷ (	BW kg	×	ATn days	×	RfDo mg/kg-day	)
Benzene		1.03E-04	= (	4.40E-02	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	4.00E-03	)
Ethylbenzene		5.17E-08	= (	5.50E-04	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	1.00E-01	)
m & p-Xylenes		NA	= (	3.20E-03	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Toluene		2.23E-06	= (	1.90E-02	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	8.00E-02	)
	Total HI	***1.72E-04***																	

Notes:

Ing-HQ – Water Ingestion Pathway Hazard Quotient
Cwater – DNAPL Concentration in Water
WIR – Water Ingestion Rate
EF – Exposure Frequency
ED – Exposure Duration
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 16a
Risk Calculations
Adult Wader: Dermal Contact with Surface Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SAwading \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	4.80E-08	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Iron	NA	= (	4.40E-07	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	2.01E-03	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
2,4 Dimethylphenol	NA	= (	4.41E-05	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	7.42E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Anthracene	NA	= (	4.47E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	3.01E-02	= (	2.28E-03	×	1	×	30	×	12	×	9,000	×	7.30E+00	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	2.77E-03	= (	2.09E-03	×	1	×	30	×	12	×	9,000	×	7.30E-01	) ÷ (	70	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	2.31E-03	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	8.31E-05	= (	6.29E-04	×	1	×	30	×	12	×	9,000	×	7.30E-02	) ÷ (	70	×	25,550	)
Chrysene	1.66E-05	= (	1.26E-03	×	1	×	30	×	12	×	9,000	×	7.30E-03	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	1.38E-02	= (	1.05E-03	×	1	×	30	×	12	×	9,000	×	7.30E+00	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	7.01E-05	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	1.16E-03	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	2.60E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.36E-03	= (	1.03E-03	×	1	×	30	×	12	×	9,000	×	7.30E-01	) ÷ (	70	×	25,550	)
m & p-Cresols	NA	= (	4.18E-05	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	2.14E-03	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
o-Cresol	NA	= (	2.83E-05	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Phenanthrene	NA	= (	1.26E-03	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Phenol	NA	= (	2.59E-06	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	1.86E-03	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	1.05E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)

Attachment I1

Table 16a
Risk Calculations
Adult Wader: Dermal Contact with Surface Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SAwading \times SFabs)}{(BW \times ATc)}$$

Equation		= (		×		×		×		×		×		) ÷ (		×		)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Benzene	5.73E-05	= (	5.75E-04	×	1	×	30	×	12	×	9,000	×	5.50E-02	) ÷ (	70	×	25,550	)
Ethylbenzene	NA	= (	3.57E-05	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
m & p-Xylenes	NA	= (	3.05E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Toluene	NA	= (	7.82E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Total CR	***4.83E-02***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (Calculated using DNAPL concentration)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 16b
Risk Calculations
Adult Wader: Dermal Contact with Surface Water (Non-Linear High Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = 1\text{-exp}\left(-\frac{(DA_{event} \times EV \times ED \times EF \times SAwading \times SFabs)}{(BW \times ATc)}\right)$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	4.80E-08	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Iron	NA	= (	4.40E-07	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	2.01E-03	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
2,4 Dimethylphenol	NA	= (	4.41E-05	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	7.42E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Anthracene	NA	= (	4.47E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	2.97E-02	= (	2.28E-03	×	1	×	30	×	12	×	9,000	×	7.30E+00	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	2.76E-03	= (	2.09E-03	×	1	×	30	×	12	×	9,000	×	7.30E-01	) ÷ (	70	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	2.31E-03	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	8.31E-05	= (	6.29E-04	×	1	×	30	×	12	×	9,000	×	7.30E-02	) ÷ (	70	×	25,550	)
Chrysene	1.66E-05	= (	1.26E-03	×	1	×	30	×	12	×	9,000	×	7.30E-03	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	1.38E-02	= (	1.05E-03	×	1	×	30	×	12	×	9,000	×	7.30E+00	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	7.01E-05	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	1.16E-03	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	2.60E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.36E-03	= (	1.03E-03	×	1	×	30	×	12	×	9,000	×	7.30E-01	) ÷ (	70	×	25,550	)
m & p-Cresols	NA	= (	4.18E-05	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	2.14E-03	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
o-Cresol	NA	= (	2.83E-05	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Phenanthrene	NA	= (	1.26E-03	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Phenol	NA	= (	2.59E-06	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	1.86E-03	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	1.05E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Benzene	5.73E-05	= (	5.75E-04	×	1	×	30	×	12	×	9,000	×	5.50E-02	) ÷ (	70	×	25,550	)

Attachment I1

Table 16b
Risk Calculations
Adult Wader: Dermal Contact with Surface Water (Non-Linear High Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = 1\text{-exp}\left(-\frac{(DA_{event} \times EV \times ED \times EF \times SAwading \times SFabs)}{(BW \times ATc)} \right)$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Ethylbenzene	NA	= (	3.57E-05	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
m & p-Xylenes	NA	= (	3.05E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Toluene	NA	= (	7.82E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Total CR	***4.77E-02***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (Calculated using DNAPL concentration)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 17
Risk Calculations
Adult Wader: Dermal Contact with Surface Water – Noncarcinogenic Effects
NSP Ashland

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SAwading)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
Cyanides	1.01E-05	= (	4.80E-08	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	2.00E-02	)
Iron	NA	= (	4.40E-07	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
2-Methylnaphthalene	2.12E+00	= (	2.01E-03	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	4.00E-03	)
2,4 Dimethylphenol	9.32E-02	= (	4.41E-05	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	2.00E-03	)
Acenaphthylene	NA	= (	7.42E-04	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Anthracene	6.30E-03	= (	4.47E-04	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	2.28E-03	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Benzo(b)fluoranthene	NA	= (	2.09E-03	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Benzo(g,h,i)perylene	NA	= (	2.31E-03	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Benzo(k)fluoranthene	NA	= (	6.29E-04	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Chrysene	NA	= (	1.26E-03	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.05E-03	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Dibenzofuran	1.48E-01	= (	7.01E-05	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	2.00E-03	)
Fluoranthene	1.23E-01	= (	1.16E-03	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	4.00E-02	)
Fluorene	2.75E-02	= (	2.60E-04	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.03E-03	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
m & p-Cresols	NA	= (	4.18E-05	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Naphthalene	4.51E-01	= (	2.14E-03	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	2.00E-02	)
o-Cresol	2.39E-03	= (	2.83E-05	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	5.00E-02	)
Phenanthrene	NA	= (	1.26E-03	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Phenol	3.65E-05	= (	2.59E-06	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	3.00E-01	)
Pyrene	2.62E-01	= (	1.86E-03	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	3.00E-02	)

Attachment I1

Table 17
Risk Calculations
Adult Wader: Dermal Contact with Surface Water – Noncarcinogenic Effects
NSP Ashland

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SAwading)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
1,2,4-Trimethylbenzene	8.91E-03	= (	1.05E-04	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	5.00E-02	)
Benzene	6.08E-01	= (	5.75E-04	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	4.00E-03	)
Ethylbenzene	1.51E-03	= (	3.57E-05	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	1.00E-01	)
m & p-Xylenes	NA	= (	3.05E-04	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Toluene	4.13E-02	= (	7.82E-04	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	8.00E-02	)
Total HI	***3.89E+00***																	

Notes:

Derm-HQ – Dermal Contact with Water Pathway Hazard Quotient
DA_{event} – Absorbed Dose per Event (Calculated using DNAPL concentration)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDabs – Absorbed Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1
Table 18a
Adult Wader Risk Summary (Linear Low Dose)
Reasonable Maximum Exposure

	Carcinogenic Risk							Target Organs	Noncarcinogenic Hazard						
Equation	CR	=	Ingestion	+	Dermal	+	Inhalation		HQ	=	Ingestion	+	Dermal	+	Inhalation
Units	unitless		unitless		unitless		unitless		unitless		unitless		unitless		unitless
Cyanides	NA	=	NA	+	NA	+	NA	*Thyroid, Systemic*	1.02E-05	=	1.13E-08	+	1.01E-05	+	NA
Iron	NA	=	NA	+	NA	+	NA		NA	=	6.89E-09	+	NA	+	NA
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA	*Respiratory*	***2.12E+00***	=	2.82E-05	+	2.12E+00	+	NA
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA	*Systemic*	9.32E-02	=	2.25E-05	+	9.32E-02	+	NA
Acenaphthylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Anthracene	NA	=	NA	+	NA	+	NA	*NOAEL*	6.30E-03	=	3.76E-08	+	6.30E-03	+	NA
Benzo(a)pyrene	***3.01E-02***	=	1.18E-08	+	3.01E-02	+	NA		NA	=	NA	+	NA	+	NA
Benzo(b)fluoranthene	***2.77E-03***	=	1.06E-09	+	2.77E-03	+	NA		NA	=	NA	+	NA	+	NA
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Benzo(k)fluoranthene	***8.31E-05***	=	3.23E-11	+	8.31E-05	+	NA		NA	=	NA	+	NA	+	NA
Chrysene	***1.66E-05***	=	1.15E-11	+	1.66E-05	+	NA		NA	=	NA	+	NA	+	NA
Dibenzo(a,h)anthracene	***1.38E-02***	=	3.23E-09	+	1.38E-02	+	NA		NA	=	NA	+	NA	+	NA
Dibenzofuran	NA	=	NA	+	NA	+	NA	*Systemic*	1.48E-01	=	1.64E-06	+	1.48E-01	+	NA
Fluoranthene	NA	=	NA	+	NA	+	NA	*Systemic, Circulatory*	1.23E-01	=	2.82E-07	+	1.23E-01	+	NA
Fluorene	NA	=	NA	+	NA	+	NA	*Circulatory*	2.75E-02	=	2.82E-07	+	2.75E-02	+	NA
Indeno(1,2,3-cd)pyrene	***1.36E-03***	=	4.70E-10	+	1.36E-03	+	NA		NA	=	NA	+	NA	+	NA
m & p-Cresols	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Naphthalene	NA	=	NA	+	NA	+	NA	*Respiratory, Systemic*	4.51E-01	=	1.22E-05	+	4.51E-01	+	NA
o-Cresol	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	2.40E-03	=	7.89E-07	+	2.39E-03	+	NA
Phenanthrene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Phenol	NA	=	NA	+	NA	+	NA	*Adrenal*	3.65E-05	=	3.76E-08	+	3.65E-05	+	NA
Pyrene	NA	=	NA	+	NA	+	NA	*Systemic*	2.62E-01	=	6.26E-07	+	2.62E-01	+	NA
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	8.91E-03	=	9.39E-08	+	8.91E-03	+	NA
Benzene	***5.73E-05***	=	9.74E-09	+	5.73E-05	+	NA	*Circulatory*	6.08E-01	=	1.03E-04	+	6.08E-01	+	NA
Ethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, Teratology*	1.51E-03	=	5.17E-08	+	1.51E-03	+	NA
m & p-Xylenes	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	NA	=	NA	+	NA	+	NA
Toluene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	4.13E-02	=	2.23E-06	+	4.13E-02	+	NA
Soil CR	***5E-02***	=	3E-08	+	***5E-02***	+	NA	**Soil HI**	***4***	=	0	+	***4***	+	NA

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Target Organ HI	
Respiratory	
Circulatory	
Systemic	
Adrenal	
CNS	
Teratology	
Skin	

Attachment I1
Table 18b
Adult Wader Risk Summary (Non-linear Low Dose)
Reasonable Maximum Exposure

	Carcinogenic Risk							Target Organs	Noncarcinogenic Hazard						
Equation	CR	=	Ingestion	+	Dermal	+	Inhalation		HQ	=	Ingestion	+	Dermal	+	Inhalation
Units	unitless		unitless		unitless		unitless		unitless		unitless		unitless		unitless
Cyanides	NA	=	NA	+	NA	+	NA	*Thyroid, Systemic*	1.02E-05	=	2.82E-08	+	1.01E-05	+	NA
Iron	NA	=	NA	+	NA	+	NA		NA	=	1.72E-08	+	NA	+	NA
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA	*Respiratory*	***2.12E+00***	=	7.05E-05	+	2.12E+00	+	NA
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA	*Systemic*	9.32E-02	=	5.64E-05	+	9.32E-02	+	NA
Acenaphthylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Anthracene	NA	=	NA	+	NA	+	NA	*NOAEL*	6.30E-03	=	9.39E-08	+	6.30E-03	+	NA
Benzo(a)pyrene	***2.97E-02***	=	2.94E-08	+	2.97E-02	+	NA		NA	=	NA	+	NA	+	NA
Benzo(b)fluoranthene	***2.76E-03***	=	2.64E-09	+	2.76E-03	+	NA		NA	=	NA	+	NA	+	NA
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Benzo(k)fluoranthene	***8.31E-05***	=	8.08E-11	+	8.31E-05	+	NA		NA	=	NA	+	NA	+	NA
Chrysene	***1.66E-05***	=	2.87E-11	+	1.66E-05	+	NA		NA	=	NA	+	NA	+	NA
Dibenzo(a,h)anthracene	***1.38E-02***	=	8.08E-09	+	1.38E-02	+	NA		NA	=	NA	+	NA	+	NA
Dibenzofuran	NA	=	NA	+	NA	+	NA	*Systemic*	1.48E-01	=	4.11E-06	+	1.48E-01	+	NA
Fluoranthene	NA	=	NA	+	NA	+	NA	*Systemic, Circulatory*	1.23E-01	=	7.05E-07	+	1.23E-01	+	NA
Fluorene	NA	=	NA	+	NA	+	NA	*Circulatory*	2.75E-02	=	7.05E-07	+	2.75E-02	+	NA
Indeno(1,2,3-cd)pyrene	***1.36E-03***	=	1.18E-09	+	1.36E-03	+	NA		NA	=	NA	+	NA	+	NA
m & p-Cresols	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Naphthalene	NA	=	NA	+	NA	+	NA	*Respiratory, Systemic*	4.51E-01	=	3.05E-05	+	4.51E-01	+	NA
o-Cresol	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	2.40E-03	=	1.97E-06	+	2.39E-03	+	NA
Phenanthrene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Phenol	NA	=	NA	+	NA	+	NA	*Adrenal*	3.66E-05	=	9.39E-08	+	3.65E-05	+	NA
Pyrene	NA	=	NA	+	NA	+	NA	*Systemic*	2.62E-01	=	1.57E-06	+	2.62E-01	+	NA
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	8.91E-03	=	2.35E-07	+	8.91E-03	+	NA
Benzene	***5.73E-05***	=	2.44E-08	+	5.73E-05	+	NA	*Circulatory*	6.08E-01	=	2.58E-04	+	6.08E-01	+	NA
Ethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, Teratology*	1.51E-03	=	1.29E-07	+	1.51E-03	+	NA
m & p-Xylenes	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	NA	=	NA	+	NA	+	NA
Toluene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	4.13E-02	=	5.58E-06	+	4.13E-02	+	NA
Soil CR	***5E-02***	=	7E-08	+	***5E-02***	+	NA	**Soil HI**	***4***	=	4.31E-04	+	***4***	+	NA

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Target Organ HI	
Respiratory	3
Circulatory	1
Systemic	1
Adrenal	4.E-05
CNS	5.E-02
Teratology	2.E-03

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Table 19
Exposure Parameters – Adult Swimmer and Wader

Exposure Pathway	Parameter	Description	Exposure Parameters			
			CTE	Source	RME	Source
Incidental Surface Water Ingestion	$WIR_{swimming}$	Surface Water Ingestion Rate (L/hour)	0.01	(a)	0.05	(b)
	WIR_{wading}	Surface Water Ingestion Rate (L/hour)	0.01	(a)	0.01	(a)
	EF	Exposure Frequency (events/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	12	(e)	12	(e)
	ET	Exposure Time (hours/event)	1 (swimming) 2 (wading)	(f)	1 (swimming) 2 (wading)	(f)
	BW	Body Weight (kg)	47	(g)	47	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	4,380	(l)	4,380	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Dermal Contact with Surface Water	$SA_{swimming}$	Skin Surface Area Exposed (cm^2)	13,533	(k)	13,533	(k)
	SA_{wading}	Skin Surface Area Exposed (cm^2)	6,767	(k)	6,767	(k)
	EF	Exposure Frequency (days/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	12	(e)	12	(e)
	EV	Event Frequency (events/day)	1		1	
	ET	Exposure Time (hours/event)	1 (swimming) 2 (wading)	(f)	1 (swimming) 2 (wading)	(f)
	BW	Body Weight (kg)	47	(g)	47	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	4,380	(l)	4,380	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Incidental Sediment Ingestion	SIR	Sediment Ingestion Rate (mg/hour)	5.60E-02	(m)	2.80E-01	(m)
	CF	Conversion Factor (kg/mg)	1E-06	--	1E-06	--
	EF	Exposure Frequency (days/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	12	(e)	12	(e)
	FI	Fraction Ingested from Contaminated Source (unitless)	1		1	
	BW	Body Weight (kg)	47	(g)	47	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	4,380	(l)	4,380	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Dermal Contact with Sediment	SA	Skin Surface Area Exposed (cm^2)	3,259	(n)	4,046	(n)
	SSAF	Soil-to-Skin Adherence Factor (mg/cm^2)	0.5	(o)	1	(o)
	CF	Conversion Factor (kg/mg)	1E-06	--	1E-06	--
	EF	Exposure Frequency (days/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	12	(e)	12	(e)
	EV	Event Frequency (events/day)	1		1	
	BW	Body Weight (kg)	47	(g)	47	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	4,380	(l)	4,380	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)

Notes:
CTE - Central Tendency Evaluation
RME - Reasonable Maximum Exposure.

(a) US EPA, 1989. Risk Assessment Guidance for Superfund, Volume I (RAGS, Part A). Value is one-fifth of that assumed to occur during a swimming event.
(b) US EPA, 1989. RAGS Part A. Value for a swimming event.
(c) One event per month for the 6 warmest months of the year.
(d) Two events per month for the 6 warmest months of the year.
(e) The default values for a residential adult, assuming the individual resides in the same residence for 9 (average) or 30 years (upperbound).
(f) US EPA, 1997. Exposure Factors Handbook, Table 1-2. Recommended values for exposure frequency of 1event per month and exposure time of 1 hours per event for swimming. The exposure time of 2 hours per event for wading is based on the estimated time spent on outdoor activities.
(g) US EPA, 1997. Exposure Factors Handbook. Body weight is the average of adult males and females
(h) 70 year lifetime is used to be consistent with the development of cancer slope factors.
(i) US EPA, 1991. Standard Default Exposure Factors. Value for adult.
(j) US EPA, 1989. RAGS, Part A.
(k) Value represents recommended skin surface area (100% for swimmers and 50% for waders).
(l) US EPA, 1989. RAGS, Part A. Averaging Time for noncarcinogens is equal to ED (year) × 365 days/year.
(m) Calculated using the equation: Sediment Ingestion Rate (mg/hour) = Surface water ingestion rate (ml/hour) × total solids (mg/ml). The average total suspended solids is 0.0056 mg/mL.
(n) The RME skin surface area represents the sum of the surface area for forearms, hands, lower legs and feet. The CTE skin surface area represents the sum of the skin surface area for hands, lower legs and feet.
(o) US EPA, 1997. Exposure Factors Handbook, (Table ??). Using loadings for the hands, arms, and legs for the irrigation worker, a weighted soil-to-skin adherence factor of 2.0 mg/cm^2 was calculated. One-half this value (1.0 mg/cm^2) used as RME assuming some

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Table 20
Risk Calculations
Adult Wader: Incidental Ingestion of Surface Water Pathway – Carcinogenic Effects
NSP Ashland

$$\text{Ing-Risk} = \frac{(\text{Cwater} \times \text{WIRwader} \times \text{EF} \times \text{ED} \times \text{ET} \times \text{SFo})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	= (	Cwater	×	WIRwader	×	EF	×	ED	×	ET	×	SFo	) ÷ (	BW	×	ATc	)
Units	unitless		mg/L		L/hour		events/year		years		hours/event		kg-day/mg		kg		days	
Cyanides	NA	= (	2.40E-05	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Iron	NA	= (	2.20E-04	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
2-Methylnaphthalene	NA	= (	1.20E-02	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
2,4 Dimethylphenol	NA	= (	4.80E-03	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Acenaphthylene	NA	= (	3.20E-03	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Anthracene	NA	= (	1.20E-03	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Benzo(a)pyrene	7.00E-09	= (	4.00E-04	×	0.01	×	12	×	12	×	2	×	7.30E+00	) ÷ (	47	×	25,550	)
Benzo(b)fluoranthene	6.30E-10	= (	3.60E-04	×	0.01	×	12	×	12	×	2	×	7.30E-01	) ÷ (	47	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	1.80E-04	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Benzo(k)fluoranthene	1.93E-11	= (	1.10E-04	×	0.01	×	12	×	12	×	2	×	7.30E-02	) ÷ (	47	×	25,550	)
Chrysene	6.85E-12	= (	3.91E-04	×	0.01	×	12	×	12	×	2	×	7.30E-03	) ÷ (	47	×	25,550	)
Dibenzo(a,h)anthracene	1.93E-09	= (	1.10E-04	×	0.01	×	12	×	12	×	2	×	7.30E+00	) ÷ (	47	×	25,550	)
Dibenzofuran	NA	= (	3.50E-04	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Fluoranthene	NA	= (	1.20E-03	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Fluorene	NA	= (	1.20E-03	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	2.80E-10	= (	1.60E-04	×	0.01	×	12	×	12	×	2	×	7.30E-01	) ÷ (	47	×	25,550	)
m & p-Cresols	NA	= (	6.20E-03	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Naphthalene	NA	= (	2.60E-02	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
o-Cresol	NA	= (	4.20E-03	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Phenanthrene	NA	= (	2.60E-03	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Phenol	NA	= (	1.20E-03	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Pyrene	NA	= (	2.00E-03	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	5.00E-04	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)

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Table 20
Risk Calculations
Adult Wader: Incidental Ingestion of Surface Water Pathway – Carcinogenic Effects
NSP Ashland

$$\text{Ing-Risk} = \frac{(\text{Cwater} \times \text{WIRwader} \times \text{EF} \times \text{ED} \times \text{ET} \times \text{SFo})}{(\text{BW} \times \text{ATc})}$$

Equation *Units*	Ing - Risk *unitless*	= (	Cwater *mg/L*	×	WIRwader *L/hour*	×	EF *events/year*	×	ED *years*	×	ET *hours/event*	×	SFo kg-day/mg	) ÷ (	BW kg	×	ATc days	)
Benzene	5.80E-09	= (	4.40E-02	×	0.01	×	12	×	12	×	2	×	5.50E-02	) ÷ (	47	×	25,550	)
Ethylbenzene	NA	= (	5.50E-04	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
m & p-Xylenes	NA	= (	3.20E-03	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Toluene	NA	= (	1.90E-02	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Total CR	***1.57E-08***																	

Notes:

Ing-Risk – Carcinogenic Risk Water Ingestion Pathway
Cwater – DNAPL Concentration in Water
WIR – Water Ingestion Rate
EF – Exposure Frequency
ED – Exposure Duration
SFo – Oral Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

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Table 21
Risk Calculations
Adult Wader: Incidental Ingestion of Surface Water Pathway – Noncarcinogenic Effects
NSP Ashland

$$\text{Inh-HQ} = \frac{(\text{Cwater} \times \text{WIRwader} \times \text{EF} \times \text{ED} \times \text{ET})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation Units	Ing - HQ unitless	= (	Cwater mg/L	×	WIRwader L/hour	×	EF days/year	×	ED years	×	ET hours/event	) ÷ (	BW kg	×	ATn days	×	RfDo mg/kg-day	)
Cyanides	1.68E-08	= (	2.40E-05	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	2.00E-02	)
Iron	1.03E-08	= (	2.20E-04	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	3.00E-01	)
2-Methylnaphthalene	4.20E-05	= (	1.20E-02	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	4.00E-03	)
2,4 Dimethylphenol	3.36E-05	= (	4.80E-03	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	2.00E-03	)
Acenaphthylene	NA	= (	3.20E-03	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Anthracene	5.60E-08	= (	1.20E-03	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	4.00E-04	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Benzo(b)fluoranthene	NA	= (	3.60E-04	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Benzo(g,h,i)perylene	NA	= (	1.80E-04	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Benzo(k)fluoranthene	NA	= (	1.10E-04	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Chrysene	NA	= (	3.91E-04	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.10E-04	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Dibenzofuran	2.45E-06	= (	3.50E-04	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	2.00E-03	)
Fluoranthene	4.20E-07	= (	1.20E-03	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	4.00E-02	)
Fluorene	4.20E-07	= (	1.20E-03	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.60E-04	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
m & p-Cresols	NA	= (	6.20E-03	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Naphthalene	1.82E-05	= (	2.60E-02	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	2.00E-02	)
o-Cresol	1.18E-06	= (	4.20E-03	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	5.00E-02	)
Phenanthrene	NA	= (	2.60E-03	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Phenol	5.60E-08	= (	1.20E-03	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	3.00E-01	)
Pyrene	9.33E-07	= (	2.00E-03	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	3.00E-02	)
1,2,4-Trimethylbenzene	1.40E-07	= (	5.00E-04	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	5.00E-02	)

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Table 21
Risk Calculations
Adult Wader: Incidental Ingestion of Surface Water Pathway – Noncarcinogenic Effects
NSP Ashland

$$\text{Inh-HQ} = \frac{(\text{Cwater} \times \text{WIRwader} \times \text{EF} \times \text{ED} \times \text{ET})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation Units	Ing - HQ unitless	= (	Cwater mg/L	×	WIRwader L/hour	×	EF days/year	×	ED years	×	ET hours/event	) ÷ (	BW kg	×	ATn days	×	RfDo mg/kg-day	)
Benzene	1.54E-04	= (	4.40E-02	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	4.00E-03	)
Ethylbenzene	7.69E-08	= (	5.50E-04	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	1.00E-01	)
m & p-Xylenes	NA	= (	3.20E-03	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Toluene	3.32E-06	= (	1.90E-02	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	8.00E-02	)
Total HI	***2.57E-04***																	

Notes:

Ing-HQ – Water Ingestion Pathway Hazard Quotient
Cwater – DNAPL Concentration in Water
WIR – Water Ingestion Rate
EF – Exposure Frequency
ED – Exposure Duration
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 22a
Risk Calculations
Adult Wader: Dermal Contact with Surface Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year)

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SAwading \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	4.80E-08	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Iron	NA	= (	4.40E-07	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
2-Methylnaphthalene	NA	= (	2.01E-03	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
2,4 Dimethylphenol	NA	= (	4.41E-05	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Acenaphthylene	NA	= (	7.42E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Anthracene	NA	= (	4.47E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Benzo(a)pyrene	1.35E-02	= (	2.28E-03	×	1	×	12	×	12	×	6,767	×	7.30E+00	) ÷ (	47	×	25,550	)
Benzo(b)fluoranthene	1.24E-03	= (	2.09E-03	×	1	×	12	×	12	×	6,767	×	7.30E-01	) ÷ (	47	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	2.31E-03	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Benzo(k)fluoranthene	3.72E-05	= (	6.29E-04	×	1	×	12	×	12	×	6,767	×	7.30E-02	) ÷ (	47	×	25,550	)
Chrysene	7.45E-06	= (	1.26E-03	×	1	×	12	×	12	×	6,767	×	7.30E-03	) ÷ (	47	×	25,550	)
Dibenzo(a,h)anthracene	6.20E-03	= (	1.05E-03	×	1	×	12	×	12	×	6,767	×	7.30E+00	) ÷ (	47	×	25,550	)
Dibenzofuran	NA	= (	7.01E-05	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Fluoranthene	NA	= (	1.16E-03	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Fluorene	NA	= (	2.60E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	6.09E-04	= (	1.03E-03	×	1	×	12	×	12	×	6,767	×	7.30E-01	) ÷ (	47	×	25,550	)
m & p-Cresols	NA	= (	4.18E-05	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Naphthalene	NA	= (	2.14E-03	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
o-Cresol	NA	= (	2.83E-05	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Phenanthrene	NA	= (	1.26E-03	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Phenol	NA	= (	2.59E-06	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Pyrene	NA	= (	1.86E-03	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	1.05E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)

Attachment I1

Table 22a
Risk Calculations
Adult Wader: Dermal Contact with Surface Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year)

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SAwading \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Benzene	2.57E-05	= (	5.75E-04	×	1	×	12	×	12	×	6,767	×	5.50E-02	) ÷ (	47	×	25,550	)
Ethylbenzene	NA	= (	3.57E-05	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
m & p-Xylenes	NA	= (	3.05E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Toluene	NA	= (	7.82E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Total CR	***2.16E-02***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (Calculated using DNAPL concentration)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 22b
Risk Calculations
Adult Wader: Dermal Contact with Surface Water (Non-Linear High Dose) – Carcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year))

$$\text{Derm-Risk} = 1\text{-exp}\left(-\frac{(DA_{event} \times EV \times ED \times EF \times SAwading \times SFabs)}{(BW \times ATc)}\right)$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	4.80E-08	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Iron	NA	= (	4.40E-07	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
2-Methylnaphthalene	NA	= (	2.01E-03	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
2,4 Dimethylphenol	NA	= (	4.41E-05	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Acenaphthylene	NA	= (	7.42E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Anthracene	NA	= (	4.47E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Benzo(a)pyrene	1.34E-02	= (	2.28E-03	×	1	×	12	×	12	×	6,767	×	7.30E+00	) ÷ (	47	×	25,550	)
Benzo(b)fluoranthene	1.24E-03	= (	2.09E-03	×	1	×	12	×	12	×	6,767	×	7.30E-01	) ÷ (	47	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	2.31E-03	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Benzo(k)fluoranthene	3.72E-05	= (	6.29E-04	×	1	×	12	×	12	×	6,767	×	7.30E-02	) ÷ (	47	×	25,550	)
Chrysene	7.45E-06	= (	1.26E-03	×	1	×	12	×	12	×	6,767	×	7.30E-03	) ÷ (	47	×	25,550	)
Dibenzo(a,h)anthracene	6.18E-03	= (	1.05E-03	×	1	×	12	×	12	×	6,767	×	7.30E+00	) ÷ (	47	×	25,550	)
Dibenzofuran	NA	= (	7.01E-05	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Fluoranthene	NA	= (	1.16E-03	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Fluorene	NA	= (	2.60E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	6.09E-04	= (	1.03E-03	×	1	×	12	×	12	×	6,767	×	7.30E-01	) ÷ (	47	×	25,550	)
m & p-Cresols	NA	= (	4.18E-05	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Naphthalene	NA	= (	2.14E-03	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
o-Cresol	NA	= (	2.83E-05	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Phenanthrene	NA	= (	1.26E-03	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Phenol	NA	= (	2.59E-06	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Pyrene	NA	= (	1.86E-03	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	1.05E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Benzene	2.57E-05	= (	5.75E-04	×	1	×	12	×	12	×	6,767	×	5.50E-02	) ÷ (	47	×	25,550	)

Attachment I1

Table 22b
Risk Calculations
Adult Wader: Dermal Contact with Surface Water (Non-Linear High Dose) – Carcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year))

$$\text{Derm-Risk} = 1\text{-exp}\left(-\frac{(DA_{event} \times EV \times ED \times EF \times SAwading \times SFabs)}{(BW \times ATc)}\right)$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Ethylbenzene	NA	= (	3.57E-05	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
m & p-Xylenes	NA	= (	3.05E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Toluene	NA	= (	7.82E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Total CR	***2.15E-02***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (Calculated using DNAPL concentration)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 23
Risk Calculations
Adult Wader: Dermal Contact with Surface Water – Noncarcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year)

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SAwading)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
Cyanides	1.14E-05	= (	4.80E-08	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	2.00E-02	)
Iron	NA	= (	4.40E-07	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
2-Methylnaphthalene	2.37E+00	= (	2.01E-03	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	4.00E-03	)
2,4 Dimethylphenol	1.04E-01	= (	4.41E-05	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	2.00E-03	)
Acenaphthylene	NA	= (	7.42E-04	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Anthracene	7.05E-03	= (	4.47E-04	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	2.28E-03	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Benzo(b)fluoranthene	NA	= (	2.09E-03	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Benzo(g,h,i)perylene	NA	= (	2.31E-03	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Benzo(k)fluoranthene	NA	= (	6.29E-04	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Chrysene	NA	= (	1.26E-03	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.05E-03	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Dibenzofuran	1.66E-01	= (	7.01E-05	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	2.00E-03	)
Fluoranthene	1.37E-01	= (	1.16E-03	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	4.00E-02	)
Fluorene	3.08E-02	= (	2.60E-04	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.03E-03	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
m & p-Cresols	NA	= (	4.18E-05	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Naphthalene	5.06E-01	= (	2.14E-03	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	2.00E-02	)
o-Cresol	2.68E-03	= (	2.83E-05	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	5.00E-02	)
Phenanthrene	NA	= (	1.26E-03	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Phenol	4.08E-05	= (	2.59E-06	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	3.00E-01	)
Pyrene	2.94E-01	= (	1.86E-03	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	3.00E-02	)

Attachment I1

Table 23
Risk Calculations
Adult Wader: Dermal Contact with Surface Water – Noncarcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year)

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SAwading)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
1,2,4-Trimethylbenzene	9.98E-03	= (	1.05E-04	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	5.00E-02	)
Benzene	6.80E-01	= (	5.75E-04	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	4.00E-03	)
Ethylbenzene	1.69E-03	= (	3.57E-05	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	1.00E-01	)
m & p-Xylenes	NA	= (	3.05E-04	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Toluene	4.63E-02	= (	7.82E-04	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	8.00E-02	)
Total HI	***4.36E+00***																	

Notes:

Derm-HQ – Dermal Contact with Water Pathway Hazard Quotient
DA_{event} – Absorbed Dose per Event (Calculated using DNAPL concentration)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDabs – Absorbed Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1
Table 24a
Adolescent Wader Risk Summary (Linear Low Dose)
Reasonable Maximum Exposure

	Carcinogenic Risk							Target Organs	Noncarcinogenic Hazard						
Equation	CR	=	Ingestion	+	Dermal	+	Inhalation		HQ	=	Ingestion	+	Dermal	+	Inhalation
Units	unitless		unitless		unitless		unitless		unitless		unitless		unitless		unitless
Cyanides	NA	=	NA	+	NA	+	NA	*Thyroid, Systemic*	1.14E-05	=	1.68E-08	+	1.14E-05	+	NA
Iron	NA	=	NA	+	NA	+	NA		NA	=	1.03E-08	+	NA	+	NA
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA	*Respiratory*	***2.37E+00***	=	4.20E-05	+	2.37E+00	+	NA
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA	*Systemic*	1.04E-01	=	3.36E-05	+	1.04E-01	+	NA
Acenaphthylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Anthracene	NA	=	NA	+	NA	+	NA	*NOAEL*	7.05E-03	=	5.60E-08	+	7.05E-03	+	NA
Benzo(a)pyrene	***1.35E-02***	=	7.00E-09	+	1.35E-02	+	NA		NA	=	NA	+	NA	+	NA
Benzo(b)fluoranthene	***1.24E-03***	=	6.30E-10	+	1.24E-03	+	NA		NA	=	NA	+	NA	+	NA
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Benzo(k)fluoranthene	***3.72E-05***	=	1.93E-11	+	3.72E-05	+	NA		NA	=	NA	+	NA	+	NA
Chrysene	7.45E-06	=	6.85E-12	+	7.45E-06	+	NA		NA	=	NA	+	NA	+	NA
Dibenzo(a,h)anthracene	***6.20E-03***	=	1.93E-09	+	6.20E-03	+	NA		NA	=	NA	+	NA	+	NA
Dibenzofuran	NA	=	NA	+	NA	+	NA	*Systemic*	1.66E-01	=	2.45E-06	+	1.66E-01	+	NA
Fluoranthene	NA	=	NA	+	NA	+	NA	*Systemic, Circulatory*	1.37E-01	=	4.20E-07	+	1.37E-01	+	NA
Fluorene	NA	=	NA	+	NA	+	NA	*Circulatory*	3.08E-02	=	4.20E-07	+	3.08E-02	+	NA
Indeno(1,2,3-cd)pyrene	***6.09E-04***	=	2.80E-10	+	6.09E-04	+	NA		NA	=	NA	+	NA	+	NA
m & p-Cresols	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Naphthalene	NA	=	NA	+	NA	+	NA	*Respiratory, Systemic*	5.06E-01	=	1.82E-05	+	5.06E-01	+	NA
o-Cresol	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	2.68E-03	=	1.18E-06	+	2.68E-03	+	NA
Phenanthrene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Phenol	NA	=	NA	+	NA	+	NA	*Adrenal*	4.09E-05	=	5.60E-08	+	4.08E-05	+	NA
Pyrene	NA	=	NA	+	NA	+	NA	*Systemic*	2.94E-01	=	9.33E-07	+	2.94E-01	+	NA
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	9.98E-03	=	1.40E-07	+	9.98E-03	+	NA
Benzene	***2.57E-05***	=	5.80E-09	+	2.57E-05	+	NA	*Circulatory*	6.81E-01	=	1.54E-04	+	6.80E-01	+	NA
Ethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, Teratology*	1.69E-03	=	7.69E-08	+	1.69E-03	+	NA
m & p-Xylenes	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	NA	=	NA	+	NA	+	NA
Toluene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	4.63E-02	=	3.32E-06	+	4.63E-02	+	NA
Soil CR	***2E-02***	=	2E-08	+	***2E-02***	+	NA	**Soil HI**	***4***	=	2.57E-04	+	***4***	+	NA

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Target Organ HI

Respiratory	3
Circulatory	1
Systemic	1
Adrenal	4.E-05
CNS	6.E-02
Teratology	2.E-03

Attachment I1
Table 24b
Adolescent Wader Risk Summary (Non-linear Low Dose)
Reasonable Maximum Exposure

	Carcinogenic Risk							Target Organs	Noncarcinogenic Hazard						
Equation	CR	=	Ingestion	+	Dermal	+	Inhalation		HQ	=	Ingestion	+	Dermal	+	Inhalation
Units	unitless		unitless		unitless		unitless		unitless		unitless		unitless		unitless
Cyanides	NA	=	NA	+	NA	+	NA	*Thyroid, Systemic*	1.14E-05	=	1.68E-08	+	1.14E-05	+	NA
Iron	NA	=	NA	+	NA	+	NA		NA	=	1.03E-08	+	NA	+	NA
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA	*Respiratory*	***2.37E+00***	=	4.20E-05	+	2.37E+00	+	NA
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA	*Systemic*	1.04E-01	=	3.36E-05	+	1.04E-01	+	NA
Acenaphthylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Anthracene	NA	=	NA	+	NA	+	NA	*NOAEL*	7.05E-03	=	5.60E-08	+	7.05E-03	+	NA
Benzo(a)pyrene	***1.34E-02***	=	7.00E-09	+	1.34E-02	+	NA		NA	=	NA	+	NA	+	NA
Benzo(b)fluoranthene	***1.24E-03***	=	6.30E-10	+	1.24E-03	+	NA		NA	=	NA	+	NA	+	NA
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Benzo(k)fluoranthene	***3.72E-05***	=	1.93E-11	+	3.72E-05	+	NA		NA	=	NA	+	NA	+	NA
Chrysene	7.45E-06	=	6.85E-12	+	7.45E-06	+	NA		NA	=	NA	+	NA	+	NA
Dibenzo(a,h)anthracene	***6.18E-03***	=	1.93E-09	+	6.18E-03	+	NA		NA	=	NA	+	NA	+	NA
Dibenzofuran	NA	=	NA	+	NA	+	NA	*Systemic*	1.66E-01	=	2.45E-06	+	1.66E-01	+	NA
Fluoranthene	NA	=	NA	+	NA	+	NA	*Systemic, Circulatory*	1.37E-01	=	4.20E-07	+	1.37E-01	+	NA
Fluorene	NA	=	NA	+	NA	+	NA	*Circulatory*	3.08E-02	=	4.20E-07	+	3.08E-02	+	NA
Indeno(1,2,3-cd)pyrene	***6.09E-04***	=	2.80E-10	+	6.09E-04	+	NA		NA	=	NA	+	NA	+	NA
m & p-Cresols	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Naphthalene	NA	=	NA	+	NA	+	NA	*Respiratory, Systemic*	5.06E-01	=	1.82E-05	+	5.06E-01	+	NA
o-Cresol	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	2.68E-03	=	1.18E-06	+	2.68E-03	+	NA
Phenanthrene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Phenol	NA	=	NA	+	NA	+	NA	*Adrenal*	4.09E-05	=	5.60E-08	+	4.08E-05	+	NA
Pyrene	NA	=	NA	+	NA	+	NA	*Systemic*	2.94E-01	=	9.33E-07	+	2.94E-01	+	NA
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	9.98E-03	=	1.40E-07	+	9.98E-03	+	NA
Benzene	***2.57E-05***	=	5.80E-09	+	2.57E-05	+	NA	*Circulatory*	6.81E-01	=	1.54E-04	+	6.80E-01	+	NA
Ethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, Teratology*	1.69E-03	=	7.69E-08	+	1.69E-03	+	NA
m & p-Xylenes	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	NA	=	NA	+	NA	+	NA
Toluene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	4.63E-02	=	3.32E-06	+	4.63E-02	+	NA
Soil CR	***2E-02***	=	2E-08	+	***2E-02***	+	NA	**Soil HI**	***4***	=	2.57E-04	+	***4***	+	NA

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Target Organ HI

Respiratory	3
Circulatory	1
Systemic	1
Adrenal	4.E-05
CNS	6.E-02
Teratology	2.E-03

Attachment I1

Table 25
Exposure Parameters – Construction Worker

Exposure Pathway	Parameter	Description	Exposure Parameters			
			CTE	Source	RME	Source
Incidental Soil Ingestion	IR	Soil Ingestion Rate (mg/day)	100	(a)	330	(b)
	EF	Exposure Frequency (days/year)	219	(c)	250	(d)
	ED	Exposure Duration (years)	1	(e)	0.5	(e)
	FI	Fraction Ingested (unitless)	1	(f)	1	(f)
	BW	Body Weight (kg)	70	(g,h,i)	70	(g,h,i)
	ATnc	Averaging Time for Noncarcinogenic Effects (days)	365	(j)	183	(j)
	ATc	Averaging Time for Carcinogenic Effects (days)	25,550	(g,h,i)	25,550	(g,h,i)
Dermal Contact with Soil	SA	Skin Surface Area Exposed (cm^2)	1,930	(k)	3,300	(k)
	SSAF	Soil-to-Skin Adherence Factor (mg/cm^2)	0.1	(l)	0.3	(l)
	CF	Conversion Factor (kg/mg)	1E-06	–	1E-06	–
	EF	Exposure Frequency (days/year)	219	(c)	250	(d)
	ED	Exposure Duration (years)	1	(e)	0.5	(e)
	EV	Event Frequency (events/day)	1	(m)	1	(m)
	BW	Body Weight (kg)	70	(g,h,i)	70	(g,h,i)
	ATnc	Averaging Time for Noncarcinogenic Effects (days)	365	(j)	183	(j)
	ATc	Averaging Time for Carcinogenic Effects (days)	25,550	(g,h,i)	25,550	(g,h,i)
Inhalation of Soil Derived Chemicals or Groundwater VOCs	IR	Inhalation Rate (m^3/hour)	1.3	(n)	2.5	(o)
	ET	Exposure Time (hour/day)	8	(p)	8	(p)
	EF	Exposure Frequency (days/year)	219	(c)	250	(d)
	ED	Exposure Duration (years)	1	(e)	1	(e)
	BW	Body Weight (kg)	70	(g,h,i)	70	(g,h,i)
	PEF	Particulate Emission Factor (m^3/kg)	1.32E+09	See Table 21e	1.32E+09	See Table 21e
	VF	Volatilization Factor (m^3/kg)	Calculated	See Table 21c	Calculated	See Table 21c
	ATnc	Averaging Time for Noncarcinogenic Effects (days)	365	(j)	183	(j)
	ATc	Averaging Time for Carcinogenic Effects (days)	25,550	(g,h,i)	25,550	(g,h,i)

Notes:
CTE - Central Tendency Evaluation
RME - Reasonable Maximum Exposure.

(a) US EPA, 2002. Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites, Exhibit 1-2. Value for outdoor workers.
(b) US EPA, 2002, Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites, Exhibit 1-2. Recommended ingestion rate for construction workers.
(c) In the absence of Site-specific information regarding future construction activities, the default industrial worker exposure frequency was used.
(d) In the absence of Site-specific information regarding future construction activities, the default industrial worker exposure frequency was used.
(e) Construction activities are assumed to occur over a 1 year period.
(f) Based on information provided in the HHRA completed by SEH (SEH, 1998) an FI of 1 was selected as the fraction ingested based on the percentage of chemical detections in subsurface soil.
(g) US EPA, 1991. Human Health Evaluation Manual, Supplemental Guidance, Standard Default Exposure Factors.
(h) US EPA, 1989. RAGS, Volume I, Human Health Evaluation Manual (Part A).
(i) 70 kg body weight and 70 year lifetime are used to be consistent with the development of cancer slope factors.
(j) US EPA, 1989. RAGS, Part A. Averaging Time for noncarcinogens is equal to ED (year) × 365 days/year.
(k) Suggested value represents the total skin surface area for head and hands, assuming that a worker wears long sleeve shirts, long pants and shoes. This value may be adjusted based on the following body part-specific surface area (mean, in cm^2), as provided in Table 6-4 of the Exposure Factors Handbook (US EPA, 1997). The skin surface area of 3,300 cm^2 is recommended by USEPA for industrial workers (Exhibit 3-5, RAGS, Part E, USEPA, 2004).

	Men	Women
Head	1,180	1,100
Hands	840	746
Forearms	1,140	1,360
Lower Legs	2,070	1,940
Feet	1,120	975

(l) USEPA, 2004. RAGS Part E, Exhibit 3-3. Recommended default values for a construction worker.
(m) USEPA, 2004. RAGS Part E, Exhibit 3-5. Recommended RME and CTE parameters for industrial scenario.
(n) US EPA, 1997. Exposure Factors Handbook, Volume 1, Table 5-23. Short-term exposures for outdoor workers, moderate activity.
(o) US EPA, 1997. Exposure Factors Handbook, Volume 1, Table 5-23. Hourly average for short-term exposures for outdoor workers.
(p) US EPA, 1997. Exposure Factors Handbook, Table 15-68. Represents the 50^{th} percentile value for time spent at work (males and females, all ages).
(q) Chemical-specific PEF calculated using methodology. Calculated PEFs for construction workers are presented on Table 21e.

Attachment I1

Table 26
Risk Calculations
Construction Worker: Dermal Contact with Ground Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year)

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SA \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SA	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	1.92E-07	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Iron	NA	= (	1.76E-06	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	4.01E-03	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
2,4 Dimethylphenol	NA	= (	8.82E-05	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	1.48E-03	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Anthracene	NA	= (	8.94E-04	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	4.37E-03	= (	2.60E-03	×	1	×	0.5	×	250	×	3,300	×	7.30E+00	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	4.01E-04	= (	2.38E-03	×	1	×	0.5	×	250	×	3,300	×	7.30E-01	) ÷ (	70	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	2.46E-03	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	1.21E-05	= (	7.16E-04	×	1	×	0.5	×	250	×	3,300	×	7.30E-02	) ÷ (	70	×	25,550	)
Chrysene	2.62E-06	= (	1.55E-03	×	1	×	0.5	×	250	×	3,300	×	7.30E-03	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	1.86E-03	= (	1.10E-03	×	1	×	0.5	×	250	×	3,300	×	7.30E+00	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	1.40E-04	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	2.32E-03	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	5.20E-04	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.86E-04	= (	1.11E-03	×	1	×	0.5	×	250	×	3,300	×	7.30E-01	) ÷ (	70	×	25,550	)
m & p-Cresols	NA	= (	8.36E-05	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	4.27E-03	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
o-Cresol	NA	= (	5.67E-05	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Phenanthrene	NA	= (	2.52E-03	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Phenol	NA	= (	5.18E-06	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	3.72E-03	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	2.11E-04	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)

Attachment I1

Table 26
Risk Calculations
Construction Worker: Dermal Contact with Ground Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year)

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SA \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SA	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Benzene	1.46E-05	= (	1.15E-03	×	1	×	0.5	×	250	×	3,300	×	5.50E-02	) ÷ (	70	×	25,550	)
Ethylbenzene	NA	= (	7.13E-05	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
m & p-Xylenes	NA	= (	6.11E-04	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Toluene	NA	= (	1.56E-03	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Total CR	***6.85E-03***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (Calculated using DNAPL concentration)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 27
Risk Calculations
Construction Worker: Dermal Contact with Ground Water – Noncarcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year)

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SA)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SA	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
Cyanides	3.10E-04	= (	1.92E-07	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	2.00E-02	)
Iron	NA	= (	1.76E-06	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
2-Methylnaphthalene	3.24E+01	= (	4.01E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	4.00E-03	)
2,4 Dimethylphenol	1.42E+00	= (	8.82E-05	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	2.00E-03	)
Acenaphthylene	NA	= (	1.48E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Anthracene	9.62E-02	= (	8.94E-04	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	2.60E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Benzo(b)fluoranthene	NA	= (	2.38E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Benzo(g,h,i)perylene	NA	= (	2.46E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Benzo(k)fluoranthene	NA	= (	7.16E-04	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Chrysene	NA	= (	1.55E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.10E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Dibenzofuran	2.26E+00	= (	1.40E-04	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	2.00E-03	)
Fluoranthene	1.87E+00	= (	2.32E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	4.00E-02	)
Fluorene	4.20E-01	= (	5.20E-04	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.11E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
m & p-Cresols	NA	= (	8.36E-05	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Naphthalene	6.90E+00	= (	4.27E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	2.00E-02	)
o-Cresol	3.66E-02	= (	5.67E-05	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	5.00E-02	)
Phenanthrene	NA	= (	2.52E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Phenol	5.57E-04	= (	5.18E-06	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	3.00E-01	)
Pyrene	4.01E+00	= (	3.72E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	3.00E-02	)

Attachment I1

Table 27
Risk Calculations
Construction Worker: Dermal Contact with Ground Water – Noncarcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year)

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SA)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SA	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
1,2,4-Trimethylbenzene	1.36E-01	= (	2.11E-04	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	5.00E-02	)
Benzene	9.28E+00	= (	1.15E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	4.00E-03	)
Ethylbenzene	2.30E-02	= (	7.13E-05	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	1.00E-01	)
m & p-Xylenes	NA	= (	6.11E-04	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Toluene	6.31E-01	= (	1.56E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	8.00E-02	)
Total HI	***5.95E+01***																	

Notes:

Derm-HQ – Dermal Contact with Water Pathway Hazard Quotient
DA_{event} – Absorbed Dose per Event (Calculated using DNAPL concentration)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDabs – Absorbed Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1
Table 28
Construction Worker Risk Summary
Reasonable Maximum Exposure

	Carcinogenic Risk							Target Organs	Noncarcinogenic Hazard						
Equation	CR	=	Ingestion	+	Dermal	+	Inhalation		HQ	=	Ingestion	+	Dermal	+	Inhalation
Units	unitless		unitless		unitless		unitless		unitless		unitless		unitless		unitless
Cyanides	NA	=	NA	+	NA	+	NA		3.10E-04	=	NA	+	3.10E-04	+	NA
Iron	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA		3.24E+01	=	NA	+	3.24E+01	+	NA
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA		1.42E+00	=	NA	+	1.42E+00	+	NA
Acenaphthylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Anthracene	NA	=	NA	+	NA	+	NA		9.62E-02	=	NA	+	9.62E-02	+	NA
Benzo(a)pyrene	4.37E-03	=	NA	+	4.37E-03	+	NA		NA	=	NA	+	NA	+	NA
Benzo(b)fluoranthene	4.01E-04	=	NA	+	4.01E-04	+	NA		NA	=	NA	+	NA	+	NA
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Benzo(k)fluoranthene	1.21E-05	=	NA	+	1.21E-05	+	NA		NA	=	NA	+	NA	+	NA
Chrysene	2.62E-06	=	NA	+	2.62E-06	+	NA		NA	=	NA	+	NA	+	NA
Dibenzo(a,h)anthracene	1.86E-03	=	NA	+	1.86E-03	+	NA		NA	=	NA	+	NA	+	NA
Dibenzofuran	NA	=	NA	+	NA	+	NA		2.26E+00	=	NA	+	2.26E+00	+	NA
Fluoranthene	NA	=	NA	+	NA	+	NA		1.87E+00	=	NA	+	1.87E+00	+	NA
Fluorene	NA	=	NA	+	NA	+	NA		4.20E-01	=	NA	+	4.20E-01	+	NA
Indeno(1,2,3-cd)pyrene	1.86E-04	=	NA	+	1.86E-04	+	NA		NA	=	NA	+	NA	+	NA
m & p-Cresols	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Naphthalene	NA	=	NA	+	NA	+	NA		6.90E+00	=	NA	+	6.90E+00	+	NA
o-Cresol	NA	=	NA	+	NA	+	NA		3.66E-02	=	NA	+	3.66E-02	+	NA
Phenanthrene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Phenol	NA	=	NA	+	NA	+	NA		5.57E-04	=	NA	+	5.57E-04	+	NA
Pyrene	NA	=	NA	+	NA	+	NA		4.01E+00	=	NA	+	4.01E+00	+	NA
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA		1.36E-01	=	NA	+	1.36E-01	+	NA
Benzene	1.46E-05	=	NA	+	1.46E-05	+	NA		9.28E+00	=	NA	+	9.28E+00	+	NA
Ethylbenzene	NA	=	NA	+	NA	+	NA		2.30E-02	=	NA	+	2.30E-02	+	NA
m & p-Xylenes	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Toluene	NA	=	NA	+	NA	+	NA		6.31E-01	=	NA	+	6.31E-01	+	NA
Soil CR	***7E-03***	=	NA	+	***7E-03***	+	NA	**Soil HI**	***59***	=	NA	+	***59***	+	NA

Notes:

NA -- Not Applicable
CR -- Cancer Risk
HQ -- Hazard Quotient
HI -- Hazard Index
CNS -- Central Nervous System

Attachment I1

Table 29
Risk Calculations
Construction Worker: Dermal Contact with Ground Water (Linear-Low Dose) – Carcinogenic Effects
NSP Ashland
(Exposure Frequency = 1 Day/Year))

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SA \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SA	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	1.92E-07	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Iron	NA	= (	1.76E-06	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	4.01E-03	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
2,4 Dimethylphenol	NA	= (	8.82E-05	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	1.48E-03	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Anthracene	NA	= (	8.94E-04	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	1.75E-05	= (	2.60E-03	×	1	×	0.5	×	1	×	3,300	×	7.30E+00	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	1.60E-06	= (	2.38E-03	×	1	×	0.5	×	1	×	3,300	×	7.30E-01	) ÷ (	70	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	2.46E-03	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	4.82E-08	= (	7.16E-04	×	1	×	0.5	×	1	×	3,300	×	7.30E-02	) ÷ (	70	×	25,550	)
Chrysene	1.05E-08	= (	1.55E-03	×	1	×	0.5	×	1	×	3,300	×	7.30E-03	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	7.43E-06	= (	1.10E-03	×	1	×	0.5	×	1	×	3,300	×	7.30E+00	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	1.40E-04	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	2.32E-03	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	5.20E-04	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	7.45E-07	= (	1.11E-03	×	1	×	0.5	×	1	×	3,300	×	7.30E-01	) ÷ (	70	×	25,550	)
m & p-Cresols	NA	= (	8.36E-05	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	4.27E-03	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
o-Cresol	NA	= (	5.67E-05	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Phenanthrene	NA	= (	2.52E-03	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Phenol	NA	= (	5.18E-06	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	3.72E-03	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	2.11E-04	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Benzene	5.83E-08	= (	1.15E-03	×	1	×	0.5	×	1	×	3,300	×	5.50E-02	) ÷ (	70	×	25,550	)
Ethylbenzene	NA	= (	7.13E-05	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)

Attachment I1

Table 29
Risk Calculations
Construction Worker: Dermal Contact with Ground Water (Linear-Low Dose) – Carcinogenic Effects
NSP Ashland
(Exposure Frequency = 1 Day/Year))

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SA \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SA	×	SFabs	) ÷ (	BW	×	ATc	)
Units	**unitless**		**mg/cm²-event**		**events/day**		**years**		**days/year**		**cm²**		**kg-day/mg**		**kg**		**days**	
m & p-Xylenes	NA	= (	6.11E-04	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Toluene	NA	= (	1.56E-03	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Total CR	***2.74E-05***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (Calculated using DNAPL concentration)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1

Table 30
Risk Calculations
Construction Worker: Dermal Contact with Ground Water – Noncarcinogenic Effects
NSP Ashland
(Exposure Frequency = 1 Day/Year)

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SA)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SA	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
Cyanides	1.24E-06	= (	1.92E-07	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	2.00E-02	)
Iron	NA	= (	1.76E-06	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
2-Methylnaphthalene	1.30E-01	= (	4.01E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	4.00E-03	)
2,4 Dimethylphenol	5.69E-03	= (	8.82E-05	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	2.00E-03	)
Acenaphthylene	NA	= (	1.48E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Anthracene	3.85E-04	= (	8.94E-04	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	2.60E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Benzo(b)fluoranthene	NA	= (	2.38E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Benzo(g,h,i)perylene	NA	= (	2.46E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Benzo(k)fluoranthene	NA	= (	7.16E-04	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Chrysene	NA	= (	1.55E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	1.10E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Dibenzofuran	9.06E-03	= (	1.40E-04	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	2.00E-03	)
Fluoranthene	7.49E-03	= (	2.32E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	4.00E-02	)
Fluorene	1.68E-03	= (	5.20E-04	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.11E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
m & p-Cresols	NA	= (	8.36E-05	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Naphthalene	2.76E-02	= (	4.27E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	2.00E-02	)
o-Cresol	1.46E-04	= (	5.67E-05	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	5.00E-02	)
Phenanthrene	NA	= (	2.52E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Phenol	2.23E-06	= (	5.18E-06	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	3.00E-01	)
Pyrene	1.60E-02	= (	3.72E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	3.00E-02	)

Attachment I1

Table 30
Risk Calculations
***Construction Worker:* Dermal Contact with Ground Water – Noncarcinogenic Effects**
NSP Ashland
(Exposure Frequency = 1 Day/Year)

$$\textbf{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SA)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SA	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
1,2,4-Trimethylbenzene	5.45E-04	= (	2.11E-04	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	5.00E-02	)
Benzene	3.71E-02	= (	1.15E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	4.00E-03	)
Ethylbenzene	9.21E-05	= (	7.13E-05	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	1.00E-01	)
m & p-Xylenes	NA	= (	6.11E-04	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Toluene	2.52E-03	= (	1.56E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	8.00E-02	)
Total HI	***2.38E-01***																	

Notes:

Derm-HQ – Dermal Contact with Water Pathway Hazard Quotient
DA_{event} – Absorbed Dose per Event (Calculated using DNAPL concentration)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDabs – Absorbed Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I1
Table 31
Construction Worker Risk Summary
Reasonable Maximum Exposure

	Carcinogenic Risk							Target Organs	Noncarcinogenic Hazard						
Equation	CR	=	Ingestion	+	Dermal	+	Inhalation		HQ	=	Ingestion	+	Dermal	+	Inhalation
Units	unitless		unitless		unitless		unitless		unitless		unitless		unitless		unitless
Cyanides	NA	=	NA	+	NA	+	NA	*Thyroid, Systemic*	1.24E-06	=	NA	+	1.24E-06	+	NA
Iron	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA	*Respiratory*	1.30E-01	=	NA	+	1.30E-01	+	NA
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA	*Systemic*	5.69E-03	=	NA	+	5.69E-03	+	NA
Acenaphthylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Anthracene	NA	=	NA	+	NA	+	NA	*NOAEL*	3.85E-04	=	NA	+	3.85E-04	+	NA
Benzo(a)pyrene	***1.75E-05***	=	NA	+	1.75E-05	+	NA		NA	=	NA	+	NA	+	NA
Benzo(b)fluoranthene	1.60E-06	=	NA	+	1.60E-06	+	NA		NA	=	NA	+	NA	+	NA
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Benzo(k)fluoranthene	4.82E-08	=	NA	+	4.82E-08	+	NA		NA	=	NA	+	NA	+	NA
Chrysene	1.05E-08	=	NA	+	1.05E-08	+	NA		NA	=	NA	+	NA	+	NA
Dibenzo(a,h)anthracene	7.43E-06	=	NA	+	7.43E-06	+	NA		NA	=	NA	+	NA	+	NA
Dibenzofuran	NA	=	NA	+	NA	+	NA	*Systemic*	9.06E-03	=	NA	+	9.06E-03	+	NA
Fluoranthene	NA	=	NA	+	NA	+	NA	*Systemic, Circulatory*	7.49E-03	=	NA	+	7.49E-03	+	NA
Fluorene	NA	=	NA	+	NA	+	NA	*Circulatory*	1.68E-03	=	NA	+	1.68E-03	+	NA
Indeno(1,2,3-cd)pyrene	7.45E-07	=	NA	+	7.45E-07	+	NA		NA	=	NA	+	NA	+	NA
m & p-Cresols	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Naphthalene	NA	=	NA	+	NA	+	NA	*Respiratory, Systemic*	2.76E-02	=	NA	+	2.76E-02	+	NA
o-Cresol	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	1.46E-04	=	NA	+	1.46E-04	+	NA
Phenanthrene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Phenol	NA	=	NA	+	NA	+	NA	*Adrenal*	2.23E-06	=	NA	+	2.23E-06	+	NA
Pyrene	NA	=	NA	+	NA	+	NA	*Systemic*	1.60E-02	=	NA	+	1.60E-02	+	NA
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	5.45E-04	=	NA	+	5.45E-04	+	NA
Benzene	5.83E-08	=	NA	+	5.83E-08	+	NA	*Circulatory*	3.71E-02	=	NA	+	3.71E-02	+	NA
Ethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, Teratology*	9.21E-05	=	NA	+	9.21E-05	+	NA
m & p-Xylenes	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	NA	=	NA	+	NA	+	NA
Toluene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	2.52E-03	=	NA	+	2.52E-03	+	NA
Soil CR	**3E-05**	=	NA	+	3E-05	+	NA	**Soil HI**	***0.24***	=	NA	+	0.24	+	NA

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Attachment I1
Table 32
DNAPL Laboratory Data
NSP Ashland

PARAMETER	Units	Result	conversion factor	Final Result	Solubility in Water	Units
Flashpoint	degrees F	100				
pH	-	7.2				
Alkalinity, bircarb, as HCO3	mg/L	570	1.00E-03	0.57	NA	mg/cm^3
Alkalinity, total as CaCO3 (unfiltered)	mg/L	470	1.00E-03	0.47	NA	mg/cm^3
Alkalinity, carbonate CaCO3	mg/L	ND (<2.3)	1.00E-03		NA	mg/cm^3
Calcium, total as Ca	mg/L	100	1.00E-03	0.10	NA	mg/cm^3
Cyanide, total	mg/L	0.024	1.00E-03	2.40E-05	NA	mg/cm^3
Hardness, total as CaCO3 (calc/unfilt)	mg/L	490	1.00E-03	0.49	NA	mg/cm^3
Iron, total	mg/L	0.22	1.00E-03	2.20E-04	NA	mg/cm^3
Magnesium, total as Mg	mg/L	45	1.00E-03	0.05	NA	mg/cm^3
Nitrate	mg/L	0.15	1.00E-03	1.50E-04	NA	mg/cm^3
Solids, total dissolved (TDS)	mg/L	680	1.00E-03	0.68	NA	mg/cm^3
Solids, total suspended (TSS)	mg/L	16	1.00E-03	0.02	NA	mg/cm^3
Sulfate	mg/L	93	1.00E-03	0.09	NA	mg/cm^3
Total Organic Carbon (TOC)	mg/L	250	1.00E-03	0.25	NA	mg/cm^3
VOCs						
Methylene Chloride	ug/L	650	1.00E-06	6.50E-04	1.30E+01	mg/cm^3
Benzene	ug/L	44000	1.00E-06	4.40E-02	1.75E+00	mg/cm^3
Toulene	ug/L	19000	1.00E-06	1.90E-02	5.26E-01	mg/cm^3
Ethylbenzene	ug/L	550	1.00E-06	5.50E-04	1.69E-01	mg/cm^3
m,p-Xylene	ug/L	3200	1.00E-06	3.20E-03	1.85E-01	mg/cm^3
1,2,4-Trimethylbenzene	ug/L	500	1.00E-06	5.00E-04	5.70E-02	mg/cm^3
Naphthalene	ug/L	8000	1.00E-06	8.00E-03	3.10E-02	mg/cm^3
SVOCs						
Acenaphthylene	ug/L	3200	1.00E-06	3.20E-03	4.24E-03	mg/cm3
Antracene	ug/L	1200	1.00E-06	1.20E-03	4.34E-05	mg/cm3
Benzo(a)pyrene	ug/L	400	1.00E-06	4.00E-04	1.62E-06	mg/cm3
Benzo(b)fluoranthene	ug/L	360	1.00E-06	3.60E-04	1.50E-06	mg/cm3
Benzo(g,h,i)perylene	ug/L	180	1.00E-06	1.80E-04	2.60E-07	mg/cm3
Benzo(k)fluoranthene	ug/L	110	1.00E-06	1.10E-04	8.00E-07	mg/cm3
Chrysene	ug/L	391	1.00E-06	3.91E-04	1.60E-06	mg/cm3
Dibenz(a,h)anthracene	ug/L	110	1.00E-06	1.10E-04	2.49E-06	mg/cm3
Dibenzofuran	ug/L	350	1.00E-06	3.50E-04	3.10E-03	mg/cm3
2,4-Dimethylphenol	ug/L	4800	1.00E-06	4.80E-03	7.87E+00	mg/cm3
Fluoranthene	ug/L	1200	1.00E-06	1.20E-03	2.06E-04	mg/cm3
Fluorene	ug/L	1200	1.00E-06	1.20E-03	1.98E-03	mg/cm3
Indeno(1,2,3-cd)pyrene	ug/L	160	1.00E-06	1.60E-04	2.20E-08	mg/cm3
2-Methylnaphthalene	ug/L	12000	1.00E-06	1.20E-02	2.46E-02	mg/cm3
2-Methylphenol	ug/L	4200	1.00E-06	4.20E-03	2.60E+01	mg/cm3
3 & 4-Methylphenol	ug/L	6200	1.00E-06	6.20E-03	2.27E+01	mg/cm3
Naphthalene	ug/L	26000	1.00E-06	2.60E-02	3.10E-02	mg/cm3
Phenanthrene	ug/L	2600	1.00E-06	2.60E-03	1.15E-03	mg/cm3
Phenol	ug/L	1200	1.00E-06	1.20E-03	8.28E+01	mg/cm3
Pyrene	ug/L	2000	1.00E-06	2.00E-03	1.35E-04	mg/cm3

Attachment I2

Calculation of Site Oily Materials in Groundwater & Oil Slicks in Surface Water using Chemical-Specific Solubility Values

Attachment I2
Table 1
Exposure Parameters – Adult Swimmer and Wader

Exposure Pathway	Parameter	Description	Exposure Parameters			
			CTE	Source	RME	Source
Incidental Surface Water Ingestion	$WIR_{swimming}$	Surface Water Ingestion Rate (L/hour)	0.01	(a)	0.05	(b)
	WIR_{wading}	Surface Water Ingestion Rate (L/hour)	0.01	(a)	0.01	(a)
	EF	Exposure Frequency (events/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	9	(e)	30	(e)
	ET	Exposure Time (hours/event)	1 (swimming) 2 (wading)	(f)	1 (swimming) 2 (wading)	(f)
	BW	Body Weight (kg)	70	(g)	70	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	3,285	(l)	10,950	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Dermal Contact with Surface Water	$SA_{swimming}$	Skin Surface Area Exposed (cm^2)	18,000	(k)	18,000	(k)
	SA_{wading}	Skin Surface Area Exposed (cm^2)	9,000	(k)	9,000	(k)
	EF	Exposure Frequency (days/yr)	6	(c)	12	(d)
	ED	Exposure Duration (years)	9	(e)	30	(e)
	EV	Event Frequency (events/day)	1		1	
	ET	Exposure Time (hours/event)	1 (swimming) 2 (wading)	(f)	1 (swimming) 2 (wading)	(f)
	BW	Body Weight (kg)	70	(g)	70	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	3,285	(l)	10,950	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Incidental Sediment Ingestion	SIR	Sediment Ingestion Rate (mg/day)	(m)		(m)	
	CF	Conversion Factor (kg/mg)	1E-06	--	1E-06	--
	EF	Exposure Frequency (days/yr)	6	(c)	12	(d)
	ED	Exposure Duration (years)	9	(e)	30	(e)
	FI	Fraction Ingested from Contaminated Source (unitless)	1		1	
	BW	Body Weight (kg)	70	(g)	70	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	3,285	(l)	10,950	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Dermal Contact with Sediment	SA	Skin Surface Area Exposed (cm^2)	4,499	(n)	5,672	(n)
	SSAF	Soil-to-Skin Adherence Factor (mg/cm^2)	0.5	(o)	1	(o)
	CF	Conversion Factor (kg/mg)	1E-06	--	1E-06	--
	EF	Exposure Frequency (days/yr)	6	(c)	12	(d)
	ED	Exposure Duration (years)	9	(e)	30	(e)
	EV	Event Frequency (events/day)	1		1	
	BW	Body Weight (kg)	70	(g)	70	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	3,285	(l)	10,950	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)

Notes:
CTE - Central Tendency Evaluation
RME - Reasonable Maximum Exposure.

(a) US EPA, 1989. Risk Assessment Guidance for Superfund, Volume I (RAGS, Part A). Value is one-fifth of that assumed to occur during a swimming event.
(b) US EPA, 1989. RAGS Part A. Value for a swimming event.
(c) One event per month for the 6 warmest months of the year.
(d) Two events per month for the 6 warmest months of the year.
(e) The default values for a residential adult, assuming the individual resides in the same residence for 9 (average) or 30 years (upperbound).
(f) US EPA, 1997. Exposure Factors Handbook, Table 1-2. Recommended values for exposure frequency of 1event per month and exposure time of 1 hours per event for swimming. The exposure time of 2 hours per event for wading is based on the estimated time spent on outdoor activities.
(g) US EPA, 1997. Exposure Factors Handbook. Body weight is the average of adult males and females
(h) 70 year lifetime is used to be consistent with the development of cancer slope factors.
(i) US EPA, 1991. Standard Default Exposure Factors. Value for adult.
(j) US EPA, 1989. RAGS, Part A.
(k) Value represents recommended skin surface area (100% for swimmers and 50% for waders).
(l) US EPA, 1989. RAGS, Part A. Averaging Time for noncarcinogens is equal to ED (year) × 365 days/year.
(m) Calculated using the equation: Sediment Ingestion Rate (mg/day) = Surface water ingestion rate (ml/day) × total solids (mg/ml).
(n) The RME skin surface area represents the sum of the surface area for forearms, hands, lower legs and feet. The CTE skin surface area represents the sum of the skin surface area for hands, lower legs and feet.
(o) US EPA, 1997. Exposure Factors Handbook, (Table ??). Using loadings for the hands, arms, and legs for the irrigation worker, a weighted soil-to-skin adherence factor of 2.0 mg/cm^2 was calculated. One-half this value (1.0 mg/cm^2) used as RME assuming some washoff; 0.5 mg/cm^2 used for CTE.

Attachment I2

Table 2
Risk Calculations
Adult Swimmer: Incidental Ingestion of Surface Water Pathway – Carcinogenic Effects
NSP Ashland

$$\text{Ing-Risk} = \frac{(\text{Cwater} \times \text{WIRswimming} \times \text{EF} \times \text{ED} \times \text{ET} \times \text{SFo})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	= (	Cwater	×	WIRswimming	×	EF	×	ED	×	ET	×	SFo	) ÷ (	BW	×	ATc	)
Units	unitless		mg/L		L/hour		events/year		years		hours/event		kg-day/mg		kg		days	
Cyanides	NA	= (	2.40E-05	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Iron	NA	= (	2.20E-04	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	2.46E-02	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
2,4 Dimethylphenol	NA	= (	7.87E+00	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	4.24E-03	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Anthracene	NA	= (	4.34E-05	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	1.19E-10	= (	1.62E-06	×	0.05	×	12	×	30	×	1	×	7.30E+00	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	1.10E-11	= (	1.50E-06	×	0.05	×	12	×	30	×	1	×	7.30E-01	) ÷ (	70	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	2.60E-07	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	5.88E-13	= (	8.00E-07	×	0.05	×	12	×	30	×	1	×	7.30E-02	) ÷ (	70	×	25,550	)
Chrysene	1.18E-13	= (	1.60E-06	×	0.05	×	12	×	30	×	1	×	7.30E-03	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	1.83E-10	= (	2.49E-06	×	0.05	×	12	×	30	×	1	×	7.30E+00	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	3.10E-03	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	2.06E-04	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	1.98E-03	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.62E-13	= (	2.20E-08	×	0.05	×	12	×	30	×	1	×	7.30E-01	) ÷ (	70	×	25,550	)
m & p-Cresols	NA	= (	2.27E+01	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	3.10E-02	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
o-Cresol	NA	= (	2.60E+01	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Phenanthrene	NA	= (	1.15E-03	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Phenol	NA	= (	8.28E+01	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	1.35E-04	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	5.70E-02	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)

Attachment I2

Table 2
Risk Calculations
Adult Swimmer: Incidental Ingestion of Surface Water Pathway – Carcinogenic Effects
NSP Ashland

$$\text{Ing-Risk} = \frac{(\text{Cwater} \times \text{WIRswimming} \times \text{EF} \times \text{ED} \times \text{ET} \times \text{SFo})}{(\text{BW} \times \text{ATc})}$$

Equation		Ing - Risk	= (	Cwater	×	WIRswimming	×	EF	×	ED	×	ET	×	SFo	) ÷ (	BW	×	ATc	)
Units		*unitless*		*mg/L*		*L/hour*		*events/year*		*years*		*hours/event*		*kg-day/mg*		*kg*		*days*	
Benzene		9.69E-07	= (	1.75E+00	×	0.05	×	12	×	30	×	1	×	5.50E-02	) ÷ (	70	×	25,550	)
Ethylbenzene		NA	= (	1.69E-01	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
m & p-Xylenes		NA	= (	1.85E-01	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
Toluene		NA	= (	5.26E-01	×	0.05	×	12	×	30	×	1	×	NV	) ÷ (	70	×	25,550	)
	Total CR	***9.69E-07***																	

Notes:

Ing-Risk – Carcinogenic Risk Water Ingestion Pathway
Cwater – Concentration in Water (Based on chemical-specific solubility)
WIR – Water Ingestion Rate
EF – Exposure Frequency
ED – Exposure Duration
SFo – Oral Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 3
Risk Calculations
Adult Swimmer: Incidental Ingestion of Surface Water Pathway – Noncarcinogenic Effects
NSP Ashland

$$\text{Inh-HQ} = \frac{(\text{Cwater} \times \text{WIRswimming} \times \text{EF} \times \text{ED} \times \text{ET})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation	Ing - HQ	= (	Cwater	×	WIRswimming	×	EF	×	ED	×	ET	) ÷ (	BW	×	ATn	×	RfDo	)
Units	unitless		mg/L		L/hour		days/year		years		hours/event		kg		days		mg/kg-day	
Cyanides	2.82E-08	= (	2.40E-05	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	2.00E-02	)
Iron	1.72E-08	= (	2.20E-04	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	3.00E-01	)
2-Methylnaphthalene	1.44E-04	= (	2.46E-02	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	4.00E-03	)
2,4 Dimethylphenol	9.24E-02	= (	7.87E+00	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	2.00E-03	)
Acenaphthylene	NA	= (	4.24E-03	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Anthracene	3.40E-09	= (	4.34E-05	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	1.62E-06	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.50E-06	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Benzo(g,h,i)perylene	NA	= (	2.60E-07	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Benzo(k)fluoranthene	NA	= (	8.00E-07	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Chrysene	NA	= (	1.60E-06	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.49E-06	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Dibenzofuran	3.64E-05	= (	3.10E-03	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	2.00E-03	)
Fluoranthene	1.21E-07	= (	2.06E-04	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	4.00E-02	)
Fluorene	1.16E-06	= (	1.98E-03	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	2.20E-08	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
m & p-Cresols	NA	= (	2.27E+01	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Naphthalene	3.64E-05	= (	3.10E-02	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	2.00E-02	)
o-Cresol	1.22E-02	= (	2.60E+01	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	5.00E-02	)
Phenanthrene	NA	= (	1.15E-03	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Phenol	6.48E-03	= (	8.28E+01	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	3.00E-01	)
Pyrene	1.06E-07	= (	1.35E-04	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	3.00E-02	)
1,2,4-Trimethylbenzene	2.68E-05	= (	5.70E-02	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	5.00E-02	)

Attachment I2

Table 3
Risk Calculations
Adult Swimmer: Incidental Ingestion of Surface Water Pathway – Noncarcinogenic Effects
NSP Ashland

$$\text{Inh-HQ} = \frac{(\text{Cwater} \times \text{WIRswimming} \times \text{EF} \times \text{ED} \times \text{ET})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation Units		Ing - HQ unitless	= (	Cwater mg/L	×	WIRswimming L/hour	×	EF days/year	×	ED years	×	ET hours/event	) ÷ (	BW kg	×	ATn days	×	RfDo mg/kg-day	)
Benzene		1.03E-02	= (	1.75E+00	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	4.00E-03	)
Ethylbenzene		3.97E-05	= (	1.69E-01	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	1.00E-01	)
m & p-Xylenes		NA	= (	1.85E-01	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	NV	)
Toluene		1.54E-04	= (	5.26E-01	×	0.05	×	12	×	30	×	1	) ÷ (	70	×	10,950	×	8.00E-02	)
	Total HI	***1.22E-01***																	

Notes:

Ing-HQ – Water Ingestion Pathway Hazard Quotient
Cwater – Concentration in Water (Based on chemical-specific solubility)
WIR – Water Ingestion Rate
EF – Exposure Frequency
ED – Exposure Duration
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 4a
Risk Calculations
Adult Swimmer: Dermal Contact with Surface Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SAswimming \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	2.40E-08	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Iron	NA	= (	2.20E-07	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	2.91E-03	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
2,4 Dimethylphenol	NA	= (	5.11E-02	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	6.96E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Anthracene	NA	= (	1.14E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	2.38E-04	= (	9.01E-06	×	1	×	30	×	12	×	18,000	×	7.30E+00	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	2.25E-05	= (	8.52E-06	×	1	×	30	×	12	×	18,000	×	7.30E-01	) ÷ (	70	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	3.30E-06	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	1.18E-06	= (	4.47E-06	×	1	×	30	×	12	×	18,000	×	7.30E-02	) ÷ (	70	×	25,550	)
Chrysene	1.31E-07	= (	4.94E-06	×	1	×	30	×	12	×	18,000	×	7.30E-03	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	6.21E-04	= (	2.35E-05	×	1	×	30	×	12	×	18,000	×	7.30E+00	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	4.39E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	1.41E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	3.03E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	3.69E-07	= (	1.40E-07	×	1	×	30	×	12	×	18,000	×	7.30E-01	) ÷ (	70	×	25,550	)
m & p-Cresols	NA	= (	2.96E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	1.80E-03	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
o-Cresol	NA	= (	2.00E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Phenanthrene	NA	= (	3.94E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Phenol	NA	= (	1.26E-01	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	8.88E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	8.50E-03	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)

Attachment I2

Table 4a
Risk Calculations
Adult Swimmer: Dermal Contact with Surface Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SAswimming \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Benzene	3.22E-03	= (	1.62E-02	×	1	×	30	×	12	×	18,000	×	5.50E-02	) ÷ (	70	×	25,550	)
Ethylbenzene	NA	= (	7.75E-03	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
m & p-Xylenes	NA	= (	1.25E-02	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Toluene	NA	= (	1.53E-02	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Total CR	***4.11E-03***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (calculated using chemical-specific solubility)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 4b
Risk Calculations
Adult Swimmer: Dermal Contact with Surface Water (Non-Linear High Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = 1\text{-exp}\left(-\frac{(DA_{event} \times EV \times ED \times EF \times SAswimming \times SFabs)}{(BW \times ATc)} \right)$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	2.40E-08	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Iron	NA	= (	2.20E-07	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	2.91E-03	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
2,4 Dimethylphenol	NA	= (	5.11E-02	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	6.96E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Anthracene	NA	= (	1.14E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	2.38E-04	= (	9.01E-06	×	1	×	30	×	12	×	18,000	×	7.30E+00	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	2.25E-05	= (	8.52E-06	×	1	×	30	×	12	×	18,000	×	7.30E-01	) ÷ (	70	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	3.30E-06	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	1.18E-06	= (	4.47E-06	×	1	×	30	×	12	×	18,000	×	7.30E-02	) ÷ (	70	×	25,550	)
Chrysene	1.31E-07	= (	4.94E-06	×	1	×	30	×	12	×	18,000	×	7.30E-03	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	6.21E-04	= (	2.35E-05	×	1	×	30	×	12	×	18,000	×	7.30E+00	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	4.39E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	1.41E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	3.03E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	3.69E-07	= (	1.40E-07	×	1	×	30	×	12	×	18,000	×	7.30E-01	) ÷ (	70	×	25,550	)
m & p-Cresols	NA	= (	2.96E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	1.80E-03	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
o-Cresol	NA	= (	2.00E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Phenanthrene	NA	= (	3.94E-04	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Phenol	NA	= (	1.26E-01	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	8.88E-05	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	8.50E-03	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Benzene	3.22E-03	= (	1.62E-02	×	1	×	30	×	12	×	18,000	×	5.50E-02	) ÷ (	70	×	25,550	)

Attachment I2

Table 4b
Risk Calculations
Adult Swimmer: Dermal Contact with Surface Water (Non-Linear High Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = 1\text{-exp}\left(-\frac{(DA_{event} \times EV \times ED \times EF \times SAswimming \times SFabs)}{(BW \times ATc)} \right)$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Ethylbenzene	NA	= (	7.75E-03	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
m & p-Xylenes	NA	= (	1.25E-02	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Toluene	NA	= (	1.53E-02	×	1	×	30	×	12	×	18,000	×	NV	) ÷ (	70	×	25,550	)
Total CR	***4.10E-03***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (calculated using chemical-specific solubility)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 5
Risk Calculations
Adult Swimmer: Dermal Contact with Surface Water – Noncarcinogenic Effects
NSP Ashland

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SAswimming)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
Cyanides	1.01E-05	= (	2.40E-08	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	2.00E-02	)
Iron	NA	= (	2.20E-07	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
2-Methylnaphthalene	6.14E+00	= (	2.91E-03	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	4.00E-03	)
2,4 Dimethylphenol	2.16E+02	= (	5.11E-02	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	2.00E-03	)
Acenaphthylene	NA	= (	6.96E-04	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Anthracene	3.22E-04	= (	1.14E-05	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	9.01E-06	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Benzo(b)fluoranthene	NA	= (	8.52E-06	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Benzo(g,h,i)perylene	NA	= (	3.30E-06	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Benzo(k)fluoranthene	NA	= (	4.47E-06	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Chrysene	NA	= (	4.94E-06	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.35E-05	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Dibenzofuran	1.86E+00	= (	4.39E-04	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	2.00E-03	)
Fluoranthene	2.98E-02	= (	1.41E-04	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	4.00E-02	)
Fluorene	6.41E-02	= (	3.03E-04	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.40E-07	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
m & p-Cresols	NA	= (	2.96E-05	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Naphthalene	7.61E-01	= (	1.80E-03	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	2.00E-02	)
o-Cresol	3.39E-03	= (	2.00E-05	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	5.00E-02	)
Phenanthrene	NA	= (	3.94E-04	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Phenol	3.56E+00	= (	1.26E-01	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	3.00E-01	)
Pyrene	2.50E-02	= (	8.88E-05	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	3.00E-02	)

Attachment I2

Table 5
Risk Calculations
Adult Swimmer: Dermal Contact with Surface Water – Noncarcinogenic Effects
NSP Ashland

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SAswimming)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
1,2,4-Trimethylbenzene	1.44E+00	= (	8.50E-03	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	5.00E-02	)
Benzene	3.42E+01	= (	1.62E-02	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	4.00E-03	)
Ethylbenzene	6.55E-01	= (	7.75E-03	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	1.00E-01	)
m & p-Xylenes	NA	= (	1.25E-02	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	NV	)
Toluene	1.62E+00	= (	1.53E-02	×	1	×	30	×	12	×	18,000	) ÷ (	70	×	10,950	×	8.00E-02	)
Total HI	***2.66E+02***																	

Notes:

Derm-HQ – Dermal Contact with Water Pathway Hazard Quotient
DA_{event} – Absorbed Dose per Event (calculated using chemical-specific solubility)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDabs – Absorbed Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2
Table 6a
Adult Swimmer Risk Summary (Linear Low Dose)
Reasonable Maximum Exposure

	Carcinogenic Risk								Target Organs	Noncarcinogenic Hazard							
Equation	CR	=	Ingestion	+	Dermal	+	Inhalation			HQ	=	Ingestion	+	Dermal	+	Inhalation	
Units	unitless		unitless		unitless		unitless			unitless		unitless		unitless		unitless	
Cyanides	NA	=	NA	+	NA	+	NA		*Thyroid, Systemic*	1.02E-05	=	2.82E-08	+	1.01E-05	+	NA	
Iron	NA	=	NA	+	NA	+	NA			NA	=	1.72E-08	+	NA	+	NA	
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA		*Respiratory*	6.14E+00	=	1.44E-04	+	6.14E+00	+	NA	
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA		*Systemic*	2.16E+02	=	9.24E-02	+	2.16E+02	+	NA	
Acenaphthylene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Anthracene	NA	=	NA	+	NA	+	NA		*NOAEL*	3.22E-04	=	3.40E-09	+	3.22E-04	+	NA	
Benzo(a)pyrene	2.38E-04	=	1.19E-10	+	2.38E-04	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(b)fluoranthene	2.25E-05	=	1.10E-11	+	2.25E-05	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(k)fluoranthene	1.18E-06	=	5.88E-13	+	1.18E-06	+	NA			NA	=	NA	+	NA	+	NA	
Chrysene	1.31E-07	=	1.18E-13	+	1.31E-07	+	NA			NA	=	NA	+	NA	+	NA	
Dibenzo(a,h)anthracene	6.21E-04	=	1.83E-10	+	6.21E-04	+	NA			NA	=	NA	+	NA	+	NA	
Dibenzofuran	NA	=	NA	+	NA	+	NA		*Systemic*	1.86E+00	=	3.64E-05	+	1.86E+00	+	NA	
Fluoranthene	NA	=	NA	+	NA	+	NA		*Systemic, Circulatory*	2.98E-02	=	1.21E-07	+	2.98E-02	+	NA	
Fluorene	NA	=	NA	+	NA	+	NA		*Circulatory*	6.41E-02	=	1.16E-06	+	6.41E-02	+	NA	
Indeno(1,2,3-cd)pyrene	3.69E-07	=	1.62E-13	+	3.69E-07	+	NA			NA	=	NA	+	NA	+	NA	
m & p-Cresols	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Naphthalene	NA	=	NA	+	NA	+	NA		*Respiratory, Systemic*	7.61E-01	=	3.64E-05	+	7.61E-01	+	NA	
o-Cresol	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	1.56E-02	=	1.22E-02	+	3.39E-03	+	NA	
Phenanthrene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Phenol	NA	=	NA	+	NA	+	NA		*Adrenal*	3.56E+00	=	6.48E-03	+	3.56E+00	+	NA	
Pyrene	NA	=	NA	+	NA	+	NA		*Systemic*	2.50E-02	=	1.06E-07	+	2.50E-02	+	NA	
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	1.44E+00	=	2.68E-05	+	1.44E+00	+	NA	
Benzene	3.22E-03	=	9.69E-07	+	3.22E-03	+	NA		*Circulatory*	3.42E+01	=	1.03E-02	+	3.42E+01	+	NA	
Ethylbenzene	NA	=	NA	+	NA	+	NA		*Systemic, Teratology*	6.55E-01	=	3.97E-05	+	6.55E-01	+	NA	
m & p-Xylenes	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	NA	=	NA	+	NA	+	NA	
Toluene	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	1.62E+00	=	1.54E-04	+	1.62E+00	+	NA	
Soil CR	***4E-03***	=	1E-06	+	***4E-03***	+	NA		**Soil HI**	***266***	=	0.1218	+	***266***	+	NA	

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Target Organ HI	
Respiratory	
Circulatory	
Systemic	
Adrenal	
CNS	
Teratology	
Skin	

Attachment I2
Table 6b
Adult Swimmer Risk Summary (Non-linear High Dose)
Reasonable Maximum Exposure

	Carcinogenic Risk							Target Organs	Noncarcinogenic Hazard						
Equation	CR	=	Ingestion	+	Dermal	+	Inhalation		HQ	=	Ingestion	+	Dermal	+	Inhalation
Units	unitless		unitless		unitless		unitless		unitless		unitless		unitless		unitless
					0										
Cyanides	NA	=	NA	+	NA	+	NA	*Thyroid, Systemic*	1.02E-05	=	2.82E-08	+	1.01E-05	+	NA
Iron	NA	=	NA	+	NA	+	NA		NA	=	1.72E-08	+	NA	+	NA
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA	*Respiratory*	***6.14E+00***	=	1.44E-04	+	6.14E+00	+	NA
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA	*Systemic*	***2.16E+02***	=	9.24E-02	+	2.16E+02	+	NA
Acenaphthylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Anthracene	NA	=	NA	+	NA	+	NA	*NOAEL*	3.22E-04	=	3.40E-09	+	3.22E-04	+	NA
Benzo(a)pyrene	***2.38E-04***	=	1.19E-10	+	2.38E-04	+	NA		NA	=	NA	+	NA	+	NA
Benzo(b)fluoranthene	***2.25E-05***	=	1.10E-11	+	2.25E-05	+	NA		NA	=	NA	+	NA	+	NA
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Benzo(k)fluoranthene	1.18E-06	=	5.88E-13	+	1.18E-06	+	NA		NA	=	NA	+	NA	+	NA
Chrysene	1.31E-07	=	1.18E-13	+	1.31E-07	+	NA		NA	=	NA	+	NA	+	NA
Dibenzo(a,h)anthracene	***6.21E-04***	=	1.83E-10	+	6.21E-04	+	NA		NA	=	NA	+	NA	+	NA
Dibenzofuran	NA	=	NA	+	NA	+	NA	*Systemic*	***1.86E+00***	=	3.64E-05	+	1.86E+00	+	NA
Fluoranthene	NA	=	NA	+	NA	+	NA	*Systemic, Circulatory*	2.98E-02	=	1.21E-07	+	2.98E-02	+	NA
Fluorene	NA	=	NA	+	NA	+	NA	*Circulatory*	6.41E-02	=	1.16E-06	+	6.41E-02	+	NA
Indeno(1,2,3-cd)pyrene	3.69E-07	=	1.62E-13	+	3.69E-07	+	NA		NA	=	NA	+	NA	+	NA
m & p-Cresols	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Naphthalene	NA	=	NA	+	NA	+	NA	*Respiratory, Systemic*	7.61E-01	=	3.64E-05	+	7.61E-01	+	NA
o-Cresol	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	1.56E-02	=	1.22E-02	+	3.39E-03	+	NA
Phenanthrene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Phenol	NA	=	NA	+	NA	+	NA	*Adrenal*	***3.56E+00***	=	6.48E-03	+	3.56E+00	+	NA
Pyrene	NA	=	NA	+	NA	+	NA	*Systemic*	2.50E-02	=	1.06E-07	+	2.50E-02	+	NA
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	***1.44E+00***	=	2.68E-05	+	1.44E+00	+	NA
Benzene	***3.22E-03***	=	9.69E-07	+	3.22E-03	+	NA	*Circulatory*	***3.42E+01***	=	1.03E-02	+	3.42E+01	+	NA
Ethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, Teratology*	6.55E-01	=	3.97E-05	+	6.55E-01	+	NA
m & p-Xylenes	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	NA	=	NA	+	NA	+	NA
Toluene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	***1.62E+00***	=	1.54E-04	+	1.62E+00	+	NA
Soil CR	***4E-03***	=	1E-06	+	***4E-03***	+	NA	**Soil HI**	***266***	=	0.1218	+	***266***	+	NA

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Target Organ HI

Respiratory	7
Circulatory	34
Systemic	222
Adrenal	4.E+00
CNS	3.E+00
Teratology	7.E-01

Attachment I2
Table 7
Exposure Parameters – Adolescent Swimmer and Wader

Exposure Pathway	Parameter	Description	Exposure Parameters			
			CTE	Source	RME	Source
Incidental Surface Water Ingestion	$WIR_{swimming}$	Surface Water Ingestion Rate (L/hour)	0.01	(a)	0.05	(b)
	WIR_{wading}	Surface Water Ingestion Rate (L/hour)	0.01	(a)	0.01	(a)
	EF	Exposure Frequency (events/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	12	(e)	12	(e)
	ET	Exposure Time (hours/event)	1 (swimming) 2 (wading)	(f)	1 (swimming) 2 (wading)	(f)
	BW	Body Weight (kg)	47	(g)	47	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	4,380	(l)	4,380	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Dermal Contact with Surface Water	$SA_{swimming}$	Skin Surface Area Exposed (cm^2)	13,533	(k)	13,533	(k)
	SA_{wading}	Skin Surface Area Exposed (cm^2)	6,767	(k)	6,767	(k)
	EF	Exposure Frequency (days/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	12	(e)	12	(e)
	EV	Event Frequency (events/day)	1		1	
	ET	Exposure Time (hours/event)	1 (swimming) 2 (wading)	(f)	1 (swimming) 2 (wading)	(f)
	BW	Body Weight (kg)	47	(g)	47	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	4,380	(l)	4,380	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Incidental Sediment Ingestion	SIR	Sediment Ingestion Rate (mg/hour)	5.60E-02	(m)	2.80E-01	(m)
	CF	Conversion Factor (kg/mg)	1E-06	--	1E-06	--
	EF	Exposure Frequency (days/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	12	(e)	12	(e)
	FI	Fraction Ingested from Contaminated Source (unitless)	1		1	
	BW	Body Weight (kg)	47	(g)	47	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	4,380	(l)	4,380	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Dermal Contact with Sediment	SA	Skin Surface Area Exposed (cm^2)	3,259	(n)	4,046	(n)
	SSAF	Soil-to-Skin Adherence Factor (mg/cm^2)	0.5	(o)	1	(o)
	CF	Conversion Factor (kg/mg)	1E-06	--	1E-06	--
	EF	Exposure Frequency (days/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	12	(e)	12	(e)
	EV	Event Frequency (events/day)	1		1	
	BW	Body Weight (kg)	47	(g)	47	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	4,380	(l)	4,380	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)

Notes:
CTE - Central Tendency Evaluation
RME - Reasonable Maximum Exposure.

(a) US EPA, 1989. Risk Assessment Guidance for Superfund, Volume I (RAGS, Part A). Value is one-fifth of that assumed to occur during a swimming event.
(b) US EPA, 1989. RAGS Part A. Value for a swimming event.
(c) One event per month for the 6 warmest months of the year.
(d) Two events per month for the 6 warmest months of the year.
(e) The default values for a residential adult, assuming the individual resides in the same residence for 9 (average) or 30 years (upperbound).
(f) US EPA, 1997. Exposure Factors Handbook, Table 1-2. Recommended values for exposure frequency of 1event per month and exposure time of 1 hours per event for swimming. The exposure time of 2 hours per event for wading is based on the estimated time spent on outdoor activities.
(g) US EPA, 1997. Exposure Factors Handbook. Body weight is the average of adult males and females
(h) 70 year lifetime is used to be consistent with the development of cancer slope factors.
(i) US EPA, 1991. Standard Default Exposure Factors. Value for adult.
(j) US EPA, 1989. RAGS, Part A.
(k) Value represents recommended skin surface area (100% for swimmers and 50% for waders).
(l) US EPA, 1989. RAGS, Part A. Averaging Time for noncarcinogens is equal to ED (year) × 365 days/year.
(m) Calculated using the equation: Sediment Ingestion Rate (mg/hour) = Surface water ingestion rate (ml/hour) × total solids (mg/ml). The average total suspended solids is 0.0056 mg/mL.
(n) The RME skin surface area represents the sum of the surface area for forearms, hands, lower legs and feet. The CTE skin surface area represents the sum of the skin surface area for hands, lower legs and feet.
(o) US EPA, 1997. Exposure Factors Handbook, (Table ??). Using loadings for the hands, arms, and legs for the irrigation worker, a weighted soil-to-skin adherence factor of 2.0 mg/cm^2 was calculated. One-half this value (1.0 mg/cm^2) used as RME assuming some

Attachment I2

Table 8
Risk Calculations
Adolescent Swimmer: Incidental Ingestion of Surface Water Pathway – Carcinogenic Effects
NSP Ashland

$$\text{Ing-Risk} = \frac{(\text{Cwater} \times \text{WIRswimming} \times \text{EF} \times \text{ED} \times \text{ET} \times \text{SFo})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	= (	Cwater	×	WIRswimming	×	EF	×	ED	×	ET	×	SFo	) ÷ (	BW	×	ATc	)
Units	unitless		mg/L		L/hour		events/year		years		hours/event		kg-day/mg		kg		days	
Cyanides	NA	= (	2.40E-05	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Iron	NA	= (	2.20E-04	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
2-Methylnaphthalene	NA	= (	2.46E-02	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
2,4 Dimethylphenol	NA	= (	7.87E+00	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Acenaphthylene	NA	= (	4.24E-03	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Anthracene	NA	= (	4.34E-05	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Benzo(a)pyrene	7.09E-11	= (	1.62E-06	×	0.05	×	12	×	12	×	1	×	7.30E+00	) ÷ (	47	×	25,550	)
Benzo(b)fluoranthene	6.57E-12	= (	1.50E-06	×	0.05	×	12	×	12	×	1	×	7.30E-01	) ÷ (	47	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	2.60E-07	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Benzo(k)fluoranthene	3.50E-13	= (	8.00E-07	×	0.05	×	12	×	12	×	1	×	7.30E-02	) ÷ (	47	×	25,550	)
Chrysene	7.00E-14	= (	1.60E-06	×	0.05	×	12	×	12	×	1	×	7.30E-03	) ÷ (	47	×	25,550	)
Dibenzo(a,h)anthracene	1.09E-10	= (	2.49E-06	×	0.05	×	12	×	12	×	1	×	7.30E+00	) ÷ (	47	×	25,550	)
Dibenzofuran	NA	= (	3.10E-03	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Fluoranthene	NA	= (	2.06E-04	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Fluorene	NA	= (	1.98E-03	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	9.63E-14	= (	2.20E-08	×	0.05	×	12	×	12	×	1	×	7.30E-01	) ÷ (	47	×	25,550	)
m & p-Cresols	NA	= (	2.27E+01	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Naphthalene	NA	= (	3.10E-02	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
o-Cresol	NA	= (	2.60E+01	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Phenanthrene	NA	= (	1.15E-03	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Phenol	NA	= (	8.28E+01	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Pyrene	NA	= (	1.35E-04	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	5.70E-02	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)

Attachment I2

Table 8
Risk Calculations
Adolescent Swimmer: Incidental Ingestion of Surface Water Pathway – Carcinogenic Effects
NSP Ashland

$$\text{Ing-Risk} = \frac{(\text{Cwater} \times \text{WIRswimming} \times \text{EF} \times \text{ED} \times \text{ET} \times \text{SFo})}{(\text{BW} \times \text{ATc})}$$

Equation / Units		Ing - Risk unitless	= (	Cwater mg/L	×	WIRswimming L/hour	×	EF events/year	×	ED years	×	ET hours/event	×	SFo kg-day/mg	) ÷ (	BW kg	×	ATc days	)
Benzene		5.77E-07	= (	1.75E+00	×	0.05	×	12	×	12	×	1	×	5.50E-02	) ÷ (	47	×	25,550	)
Ethylbenzene		NA	= (	1.69E-01	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
m & p-Xylenes		NA	= (	1.85E-01	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
Toluene		NA	= (	5.26E-01	×	0.05	×	12	×	12	×	1	×	NV	) ÷ (	47	×	25,550	)
	Total CR	***5.77E-07***																	

Notes:

Ing-Risk – Carcinogenic Risk Water Ingestion Pathway
Cwater – Concentration in Water (Based on chemical-specific solubility)
WIR – Water Ingestion Rate
EF – Exposure Frequency
ED – Exposure Duration
SFo – Oral Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 9
Risk Calculations
Adolescent Swimmer: Incidental Ingestion of Surface Water Pathway – Noncarcinogenic Effects
NSP Ashland

$$\text{Inh-HQ} = \frac{(\text{Cwater} \times \text{WIRswimming} \times \text{EF} \times \text{ED} \times \text{ET})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation	Ing - HQ	= (	Cwater	×	WIRswimming	×	EF	×	ED	×	ET	) ÷ (	BW	×	ATn	×	RfDo	)
Units	unitless		mg/L		L/hour		days/year		years		hours/event		kg		days		mg/kg-day	
Cyanides	4.20E-08	= (	2.40E-05	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	2.00E-02	)
Iron	2.56E-08	= (	2.20E-04	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	3.00E-01	)
2-Methylnaphthalene	2.15E-04	= (	2.46E-02	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	4.00E-03	)
2,4 Dimethylphenol	1.38E-01	= (	7.87E+00	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	2.00E-03	)
Acenaphthylene	NA	= (	4.24E-03	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Anthracene	5.06E-09	= (	4.34E-05	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	1.62E-06	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.50E-06	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Benzo(g,h,i)perylene	NA	= (	2.60E-07	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Benzo(k)fluoranthene	NA	= (	8.00E-07	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Chrysene	NA	= (	1.60E-06	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.49E-06	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Dibenzofuran	5.42E-05	= (	3.10E-03	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	2.00E-03	)
Fluoranthene	1.80E-07	= (	2.06E-04	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	4.00E-02	)
Fluorene	1.73E-06	= (	1.98E-03	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	2.20E-08	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
m & p-Cresols	NA	= (	2.27E+01	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Naphthalene	5.42E-05	= (	3.10E-02	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	2.00E-02	)
o-Cresol	1.82E-02	= (	2.60E+01	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	5.00E-02	)
Phenanthrene	NA	= (	*1.15E-03*	×	*0.05*	×	*12*	×	*12*	×	*1*	) ÷ (	*47*	×	4,380	×	NV	)
Phenol	9.65E-03	= (	8.28E+01	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	3.00E-01	)
Pyrene	1.57E-07	= (	1.35E-04	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	3.00E-02	)
1,2,4-Trimethylbenzene	3.99E-05	= (	5.70E-02	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	5.00E-02	)

Attachment I2

Table 9
Risk Calculations
Adolescent Swimmer: Incidental Ingestion of Surface Water Pathway – Noncarcinogenic Effects
NSP Ashland

$$\text{Inh-HQ} = \frac{(\text{Cwater} \times \text{WIRswimming} \times \text{EF} \times \text{ED} \times \text{ET})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation Units	Ing - HQ unitless	= (	Cwater mg/L	×	WIRswimming L/hour	×	EF days/year	×	ED years	×	ET hours/event	) ÷ (	BW kg	×	ATn days	×	RfDo mg/kg-day	)
Benzene	1.53E-02	= (	1.75E+00	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	4.00E-03	)
Ethylbenzene	5.91E-05	= (	1.69E-01	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	1.00E-01	)
m & p-Xylenes	NA	= (	1.85E-01	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	NV	)
Toluene	2.30E-04	= (	5.26E-01	×	0.05	×	12	×	12	×	1	) ÷ (	47	×	4,380	×	8.00E-02	)
Total HI	***1.81E-01***																	

Notes:

Ing-HQ – Water Ingestion Pathway Hazard Quotient
Cwater – Concentration in Water (Based on chemical-specific solubility)
WIR – Water Ingestion Rate
EF – Exposure Frequency
ED – Exposure Duration
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 10a
Risk Calculations
Adolescent Swimmer: Dermal Contact with Surface Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SAswimming \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	2.40E-08	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Iron	NA	= (	2.20E-07	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
2-Methylnaphthalene	NA	= (	2.91E-03	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
2,4 Dimethylphenol	NA	= (	5.11E-02	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Acenaphthylene	NA	= (	6.96E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Anthracene	NA	= (	1.14E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Benzo(a)pyrene	1.07E-04	= (	9.01E-06	×	1	×	12	×	12	×	13,533	×	7.30E+00	) ÷ (	47	×	25,550	)
Benzo(b)fluoranthene	1.01E-05	= (	8.52E-06	×	1	×	12	×	12	×	13,533	×	7.30E-01	) ÷ (	47	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	3.30E-06	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Benzo(k)fluoranthene	5.29E-07	= (	4.47E-06	×	1	×	12	×	12	×	13,533	×	7.30E-02	) ÷ (	47	×	25,550	)
Chrysene	5.86E-08	= (	4.94E-06	×	1	×	12	×	12	×	13,533	×	7.30E-03	) ÷ (	47	×	25,550	)
Dibenzo(a,h)anthracene	2.78E-04	= (	2.35E-05	×	1	×	12	×	12	×	13,533	×	7.30E+00	) ÷ (	47	×	25,550	)
Dibenzofuran	NA	= (	4.39E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Fluoranthene	NA	= (	1.41E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Fluorene	NA	= (	3.03E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.65E-07	= (	1.40E-07	×	1	×	12	×	12	×	13,533	×	7.30E-01	) ÷ (	47	×	25,550	)
m & p-Cresols	NA	= (	2.96E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Naphthalene	NA	= (	1.80E-03	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
o-Cresol	NA	= (	2.00E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Phenanthrene	NA	= (	3.94E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Phenol	NA	= (	1.26E-01	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Pyrene	NA	= (	8.88E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	8.50E-03	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)

Attachment I2

Table 10a
Risk Calculations
Adolescent Swimmer: Dermal Contact with Surface Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SAswimming \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Benzene	1.44E-03	= (	1.62E-02	×	1	×	12	×	12	×	13,533	×	5.50E-02	) ÷ (	47	×	25,550	)
Ethylbenzene	NA	= (	7.75E-03	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
m & p-Xylenes	NA	= (	1.25E-02	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Toluene	NA	= (	1.53E-02	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Total CR	***1.84E-03***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (calculated using chemical-specific solubility)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 10b
Risk Calculations
Adolescent Swimmer: Dermal Contact with Surface Water (Non-Linear High Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = 1\text{-exp}\left(-\frac{(DA_{event} \times EV \times ED \times EF \times SAswimming \times SFabs)}{(BW \times ATc)}\right)$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	2.40E-08	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Iron	NA	= (	2.20E-07	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
2-Methylnaphthalene	NA	= (	2.91E-03	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
2,4 Dimethylphenol	NA	= (	5.11E-02	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Acenaphthylene	NA	= (	6.96E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Anthracene	NA	= (	1.14E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Benzo(a)pyrene	1.07E-04	= (	9.01E-06	×	1	×	12	×	12	×	13,533	×	7.30E+00	) ÷ (	47	×	25,550	)
Benzo(b)fluoranthene	1.01E-05	= (	8.52E-06	×	1	×	12	×	12	×	13,533	×	7.30E-01	) ÷ (	47	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	3.30E-06	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Benzo(k)fluoranthene	5.29E-07	= (	4.47E-06	×	1	×	12	×	12	×	13,533	×	7.30E-02	) ÷ (	47	×	25,550	)
Chrysene	5.86E-08	= (	4.94E-06	×	1	×	12	×	12	×	13,533	×	7.30E-03	) ÷ (	47	×	25,550	)
Dibenzo(a,h)anthracene	2.78E-04	= (	2.35E-05	×	1	×	12	×	12	×	13,533	×	7.30E+00	) ÷ (	47	×	25,550	)
Dibenzofuran	NA	= (	4.39E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Fluoranthene	NA	= (	1.41E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Fluorene	NA	= (	3.03E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.65E-07	= (	1.40E-07	×	1	×	12	×	12	×	13,533	×	7.30E-01	) ÷ (	47	×	25,550	)
m & p-Cresols	NA	= (	2.96E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Naphthalene	NA	= (	1.80E-03	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
o-Cresol	NA	= (	2.00E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Phenanthrene	NA	= (	3.94E-04	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Phenol	NA	= (	1.26E-01	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Pyrene	NA	= (	8.88E-05	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	8.50E-03	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Benzene	1.44E-03	= (	1.62E-02	×	1	×	12	×	12	×	13,533	×	5.50E-02	) ÷ (	47	×	25,550	)

Attachment I2

Table 10b
Risk Calculations
Adolescent Swimmer: Dermal Contact with Surface Water (Non-Linear High Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = 1\text{-exp}\left(-\frac{(DA_{event} \times EV \times ED \times EF \times SAswimming \times SFabs)}{(BW \times ATc)}\right)$$

Equation / Units	Derm-Risk unitless	= (	DA_{event} mg/cm²-event	×	EV events/day	×	ED years	×	EF days/year	×	SAswimming cm²	×	SFabs kg-day/mg	) ÷ (	BW kg	×	ATc days	)
Ethylbenzene	NA	= (	7.75E-03	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
m & p-Xylenes	NA	= (	1.25E-02	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Toluene	NA	= (	1.53E-02	×	1	×	12	×	12	×	13,533	×	NV	) ÷ (	47	×	25,550	)
Total CR	***1.84E-03***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (calculated using chemical-specific solubility)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 11
Risk Calculations
Adolescent Swimmer: Dermal Contact with Surface Water – Noncarcinogenic Effects
NSP Ashland

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SAswimming)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
Cyanides	1.14E-05	= (	2.40E-08	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	2.00E-02	)
Iron	NA	= (	2.20E-07	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
2-Methylnaphthalene	6.88E+00	= (	2.91E-03	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	4.00E-03	)
2,4 Dimethylphenol	2.42E+02	= (	5.11E-02	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	2.00E-03	)
Acenaphthylene	NA	= (	6.96E-04	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Anthracene	3.61E-04	= (	1.14E-05	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	9.01E-06	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Benzo(b)fluoranthene	NA	= (	8.52E-06	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Benzo(g,h,i)perylene	NA	= (	3.30E-06	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Benzo(k)fluoranthene	NA	= (	4.47E-06	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Chrysene	NA	= (	4.94E-06	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.35E-05	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Dibenzofuran	2.08E+00	= (	4.39E-04	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	2.00E-03	)
Fluoranthene	3.33E-02	= (	1.41E-04	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	4.00E-02	)
Fluorene	7.18E-02	= (	3.03E-04	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.40E-07	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
m & p-Cresols	NA	= (	2.96E-05	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Naphthalene	8.52E-01	= (	1.80E-03	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	2.00E-02	)
o-Cresol	3.79E-03	= (	2.00E-05	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	5.00E-02	)
Phenanthrene	NA	= (	3.94E-04	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Phenol	3.98E+00	= (	1.26E-01	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	3.00E-01	)
Pyrene	2.80E-02	= (	8.88E-05	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	3.00E-02	)

Attachment I2

Table 11
Risk Calculations
Adolescent Swimmer: Dermal Contact with Surface Water – Noncarcinogenic Effects
NSP Ashland

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SAswimming)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAswimming	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
1,2,4-Trimethylbenzene	1.61E+00	= (	8.50E-03	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	5.00E-02	)
Benzene	3.83E+01	= (	1.62E-02	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	4.00E-03	)
Ethylbenzene	7.33E-01	= (	7.75E-03	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	1.00E-01	)
m & p-Xylenes	NA	= (	1.25E-02	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	NV	)
Toluene	1.81E+00	= (	1.53E-02	×	1	×	12	×	12	×	13,533	) ÷ (	47	×	4,380	×	8.00E-02	)
Total HI	***2.98E+02***																	

Notes:

Derm-HQ – Dermal Contact with Water Pathway Hazard Quotient
DA_{event} – Absorbed Dose per Event (calculated using chemical-specific solubility)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDabs – Absorbed Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 12a
Adolescent Swimmer Risk Summary (Linear Low Dose)
Reasonable Maximum Exposure

	Carcinogenic Risk								Target Organs	Noncarcinogenic Hazard							
Equation Units	CR unitless	=	Ingestion unitless	+	Dermal unitless	+	Inhalation unitless			HQ unitless	=	Ingestion unitless	+	Dermal unitless	+	Inhalation unitless	
Cyanides	NA	=	NA	+	NA	+	NA		*Thyroid, Systemic*	1.14E-05	=	4.20E-08	+	1.14E-05	+	NA	
Iron	NA	=	NA	+	NA	+	NA			NA	=	2.56E-08	+	NA	+	NA	
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA		*Respiratory*	6.88E+00	=	2.15E-04	+	6.88E+00	+	NA	
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA		*Systemic*	2.42E+02	=	1.38E-01	+	2.42E+02	+	NA	
Acenaphthylene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Anthracene	NA	=	NA	+	NA	+	NA		*NOAEL*	3.61E-04	=	5.06E-09	+	3.61E-04	+	NA	
Benzo(a)pyrene	1.07E-04	=	7.09E-11	+	1.07E-04	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(b)fluoranthene	1.01E-05	=	6.57E-12	+	1.01E-05	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(k)fluoranthene	5.29E-07	=	3.50E-13	+	5.29E-07	+	NA			NA	=	NA	+	NA	+	NA	
Chrysene	5.86E-08	=	7.00E-14	+	5.86E-08	+	NA			NA	=	NA	+	NA	+	NA	
Dibenzo(a,h)anthracene	2.78E-04	=	1.09E-10	+	2.78E-04	+	NA			NA	=	NA	+	NA	+	NA	
Dibenzofuran	NA	=	NA	+	NA	+	NA		*Systemic*	2.08E+00	=	5.42E-05	+	2.08E+00	+	NA	
Fluoranthene	NA	=	NA	+	NA	+	NA		*Systemic, Circulatory*	3.33E-02	=	1.80E-07	+	3.33E-02	+	NA	
Fluorene	NA	=	NA	+	NA	+	NA		*Circulatory*	7.18E-02	=	1.73E-06	+	7.18E-02	+	NA	
Indeno(1,2,3-cd)pyrene	1.65E-07	=	9.63E-14	+	1.65E-07	+	NA			NA	=	NA	+	NA	+	NA	
m & p-Cresols	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Naphthalene	NA	=	NA	+	NA	+	NA		*Respiratory, Systemic*	8.52E-01	=	5.42E-05	+	8.52E-01	+	NA	
o-Cresol	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	2.20E-02	=	1.82E-02	+	3.79E-03	+	NA	
Phenanthrene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Phenol	NA	=	NA	+	NA	+	NA		*Adrenal*	3.99E+00	=	9.65E-03	+	3.98E+00	+	NA	
Pyrene	NA	=	NA	+	NA	+	NA		*Systemic*	2.80E-02	=	1.57E-07	+	2.80E-02	+	NA	
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	1.61E+00	=	3.99E-05	+	1.61E+00	+	NA	
Benzene	1.44E-03	=	5.77E-07	+	1.44E-03	+	NA		*Circulatory*	3.83E+01	=	1.53E-02	+	3.83E+01	+	NA	
Ethylbenzene	NA	=	NA	+	NA	+	NA		*Systemic, Teratology*	7.34E-01	=	5.91E-05	+	7.33E-01	+	NA	
m & p-Xylenes	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	NA	=	NA	+	NA	+	NA	
Toluene	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	1.81E+00	=	2.30E-04	+	1.81E+00	+	NA	
Soil CR	***2E-03***	=	NA	+	***2E-03***	+	NA		**Soil HI**	***298***	=	NA	+	***298***	+	NA	

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Target Organ HI	
Respiratory	8
Circulatory	38
Systemic	248
Adrenal	4.E+00
CNS	3.E+00
Teratology	7.E-01

Attachment I2
Table 12b
Adolescent Swimmer Risk Summary (Non-linear Low Dose)
Reasonable Maximum Exposure

	Carcinogenic Risk								Target Organs	Noncarcinogenic Hazard							
Equation	CR	=	Ingestion	+	Dermal	+	Inhalation			HQ	=	Ingestion	+	Dermal	+	Inhalation	
Units	unitless		unitless		unitless		unitless			unitless		unitless		unitless		unitless	
					0												
Cyanides	NA	=	NA	+	NA	+	NA		*Thyroid, Systemic*	1.14E-05	=	4.20E-08	+	1.14E-05	+	NA	
Iron	NA	=	NA	+	NA	+	NA			NA	=	2.56E-08	+	NA	+	NA	
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA		*Respiratory*	***6.88E+00***	=	2.15E-04	+	6.88E+00	+	NA	
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA		*Systemic*	***2.42E+02***	=	1.38E-01	+	2.42E+02	+	NA	
Acenaphthylene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Anthracene	NA	=	NA	+	NA	+	NA		*NOAEL*	3.61E-04	=	5.06E-09	+	3.61E-04	+	NA	
Benzo(a)pyrene	***1.07E-04***	=	7.09E-11	+	1.07E-04	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(b)fluoranthene	***1.01E-05***	=	6.57E-12	+	1.01E-05	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(k)fluoranthene	5.29E-07	=	3.50E-13	+	5.29E-07	+	NA			NA	=	NA	+	NA	+	NA	
Chrysene	5.86E-08	=	7.00E-14	+	5.86E-08	+	NA			NA	=	NA	+	NA	+	NA	
Dibenzo(a,h)anthracene	***2.78E-04***	=	1.09E-10	+	2.78E-04	+	NA			NA	=	NA	+	NA	+	NA	
Dibenzofuran	NA	=	NA	+	NA	+	NA		*Systemic*	***2.08E+00***	=	5.42E-05	+	2.08E+00	+	NA	
Fluoranthene	NA	=	NA	+	NA	+	NA		*Systemic, Circulatory*	3.33E-02	=	1.80E-07	+	3.33E-02	+	NA	
Fluorene	NA	=	NA	+	NA	+	NA		*Circulatory*	7.18E-02	=	1.73E-06	+	7.18E-02	+	NA	
Indeno(1,2,3-cd)pyrene	1.65E-07	=	9.63E-14	+	1.65E-07	+	NA			NA	=	NA	+	NA	+	NA	
m & p-Cresols	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Naphthalene	NA	=	NA	+	NA	+	NA		*Respiratory, Systemic*	8.52E-01	=	5.42E-05	+	8.52E-01	+	NA	
o-Cresol	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	2.20E-02	=	1.82E-02	+	3.79E-03	+	NA	
Phenanthrene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Phenol	NA	=	NA	+	NA	+	NA		*Adrenal*	***3.99E+00***	=	9.65E-03	+	3.98E+00	+	NA	
Pyrene	NA	=	NA	+	NA	+	NA		*Systemic*	2.80E-02	=	1.57E-07	+	2.80E-02	+	NA	
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	***1.61E+00***	=	3.99E-05	+	1.61E+00	+	NA	
Benzene	***1.44E-03***	=	5.77E-07	+	1.44E-03	+	NA		*Circulatory*	***3.83E+01***	=	1.53E-02	+	3.83E+01	+	NA	
Ethylbenzene	NA	=	NA	+	NA	+	NA		*Systemic, Teratology*	7.34E-01	=	5.91E-05	+	7.33E-01	+	NA	
m & p-Xylenes	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	NA	=	NA	+	NA	+	NA	
Toluene	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	***1.81E+00***	=	2.30E-04	+	1.81E+00	+	NA	
Soil CR	***2E-03***	=	6E-07	+	***2E-03***	+	NA		**Soil HI**	***298***	=	1.8E-01	+	***298***	+	NA	

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Target Organ HI	
Respiratory	8
Circulatory	38
Systemic	248
Adrenal	4.E+00
CNS	3.E+00
Teratology	7.E-01

Attachment I2

Table 13
Exposure Parameters – Adult Swimmer and Wader

Exposure Pathway	Parameter	Description	Exposure Parameters			
			CTE	Source	RME	Source
Incidental Surface Water Ingestion	$WIR_{swimming}$	Surface Water Ingestion Rate (L/hour)	0.01	(a)	0.05	(b)
	WIR_{wading}	Surface Water Ingestion Rate (L/hour)	0.01	(a)	0.01	(a)
	EF	Exposure Frequency (events/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	9	(e)	30	(e)
	ET	Exposure Time (hours/event)	1 (swimming) 2 (wading)	(f)	1 (swimming) 2 (wading)	(f)
	BW	Body Weight (kg)	70	(g)	70	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	3,285	(l)	10,950	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Dermal Contact with Surface Water	$SA_{swimming}$	Skin Surface Area Exposed (cm^2)	18,000	(k)	18,000	(k)
	SA_{wading}	Skin Surface Area Exposed (cm^2)	9,000	(k)	9,000	(k)
	EF	Exposure Frequency (days/yr)	6	(c)	12	(d)
	ED	Exposure Duration (years)	9	(e)	30	(e)
	EV	Event Frequency (events/day)	1		1	
	ET	Exposure Time (hours/event)	1 (swimming) 2 (wading)	(f)	1 (swimming) 2 (wading)	(f)
	BW	Body Weight (kg)	70	(g)	70	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	3,285	(l)	10,950	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Incidental Sediment Ingestion	SIR	Sediment Ingestion Rate (mg/day)	(m)		(m)	
	CF	Conversion Factor (kg/mg)	1E-06	--	1E-06	--
	EF	Exposure Frequency (days/yr)	6	(c)	12	(d)
	ED	Exposure Duration (years)	9	(e)	30	(e)
	FI	Fraction Ingested from Contaminated Source (unitless)	1		1	
	BW	Body Weight (kg)	70	(g)	70	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	3,285	(l)	10,950	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Dermal Contact with Sediment	SA	Skin Surface Area Exposed (cm^2)	4,499	(n)	5,672	(n)
	SSAF	Soil-to-Skin Adherence Factor (mg/cm^2)	0.5	(o)	1	(o)
	CF	Conversion Factor (kg/mg)	1E-06	--	1E-06	--
	EF	Exposure Frequency (days/yr)	6	(c)	12	(d)
	ED	Exposure Duration (years)	9	(e)	30	(e)
	EV	Event Frequency (events/day)	1		1	
	BW	Body Weight (kg)	70	(g)	70	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	3,285	(l)	10,950	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)

Notes:
CTE - Central Tendency Evaluation
RME - Reasonable Maximum Exposure.

(a) US EPA, 1989. Risk Assessment Guidance for Superfund, Volume I (RAGS, Part A). Value is one-fifth of that assumed to occur during a swimming event.
(b) US EPA, 1989. RAGS Part A. Value for a swimming event.
(c) One event per month for the 6 warmest months of the year.
(d) Two events per month for the 6 warmest months of the year.
(e) The default values for a residential adult, assuming the individual resides in the same residence for 9 (average) or 30 years (upperbound).
(f) US EPA, 1997. Exposure Factors Handbook, Table 1-2. Recommended values for exposure frequency of 1event per month and exposure time of 1 hours per event for swimming. The exposure time of 2 hours per event for wading is based on the estimated time spent on outdoor activities.
(g) US EPA, 1997. Exposure Factors Handbook. Body weight is the average of adult males and females
(h) 70 year lifetime is used to be consistent with the development of cancer slope factors.
(i) US EPA, 1991. Standard Default Exposure Factors. Value for adult.
(j) US EPA, 1989. RAGS, Part A.
(k) Value represents recommended skin surface area (100% for swimmers and 50% for waders).
(l) US EPA, 1989. RAGS, Part A. *Averaging Time for noncarcinogens is equal to ED (year) × 365 days/year.*
(m) Calculated using the equation: Sediment Ingestion Rate (mg/day) = Surface water ingestion rate (ml/day) × total solids (mg/ml).
(n) The RME skin surface area represents the sum of the surface area for forearms, hands, lower legs and feet. The CTE skin surface area represents the sum of the skin surface area for hands, lower legs and feet.
(o) US EPA, 1997. Exposure Factors Handbook, (Table ??). Using loadings for the hands, arms, and legs for the irrigation worker, a weighted soil-to-skin adherence factor of 2.0 mg/cm^2 was calculated. One-half this value (1.0 mg/cm^2) used as RME assuming some washoff; 0.5 mg/cm^2 used for CTE.

Attachment I2

Table 14
Risk Calculations
Adult Wader: Incidental Ingestion of Surface Water Pathway – Carcinogenic Effects
NSP Ashland

$$\text{Ing-Risk} = \frac{(\text{Cwater} \times \text{WIRwader} \times \text{EF} \times \text{ED} \times \text{ET} \times \text{SFo})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	= (	Cwater	×	WIRwader	×	EF	×	ED	×	ET	×	SFo	) ÷ (	BW	×	ATc	)
Units	unitless		mg/L		L/hour		events/year		years		hours/event		kg-day/mg		kg		days	
Cyanides	NA	= (	2.40E-05	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Iron	NA	= (	2.20E-04	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	2.46E-02	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
2,4 Dimethylphenol	NA	= (	7.87E+00	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	4.24E-03	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Anthracene	NA	= (	4.34E-05	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	4.76E-11	= (	1.62E-06	×	0.01	×	12	×	30	×	2	×	7.30E+00	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	4.41E-12	= (	1.50E-06	×	0.01	×	12	×	30	×	2	×	7.30E-01	) ÷ (	70	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	2.60E-07	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	2.35E-13	= (	8.00E-07	×	0.01	×	12	×	30	×	2	×	7.30E-02	) ÷ (	70	×	25,550	)
Chrysene	4.70E-14	= (	1.60E-06	×	0.01	×	12	×	30	×	2	×	7.30E-03	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	7.32E-11	= (	2.49E-06	×	0.01	×	12	×	30	×	2	×	7.30E+00	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	3.10E-03	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	2.06E-04	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	1.98E-03	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	6.47E-14	= (	2.20E-08	×	0.01	×	12	×	30	×	2	×	7.30E-01	) ÷ (	70	×	25,550	)
m & p-Cresols	NA	= (	2.27E+01	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	3.10E-02	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
o-Cresol	NA	= (	2.60E+01	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Phenanthrene	NA	= (	1.15E-03	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Phenol	NA	= (	8.28E+01	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	1.35E-04	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	5.70E-02	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)

Attachment I2

Table 14
Risk Calculations
Adult Wader: Incidental Ingestion of Surface Water Pathway – Carcinogenic Effects
NSP Ashland

$$\text{Ing-Risk} = \frac{(\text{Cwater} \times \text{WIRwader} \times \text{EF} \times \text{ED} \times \text{ET} \times \text{SFo})}{(\text{BW} \times \text{ATc})}$$

Equation Units		Ing - Risk unitless	= (	Cwater mg/L	×	WIRwader L/hour	×	EF events/year	×	ED years	×	ET hours/event	×	SFo kg-day/mg	) ÷ (	BW kg	×	ATc days	)
Benzene		3.87E-07	= (	1.75E+00	×	0.01	×	12	×	30	×	2	×	5.50E-02	) ÷ (	70	×	25,550	)
Ethylbenzene		NA	= (	1.69E-01	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
m & p-Xylenes		NA	= (	1.85E-01	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
Toluene		NA	= (	5.26E-01	×	0.01	×	12	×	30	×	2	×	NV	) ÷ (	70	×	25,550	)
	Total CR	***3.88E-07***																	

Notes:

Ing-Risk – Carcinogenic Risk Water Ingestion Pathway
Cwater – Concentration in Water (Based on chemical-specific solubility)
WIR – Water Ingestion Rate
EF – Exposure Frequency
ED – Exposure Duration
SFo – Oral Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 15
Risk Calculations
Adult Wader: Incidental Ingestion of Surface Water Pathway – Noncarcinogenic Effects
NSP Ashland

$$\text{Inh-HQ} = \frac{(\text{Cwater} \times \text{WIRwader} \times \text{EF} \times \text{ED} \times \text{ET})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation Units	Ing - HQ unitless	=	Cwater mg/L	×	WIRwader L/hour	×	EF days/year	×	ED years	×	ET hours/event	) ÷ (	BW kg	×	ATn days	×	RfDo mg/kg-day	)
Cyanides	1.13E-08	= (	2.40E-05	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	2.00E-02	)
Iron	6.89E-09	= (	2.20E-04	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	3.00E-01	)
2-Methylnaphthalene	5.78E-05	= (	2.46E-02	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	4.00E-03	)
2,4 Dimethylphenol	3.70E-02	= (	7.87E+00	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	2.00E-03	)
Acenaphthylene	NA	= (	4.24E-03	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Anthracene	1.36E-09	= (	4.34E-05	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	1.62E-06	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.50E-06	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Benzo(g,h,i)perylene	NA	= (	2.60E-07	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Benzo(k)fluoranthene	NA	= (	8.00E-07	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Chrysene	NA	= (	1.60E-06	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.49E-06	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Dibenzofuran	1.46E-05	= (	3.10E-03	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	2.00E-03	)
Fluoranthene	4.84E-08	= (	2.06E-04	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	4.00E-02	)
Fluorene	4.65E-07	= (	1.98E-03	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	2.20E-08	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
m & p-Cresols	NA	= (	2.27E+01	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Naphthalene	1.46E-05	= (	3.10E-02	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	2.00E-02	)
o-Cresol	4.88E-03	= (	2.60E+01	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	5.00E-02	)
Phenanthrene	NA	= (	1.15E-03	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	NV	)
Phenol	2.59E-03	= (	8.28E+01	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	3.00E-01	)
Pyrene	4.23E-08	= (	1.35E-04	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	3.00E-02	)
1,2,4-Trimethylbenzene	1.07E-05	= (	5.70E-02	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	5.00E-02	)

Attachment I2

Table 15
Risk Calculations
Adult Wader: Incidental Ingestion of Surface Water Pathway – Noncarcinogenic Effects
NSP Ashland

$$\text{Inh-HQ} = \frac{(\text{Cwater} \times \text{WIRwader} \times \text{EF} \times \text{ED} \times \text{ET})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation Units	Ing - HQ unitless	= (	Cwater mg/L	×	WIRwader L/hour	×	EF days/year	×	ED years	×	ET hours/event	) ÷ (	BW kg	×	ATn days	×	RfDo mg/kg-day	)
Benzene	4.11E-03	= (	1.75E+00	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	4.00E-03	)
Ethylbenzene	1.59E-05	= (	1.69E-01	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	1.00E-01	)
m & p-Xylenes	*NA*	= (	*1.85E-01*	×	*0.01*	×	12	×	*30*	×	2	) ÷ (	70	×	10,950	×	NV	)
Toluene	6.18E-05	= (	5.26E-01	×	0.01	×	12	×	30	×	2	) ÷ (	70	×	10,950	×	8.00E-02	)
Total HI	***4.87E-02***																	

Notes:

Ing-HQ – Water Ingestion Pathway Hazard Quotient
Cwater – *Concentration in Water* (Based on chemical-specific solubility)
WIR – Water Ingestion Rate
EF – Exposure Frequency
ED – Exposure Duration
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 16a
Risk Calculations
Adult Wader: Dermal Contact with Surface Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SAwading \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	4.80E-08	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Iron	NA	= (	4.40E-07	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	4.11E-03	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
2,4 Dimethylphenol	NA	= (	7.23E-02	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	9.84E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Anthracene	NA	= (	1.62E-05	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	1.22E-04	= (	9.23E-06	×	1	×	30	×	12	×	9,000	×	7.30E+00	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	1.15E-05	= (	8.72E-06	×	1	×	30	×	12	×	9,000	×	7.30E-01	) ÷ (	70	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	3.34E-06	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	6.05E-07	= (	4.57E-06	×	1	×	30	×	12	×	9,000	×	7.30E-02	) ÷ (	70	×	25,550	)
Chrysene	6.80E-08	= (	5.15E-06	×	1	×	30	×	12	×	9,000	×	7.30E-03	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	3.14E-04	= (	2.37E-05	×	1	×	30	×	12	×	9,000	×	7.30E+00	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	6.21E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	1.99E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	4.29E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.87E-07	= (	1.41E-07	×	1	×	30	×	12	×	9,000	×	7.30E-01	) ÷ (	70	×	25,550	)
m & p-Cresols	NA	= (	4.18E-05	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	2.55E-03	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
o-Cresol	NA	= (	2.83E-05	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Phenanthrene	NA	= (	5.58E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Phenol	NA	= (	1.79E-01	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	1.26E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	1.20E-02	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)

Attachment I2

Table 16a
Risk Calculations
Adult Wader: Dermal Contact with Surface Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SAwading \times SFabs)}{(BW \times ATc)}$$

Equation		Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	×	SFabs	) ÷ (	BW	×	ATc	)
Units		unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Benzene		2.28E-03	= (	2.29E-02	×	1	×	30	×	12	×	9,000	×	5.50E-02	) ÷ (	70	×	25,550	)
Ethylbenzene		NA	= (	1.10E-02	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
m & p-Xylenes		NA	= (	1.77E-02	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Toluene		NA	= (	2.16E-02	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
	Total CR	***2.73E-03***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (calculated using chemical-specific solubility)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 16b
Risk Calculations
Adult Wader: Dermal Contact with Surface Water (Non-Linear High Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = 1\text{-exp}\left(-\frac{(DA_{event} \times EV \times ED \times EF \times SAwading \times SFabs)}{(BW \times ATc)}\right)$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	4.80E-08	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Iron	NA	= (	4.40E-07	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	4.11E-03	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
2,4 Dimethylphenol	NA	= (	7.23E-02	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	9.84E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Anthracene	NA	= (	1.62E-05	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	1.22E-04	= (	9.23E-06	×	1	×	30	×	12	×	9,000	×	7.30E+00	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	1.15E-05	= (	8.72E-06	×	1	×	30	×	12	×	9,000	×	7.30E-01	) ÷ (	70	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	3.34E-06	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	6.05E-07	= (	4.57E-06	×	1	×	30	×	12	×	9,000	×	7.30E-02	) ÷ (	70	×	25,550	)
Chrysene	6.80E-08	= (	5.15E-06	×	1	×	30	×	12	×	9,000	×	7.30E-03	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	3.13E-04	= (	2.37E-05	×	1	×	30	×	12	×	9,000	×	7.30E+00	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	6.21E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	1.99E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	4.29E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.87E-07	= (	1.41E-07	×	1	×	30	×	12	×	9,000	×	7.30E-01	) ÷ (	70	×	25,550	)
m & p-Cresols	NA	= (	4.18E-05	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	2.55E-03	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
o-Cresol	NA	= (	2.83E-05	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Phenanthrene	NA	= (	5.58E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Phenol	NA	= (	1.79E-01	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	1.26E-04	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	1.20E-02	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Benzene	2.28E-03	= (	2.29E-02	×	1	×	30	×	12	×	9,000	×	5.50E-02	) ÷ (	70	×	25,550	)

Attachment I2

Table 16b
Risk Calculations
Adult Wader: Dermal Contact with Surface Water (Non-Linear High Dose) – Carcinogenic Effects
NSP Ashland

$$\text{Derm-Risk} = 1\text{-exp}\left(-\frac{(DA_{event} \times EV \times ED \times EF \times SAwading \times SFabs)}{(BW \times ATc)} \right)$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Ethylbenzene	NA	= (	1.10E-02	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
m & p-Xylenes	NA	= (	1.77E-02	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Toluene	NA	= (	2.16E-02	×	1	×	30	×	12	×	9,000	×	NV	) ÷ (	70	×	25,550	)
Total CR	***2.72E-03***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (calculated using chemical-specific solubility)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 17
Risk Calculations
Adult Wader: Dermal Contact with Surface Water – Noncarcinogenic Effects
NSP Ashland

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SAwading)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
Cyanides	1.01E-05	= (	4.80E-08	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	2.00E-02	)
Iron	NA	= (	4.40E-07	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
2-Methylnaphthalene	4.34E+00	= (	4.11E-03	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	4.00E-03	)
2,4 Dimethylphenol	1.53E+02	= (	7.23E-02	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	2.00E-03	)
Acenaphthylene	NA	= (	9.84E-04	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Anthracene	2.28E-04	= (	1.62E-05	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	9.23E-06	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Benzo(b)fluoranthene	NA	= (	8.72E-06	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Benzo(g,h,i)perylene	NA	= (	3.34E-06	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Benzo(k)fluoranthene	NA	= (	4.57E-06	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Chrysene	NA	= (	5.15E-06	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.37E-05	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Dibenzofuran	1.31E+00	= (	6.21E-04	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	2.00E-03	)
Fluoranthene	2.10E-02	= (	1.99E-04	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	4.00E-02	)
Fluorene	4.54E-02	= (	4.29E-04	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.41E-07	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
m & p-Cresols	NA	= (	4.18E-05	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Naphthalene	5.38E-01	= (	2.55E-03	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	2.00E-02	)
o-Cresol	2.39E-03	= (	2.83E-05	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	5.00E-02	)
Phenanthrene	NA	= (	5.58E-04	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Phenol	2.52E+00	= (	1.79E-01	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	3.00E-01	)
Pyrene	1.77E-02	= (	1.26E-04	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	3.00E-02	)

Attachment I2

Table 17
Risk Calculations
Adult Wader: Dermal Contact with Surface Water – Noncarcinogenic Effects
NSP Ashland

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SAwading)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
1,2,4-Trimethylbenzene	1.02E+00	= (	1.20E-02	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	5.00E-02	)
Benzene	2.42E+01	= (	2.29E-02	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	4.00E-03	)
Ethylbenzene	4.63E-01	= (	1.10E-02	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	1.00E-01	)
m & p-Xylenes	NA	= (	1.77E-02	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	NV	)
Toluene	1.14E+00	= (	2.16E-02	×	1	×	30	×	12	×	9,000	) ÷ (	70	×	10,950	×	8.00E-02	)
Total HI	***1.88E+02***																	

Notes:

Derm-HQ – Dermal Contact with Water Pathway Hazard Quotient
DA_{event} – Absorbed Dose per Event (calculated using chemical-specific solubility)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDabs – Absorbed Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2
Table 18a
Adult Wader Risk Summary (Linear Low Dose)
Reasonable Maximum Exposure

	Carcinogenic Risk							Target Organs	Noncarcinogenic Hazard						
Equation	CR	=	Ingestion	+	Dermal	+	Inhalation		HQ	=	Ingestion	+	Dermal	+	Inhalation
Units	unitless		unitless		unitless		unitless		unitless		unitless		unitless		unitless
Cyanides	NA	=	NA	+	NA	+	NA	*Thyroid, Systemic*	1.02E-05	=	1.13E-08	+	1.01E-05	+	NA
Iron	NA	=	NA	+	NA	+	NA		NA	=	6.89E-09	+	NA	+	NA
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA	*Respiratory*	***4.34E+00***	=	5.78E-05	+	4.34E+00	+	NA
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA	*Systemic*	***1.53E+02***	=	3.70E-02	+	1.53E+02	+	NA
Acenaphthylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Anthracene	NA	=	NA	+	NA	+	NA	*NOAEL*	2.28E-04	=	1.36E-09	+	2.28E-04	+	NA
Benzo(a)pyrene	***1.22E-04***	=	4.76E-11	+	1.22E-04	+	NA		NA	=	NA	+	NA	+	NA
Benzo(b)fluoranthene	***1.15E-05***	=	4.41E-12	+	1.15E-05	+	NA		NA	=	NA	+	NA	+	NA
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Benzo(k)fluoranthene	6.05E-07	=	2.35E-13	+	6.05E-07	+	NA		NA	=	NA	+	NA	+	NA
Chrysene	6.80E-08	=	4.70E-14	+	6.80E-08	+	NA		NA	=	NA	+	NA	+	NA
Dibenzo(a,h)anthracene	***3.14E-04***	=	7.32E-11	+	3.14E-04	+	NA		NA	=	NA	+	NA	+	NA
Dibenzofuran	NA	=	NA	+	NA	+	NA	*Systemic*	***1.31E+00***	=	1.46E-05	+	1.31E+00	+	NA
Fluoranthene	NA	=	NA	+	NA	+	NA	*Systemic, Circulatory*	2.10E-02	=	4.84E-08	+	2.10E-02	+	NA
Fluorene	NA	=	NA	+	NA	+	NA	*Circulatory*	4.54E-02	=	4.65E-07	+	4.54E-02	+	NA
Indeno(1,2,3-cd)pyrene	1.87E-07	=	6.47E-14	+	1.87E-07	+	NA		NA	=	NA	+	NA	+	NA
m & p-Cresols	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Naphthalene	NA	=	NA	+	NA	+	NA	*Respiratory, Systemic*	5.38E-01	=	1.46E-05	+	5.38E-01	+	NA
o-Cresol	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	7.28E-03	=	4.88E-03	+	2.39E-03	+	NA
Phenanthrene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Phenol	NA	=	NA	+	NA	+	NA	*Adrenal*	***2.52E+00***	=	2.59E-03	+	2.52E+00	+	NA
Pyrene	NA	=	NA	+	NA	+	NA	*Systemic*	1.77E-02	=	4.23E-08	+	1.77E-02	+	NA
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	***1.02E+00***	=	1.07E-05	+	1.02E+00	+	NA
Benzene	***2.28E-03***	=	3.87E-07	+	2.28E-03	+	NA	*Circulatory*	***2.42E+01***	=	4.11E-03	+	2.42E+01	+	NA
Ethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, Teratology*	4.63E-01	=	1.59E-05	+	4.63E-01	+	NA
m & p-Xylenes	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	NA	=	NA	+	NA	+	NA
Toluene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	***1.14E+00***	=	6.18E-05	+	1.14E+00	+	NA
Soil CR	***3E-03***	=	4E-07	+	***3E-03***	+	NA	**Soil HI**	***188***	=	0	+	***188***	+	NA

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Target Organ HI	
Respiratory	
Circulatory	
Systemic	
Adrenal	
CNS	
Teratology	
Skin	

Attachment I2
Table 18b
Adult Wader Risk Summary (Non-linear Low Dose)
Reasonable Maximum Exposure

	Carcinogenic Risk							Target Organs	Noncarcinogenic Hazard						
Equation Units	CR unitless	=	Ingestion unitless	+	Dermal unitless	+	Inhalation unitless		HQ unitless	=	Ingestion unitless	+	Dermal unitless	+	Inhalation unitless
Cyanides	NA	=	NA	+	NA	+	NA	*Thyroid, Systemic*	1.02E-05	=	2.82E-08	+	1.01E-05	+	NA
Iron	NA	=	NA	+	NA	+	NA		NA	=	1.72E-08	+	NA	+	NA
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA	*Respiratory*	***4.34E+00***	=	7.05E-05	+	4.34E+00	+	NA
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA	*Systemic*	***1.53E+02***	=	5.64E-05	+	1.53E+02	+	NA
Acenaphthylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Anthracene	NA	=	NA	+	NA	+	NA	*NOAEL*	2.28E-04	=	9.39E-08	+	2.28E-04	+	NA
Benzo(a)pyrene	***1.22E-04***	=	2.94E-08	+	1.22E-04	+	NA		NA	=	NA	+	NA	+	NA
Benzo(b)fluoranthene	***1.15E-05***	=	2.64E-09	+	1.15E-05	+	NA		NA	=	NA	+	NA	+	NA
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Benzo(k)fluoranthene	6.05E-07	=	8.08E-11	+	6.05E-07	+	NA		NA	=	NA	+	NA	+	NA
Chrysene	6.81E-08	=	2.87E-11	+	6.80E-08	+	NA		NA	=	NA	+	NA	+	NA
Dibenzo(a,h)anthracene	***3.13E-04***	=	8.08E-09	+	3.13E-04	+	NA		NA	=	NA	+	NA	+	NA
Dibenzofuran	NA	=	NA	+	NA	+	NA	*Systemic*	***1.31E+00***	=	4.11E-06	+	1.31E+00	+	NA
Fluoranthene	NA	=	NA	+	NA	+	NA	*Systemic, Circulatory*	2.10E-02	=	7.05E-07	+	2.10E-02	+	NA
Fluorene	NA	=	NA	+	NA	+	NA	*Circulatory*	4.54E-02	=	7.05E-07	+	4.54E-02	+	NA
Indeno(1,2,3-cd)pyrene	1.88E-07	=	1.18E-09	+	1.87E-07	+	NA		NA	=	NA	+	NA	+	NA
m & p-Cresols	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Naphthalene	NA	=	NA	+	NA	+	NA	*Respiratory, Systemic*	5.38E-01	=	3.05E-05	+	5.38E-01	+	NA
o-Cresol	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	2.40E-03	=	1.97E-06	+	2.39E-03	+	NA
Phenanthrene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Phenol	NA	=	NA	+	NA	+	NA	*Adrenal*	***2.52E+00***	=	9.39E-08	+	2.52E+00	+	NA
Pyrene	NA	=	NA	+	NA	+	NA	*Systemic*	1.77E-02	=	1.57E-06	+	1.77E-02	+	NA
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	***1.02E+00***	=	2.35E-07	+	1.02E+00	+	NA
Benzene	***2.28E-03***	=	2.44E-08	+	2.28E-03	+	NA	*Circulatory*	***2.42E+01***	=	2.58E-04	+	2.42E+01	+	NA
Ethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, Teratology*	4.63E-01	=	1.29E-07	+	4.63E-01	+	NA
m & p-Xylenes	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	NA	=	NA	+	NA	+	NA
Toluene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	***1.14E+00***	=	5.58E-06	+	1.14E+00	+	NA
Soil CR	***3E-03***	=	7E-08	+	***3E-03***	+	NA	**Soil HI**	***188***	=	4.31E-04	+	***188***	+	NA

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Target Organ HI	
Respiratory	5
Circulatory	24
Systemic	157
Adrenal	3.E+00
CNS	2.E+00
Teratology	5.E-01

Attachment I2
Table 19
Exposure Parameters – Adult Swimmer and Wader

Exposure Pathway	Parameter	Description	Exposure Parameters			
			CTE	Source	RME	Source
Incidental Surface Water Ingestion	$WIR_{swimming}$	Surface Water Ingestion Rate (L/hour)	0.01	(a)	0.05	(b)
	WIR_{wading}	Surface Water Ingestion Rate (L/hour)	0.01	(a)	0.01	(a)
	EF	Exposure Frequency (events/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	12	(e)	12	(e)
	ET	Exposure Time (hours/event)	1 (swimming) 2 (wading)	(f)	1 (swimming) 2 (wading)	(f)
	BW	Body Weight (kg)	47	(g)	47	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	4,380	(l)	4,380	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Dermal Contact with Surface Water	$SA_{swimming}$	Skin Surface Area Exposed (cm^2)	13,533	(k)	13,533	(k)
	SA_{wading}	Skin Surface Area Exposed (cm^2)	6,767	(k)	6,767	(k)
	EF	Exposure Frequency (days/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	12	(e)	12	(e)
	EV	Event Frequency (events/day)	1		1	
	ET	Exposure Time (hours/event)	1 (swimming) 2 (wading)	(f)	1 (swimming) 2 (wading)	(f)
	BW	Body Weight (kg)	47	(g)	47	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	4,380	(l)	4,380	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Incidental Sediment Ingestion	SIR	Sediment Ingestion Rate (mg/hour)	5.60E-02	(m)	2.80E-01	(m)
	CF	Conversion Factor (kg/mg)	1E-06	--	1E-06	--
	EF	Exposure Frequency (days/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	12	(e)	12	(e)
	FI	Fraction Ingested from Contaminated Source (unitless)	1		1	
	BW	Body Weight (kg)	47	(g)	47	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	4,380	(l)	4,380	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)
Dermal Contact with Sediment	SA	Skin Surface Area Exposed (cm^2)	3,259	(n)	4,046	(n)
	SSAF	Soil-to-Skin Adherence Factor (mg/cm^2)	0.5	(o)	1	(o)
	CF	Conversion Factor (kg/mg)	1E-06	--	1E-06	--
	EF	Exposure Frequency (days/year)	6	(c)	12	(d)
	ED	Exposure Duration (years)	12	(e)	12	(e)
	EV	Event Frequency (events/day)	1		1	
	BW	Body Weight (kg)	47	(g)	47	(g)
	ATn	Averaging Time for Noncarcinogenic Effects (days)	4,380	(l)	4,380	(l)
	ATc	Averaging Time Carcinogens (days)	25,550	(h,i, j)	25,550	(h,i, j)

Notes:
CTE - Central Tendency Evaluation
RME - Reasonable Maximum Exposure.

(a) US EPA, 1989. Risk Assessment Guidance for Superfund, Volume I (RAGS, Part A). Value is one-fifth of that assumed to occur during a swimming event.
(b) US EPA, 1989. RAGS Part A. Value for a swimming event.
(c) One event per month for the 6 warmest months of the year.
(d) Two events per month for the 6 warmest months of the year.
(e) The default values for a residential adult, assuming the individual resides in the same residence for 9 (average) or 30 years (upperbound).
(f) US EPA, 1997. Exposure Factors Handbook, Table 1-2. Recommended values for exposure frequency of 1event per month and exposure time of 1 hours per event for swimming. The exposure time of 2 hours per event for wading is based on the estimated time spent on outdoor activities.
(g) US EPA, 1997. Exposure Factors Handbook. Body weight is the average of adult males and females
(h) 70 year lifetime is used to be consistent with the development of cancer slope factors.
(i) US EPA, 1991. Standard Default Exposure Factors. Value for adult.
(j) US EPA, 1989. RAGS, Part A.
(k) Value represents recommended skin surface area (100% for swimmers and 50% for waders).
(l) US EPA, 1989. RAGS, Part A. Averaging Time for noncarcinogens is equal to ED (year) × 365 days/year.
(m) Calculated using the equation: Sediment Ingestion Rate (mg/hour) = Surface water ingestion rate (ml/hour) × total solids (mg/ml). The average total suspended solids is 0.0056 mg/mL.
(n) The RME skin surface area represents the sum of the surface area for forearms, hands, lower legs and feet. The CTE skin surface area represents the sum of the skin surface area for hands, lower legs and feet.
(o) US EPA, 1997. Exposure Factors Handbook, (Table ??). Using loadings for the hands, arms, and legs for the irrigation worker, a weighted soil-to-skin adherence factor of 2.0 mg/cm^2 was calculated. One-half this value (1.0 mg/cm^2) used as RME assuming some

Attachment I2

Table 20
Risk Calculations
Adult Wader: Incidental Ingestion of Surface Water Pathway – Carcinogenic Effects
NSP Ashland

$$\text{Ing-Risk} = \frac{(\text{Cwater} \times \text{WIRwader} \times \text{EF} \times \text{ED} \times \text{ET} \times \text{SFo})}{(\text{BW} \times \text{ATc})}$$

Equation	Ing - Risk	= (	Cwater	×	WIRwader	×	EF	×	ED	×	ET	×	SFo	) ÷ (	BW	×	ATc	)
Units	unitless		mg/L		L/hour		events/year		years		hours/event		kg-day/mg		kg		days	
Cyanides	NA	= (	2.40E-05	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Iron	NA	= (	2.20E-04	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
2-Methylnaphthalene	NA	= (	2.46E-02	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
2,4 Dimethylphenol	NA	= (	7.87E+00	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Acenaphthylene	NA	= (	4.24E-03	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Anthracene	NA	= (	4.34E-05	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Benzo(a)pyrene	2.84E-11	= (	1.62E-06	×	0.01	×	12	×	12	×	2	×	7.30E+00	) ÷ (	47	×	25,550	)
Benzo(b)fluoranthene	2.63E-12	= (	1.50E-06	×	0.01	×	12	×	12	×	2	×	7.30E-01	) ÷ (	47	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	2.60E-07	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Benzo(k)fluoranthene	1.40E-13	= (	8.00E-07	×	0.01	×	12	×	12	×	2	×	7.30E-02	) ÷ (	47	×	25,550	)
Chrysene	2.80E-14	= (	1.60E-06	×	0.01	×	12	×	12	×	2	×	7.30E-03	) ÷ (	47	×	25,550	)
Dibenzo(a,h)anthracene	4.36E-11	= (	2.49E-06	×	0.01	×	12	×	12	×	2	×	7.30E+00	) ÷ (	47	×	25,550	)
Dibenzofuran	NA	= (	3.10E-03	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Fluoranthene	NA	= (	2.06E-04	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Fluorene	NA	= (	1.98E-03	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	3.85E-14	= (	2.20E-08	×	0.01	×	12	×	12	×	2	×	7.30E-01	) ÷ (	47	×	25,550	)
m & p-Cresols	NA	= (	2.27E+01	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Naphthalene	NA	= (	3.10E-02	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
o-Cresol	NA	= (	2.60E+01	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Phenanthrene	NA	= (	1.15E-03	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Phenol	NA	= (	8.28E+01	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Pyrene	NA	= (	1.35E-04	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	5.70E-02	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)

Attachment I2

Table 20
Risk Calculations
Adult Wader: Incidental Ingestion of Surface Water Pathway – Carcinogenic Effects
NSP Ashland

$$\text{Ing-Risk} = \frac{(\text{Cwater} \times \text{WIRwader} \times \text{EF} \times \text{ED} \times \text{ET} \times \text{SFo})}{(\text{BW} \times \text{ATc})}$$

Equation		Ing - Risk	= (	Cwater	×	WIRwader	×	EF	×	ED	×	ET	×	SFo	) ÷ (	BW	×	ATc	)
Units		unitless		mg/L		L/hour		events/year		years		hours/event		kg-day/mg		kg		days	
Benzene		2.31E-07	= (	1.75E+00	×	0.01	×	12	×	12	×	2	×	5.50E-02	) ÷ (	47	×	25,550	)
Ethylbenzene		NA	= (	1.69E-01	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
m & p-Xylenes		NA	= (	1.85E-01	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
Toluene		NA	= (	5.26E-01	×	0.01	×	12	×	12	×	2	×	NV	) ÷ (	47	×	25,550	)
	Total CR	***2.31E-07***																	

Notes:

Ing-Risk – Carcinogenic Risk Water Ingestion Pathway
Cwater – Concentration in Water (Based on chemical-specific solubility)
WIR – Water Ingestion Rate
EF – Exposure Frequency
ED – Exposure Duration
SFo – Oral Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 21
Risk Calculations
Adult Wader: Incidental Ingestion of Surface Water Pathway – Noncarcinogenic Effects
NSP Ashland

$$\text{Inh-HQ} = \frac{(\text{Cwater} \times \text{WIRwader} \times \text{EF} \times \text{ED} \times \text{ET})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation	Ing - HQ	= (	Cwater	×	WIRwader	×	EF	×	ED	×	ET	) ÷ (	BW	×	ATn	×	RfDo	)
Units	unitless		mg/L		L/hour		days/year		years		hours/event		kg		days		mg/kg-day	
Cyanides	1.68E-08	= (	2.40E-05	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	2.00E-02	)
Iron	1.03E-08	= (	2.20E-04	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	3.00E-01	)
2-Methylnaphthalene	8.60E-05	= (	2.46E-02	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	4.00E-03	)
2,4 Dimethylphenol	5.51E-02	= (	7.87E+00	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	2.00E-03	)
Acenaphthylene	NA	= (	4.24E-03	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Anthracene	2.02E-09	= (	4.34E-05	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	1.62E-06	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Benzo(b)fluoranthene	NA	= (	1.50E-06	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Benzo(g,h,i)perylene	NA	= (	2.60E-07	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Benzo(k)fluoranthene	NA	= (	8.00E-07	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Chrysene	NA	= (	1.60E-06	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.49E-06	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Dibenzofuran	2.17E-05	= (	3.10E-03	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	2.00E-03	)
Fluoranthene	7.20E-08	= (	2.06E-04	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	4.00E-02	)
Fluorene	6.93E-07	= (	1.98E-03	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	2.20E-08	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
m & p-Cresols	NA	= (	2.27E+01	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Naphthalene	2.17E-05	= (	3.10E-02	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	2.00E-02	)
o-Cresol	7.27E-03	= (	2.60E+01	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	5.00E-02	)
Phenanthrene	NA	= (	1.15E-03	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Phenol	3.86E-03	= (	8.28E+01	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	3.00E-01	)
Pyrene	6.30E-08	= (	1.35E-04	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	3.00E-02	)
1,2,4-Trimethylbenzene	1.59E-05	= (	5.70E-02	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	5.00E-02	)

Attachment I2

Table 21
Risk Calculations
Adult Wader: Incidental Ingestion of Surface Water Pathway – Noncarcinogenic Effects
NSP Ashland

$$\text{Inh-HQ} = \frac{(\text{Cwater} \times \text{WIRwader} \times \text{EF} \times \text{ED} \times \text{ET})}{(\text{BW} \times \text{ATn} \times \text{RfDo})}$$

Equation Units	Ing - HQ unitless	= (	Cwater mg/L	×	WIRwader L/hour	×	EF days/year	×	ED years	×	ET hours/event	) ÷ (	BW kg	×	ATn days	×	RfDo mg/kg-day	)
Benzene	6.12E-03	= (	1.75E+00	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	4.00E-03	)
Ethylbenzene	2.36E-05	= (	1.69E-01	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	1.00E-01	)
m & p-Xylenes	NA	= (	1.85E-01	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	NV	)
Toluene	9.20E-05	= (	5.26E-01	×	0.01	×	12	×	12	×	2	) ÷ (	47	×	4,380	×	8.00E-02	)
Total HI	***7.26E-02***																	

Notes:

Ing-HQ – Water Ingestion Pathway Hazard Quotient
Cwater – Concentration in Water (Based on chemical-specific solubility)
WIR – Water Ingestion Rate
EF – Exposure Frequency
ED – Exposure Duration
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDo – Oral Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 22a
Risk Calculations
Adult Wader: Dermal Contact with Surface Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year)

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SAwading \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	4.80E-08	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Iron	NA	= (	4.40E-07	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
2-Methylnaphthalene	NA	= (	4.11E-03	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
2,4 Dimethylphenol	NA	= (	7.23E-02	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Acenaphthylene	NA	= (	9.84E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Anthracene	NA	= (	1.62E-05	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Benzo(a)pyrene	5.47E-05	= (	9.23E-06	×	1	×	12	×	12	×	6,767	×	7.30E+00	) ÷ (	47	×	25,550	)
Benzo(b)fluoranthene	5.17E-06	= (	8.72E-06	×	1	×	12	×	12	×	6,767	×	7.30E-01	) ÷ (	47	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	3.34E-06	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Benzo(k)fluoranthene	2.71E-07	= (	4.57E-06	×	1	×	12	×	12	×	6,767	×	7.30E-02	) ÷ (	47	×	25,550	)
Chrysene	3.05E-08	= (	5.15E-06	×	1	×	12	×	12	×	6,767	×	7.30E-03	) ÷ (	47	×	25,550	)
Dibenzo(a,h)anthracene	1.40E-04	= (	2.37E-05	×	1	×	12	×	12	×	6,767	×	7.30E+00	) ÷ (	47	×	25,550	)
Dibenzofuran	NA	= (	6.21E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Fluoranthene	NA	= (	1.99E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Fluorene	NA	= (	4.29E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	8.38E-08	= (	1.41E-07	×	1	×	12	×	12	×	6,767	×	7.30E-01	) ÷ (	47	×	25,550	)
m & p-Cresols	NA	= (	4.18E-05	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Naphthalene	NA	= (	2.55E-03	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
o-Cresol	NA	= (	2.83E-05	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Phenanthrene	NA	= (	5.58E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Phenol	NA	= (	1.79E-01	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Pyrene	NA	= (	1.26E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	1.20E-02	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)

Attachment I2

Table 22a
Risk Calculations
Adult Wader: Dermal Contact with Surface Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year)

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SAwading \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Benzene	1.02E-03	= (	2.29E-02	×	1	×	12	×	12	×	6,767	×	5.50E-02	) ÷ (	47	×	25,550	)
Ethylbenzene	NA	= (	1.10E-02	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
m & p-Xylenes	NA	= (	1.77E-02	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Toluene	NA	= (	2.16E-02	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Total CR	***1.22E-03***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (calculated using chemical-specific solubility)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 22b
Risk Calculations
Adult Wader: Dermal Contact with Surface Water (Non-Linear High Dose) – Carcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year))

$$\text{Derm-Risk} = 1\text{-exp}\left(-\frac{(DA_{event} \times EV \times ED \times EF \times SAwading \times SFabs)}{(BW \times ATc)}\right)$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	4.80E-08	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Iron	NA	= (	4.40E-07	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
2-Methylnaphthalene	NA	= (	4.11E-03	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
2,4 Dimethylphenol	NA	= (	7.23E-02	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Acenaphthylene	NA	= (	9.84E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Anthracene	NA	= (	1.62E-05	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Benzo(a)pyrene	5.47E-05	= (	9.23E-06	×	1	×	12	×	12	×	6,767	×	7.30E+00	) ÷ (	47	×	25,550	)
Benzo(b)fluoranthene	5.17E-06	= (	8.72E-06	×	1	×	12	×	12	×	6,767	×	7.30E-01	) ÷ (	47	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	3.34E-06	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Benzo(k)fluoranthene	2.71E-07	= (	4.57E-06	×	1	×	12	×	12	×	6,767	×	7.30E-02	) ÷ (	47	×	25,550	)
Chrysene	3.05E-08	= (	5.15E-06	×	1	×	12	×	12	×	6,767	×	7.30E-03	) ÷ (	47	×	25,550	)
Dibenzo(a,h)anthracene	1.40E-04	= (	2.37E-05	×	1	×	12	×	12	×	6,767	×	7.30E+00	) ÷ (	47	×	25,550	)
Dibenzofuran	NA	= (	6.21E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Fluoranthene	NA	= (	1.99E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Fluorene	NA	= (	4.29E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Indeno(1,2,3-cd)pyrene	8.38E-08	= (	1.41E-07	×	1	×	12	×	12	×	6,767	×	7.30E-01	) ÷ (	47	×	25,550	)
m & p-Cresols	NA	= (	4.18E-05	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Naphthalene	NA	= (	2.55E-03	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
o-Cresol	NA	= (	2.83E-05	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Phenanthrene	NA	= (	5.58E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Phenol	NA	= (	1.79E-01	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Pyrene	NA	= (	1.26E-04	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	1.20E-02	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Benzene	1.02E-03	= (	2.29E-02	×	1	×	12	×	12	×	6,767	×	5.50E-02	) ÷ (	47	×	25,550	)

Attachment I2

Table 22b
Risk Calculations
Adult Wader: Dermal Contact with Surface Water (Non-Linear High Dose) – Carcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year))

$$\text{Derm-Risk} = 1\text{-exp}\left(-\frac{(DA_{event} \times EV \times ED \times EF \times SAwading \times SFabs)}{(BW \times ATc)} \right)$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Ethylbenzene	NA	= (	1.10E-02	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
m & p-Xylenes	NA	= (	1.77E-02	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Toluene	NA	= (	2.16E-02	×	1	×	12	×	12	×	6,767	×	NV	) ÷ (	47	×	25,550	)
Total CR	***1.22E-03***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (calculated using chemical-specific solubility)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 23
Risk Calculations
Adult Wader: Dermal Contact with Surface Water – Noncarcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year)

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SAwading)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
Cyanides	1.14E-05	= (	4.80E-08	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	2.00E-02	)
Iron	NA	= (	4.40E-07	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
2-Methylnaphthalene	4.86E+00	= (	4.11E-03	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	4.00E-03	)
2,4 Dimethylphenol	1.71E+02	= (	7.23E-02	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	2.00E-03	)
Acenaphthylene	NA	= (	9.84E-04	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Anthracene	2.55E-04	= (	1.62E-05	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	9.23E-06	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Benzo(b)fluoranthene	NA	= (	8.72E-06	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Benzo(g,h,i)perylene	NA	= (	3.34E-06	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Benzo(k)fluoranthene	NA	= (	4.57E-06	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Chrysene	NA	= (	5.15E-06	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.37E-05	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Dibenzofuran	1.47E+00	= (	6.21E-04	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	2.00E-03	)
Fluoranthene	2.36E-02	= (	1.99E-04	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	4.00E-02	)
Fluorene	5.08E-02	= (	4.29E-04	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.41E-07	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
m & p-Cresols	NA	= (	4.18E-05	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Naphthalene	6.03E-01	= (	2.55E-03	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	2.00E-02	)
o-Cresol	2.68E-03	= (	2.83E-05	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	5.00E-02	)
Phenanthrene	NA	= (	5.58E-04	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Phenol	2.82E+00	= (	1.79E-01	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	3.00E-01	)
Pyrene	1.98E-02	= (	1.26E-04	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	3.00E-02	)

Attachment I2

Table 23
Risk Calculations
Adult Wader: Dermal Contact with Surface Water – Noncarcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year)

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SAwading)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SAwading	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
1,2,4-Trimethylbenzene	1.14E+00	= (	1.20E-02	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	5.00E-02	)
Benzene	2.71E+01	= (	2.29E-02	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	4.00E-03	)
Ethylbenzene	5.19E-01	= (	1.10E-02	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	1.00E-01	)
m & p-Xylenes	NA	= (	1.77E-02	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	NV	)
Toluene	1.28E+00	= (	2.16E-02	×	1	×	12	×	12	×	6,767	) ÷ (	47	×	4,380	×	8.00E-02	)
Total HI	***2.11E+02***																	

Notes:

Derm-HQ – Dermal Contact with Water Pathway Hazard Quotient
DA_{event} – Absorbed Dose per Event (calculated using chemical-specific solubility)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDabs – Absorbed Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2
Table 24a
Adolescent Wader Risk Summary (Linear Low Dose)
Reasonable Maximum Exposure

	Carcinogenic Risk							Target Organs	Noncarcinogenic Hazard						
Equation Units	CR unitless	=	Ingestion unitless	+	Dermal unitless	+	Inhalation unitless		HQ unitless	=	Ingestion unitless	+	Dermal unitless	+	Inhalation unitless
Cyanides	NA	=	NA	+	NA	+	NA	*Thyroid, Systemic*	1.14E-05	=	1.68E-08	+	1.14E-05	+	NA
Iron	NA	=	NA	+	NA	+	NA		NA	=	1.03E-08	+	NA	+	NA
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA	*Respiratory*	***4.86E+00***	=	8.60E-05	+	4.86E+00	+	NA
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA	*Systemic*	***1.71E+02***	=	5.51E-02	+	1.71E+02	+	NA
Acenaphthylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Anthracene	NA	=	NA	+	NA	+	NA	*NOAEL*	2.55E-04	=	2.02E-09	+	2.55E-04	+	NA
Benzo(a)pyrene	***5.47E-05***	=	2.84E-11	+	5.47E-05	+	NA		NA	=	NA	+	NA	+	NA
Benzo(b)fluoranthene	5.17E-06	=	2.63E-12	+	5.17E-06	+	NA		NA	=	NA	+	NA	+	NA
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Benzo(k)fluoranthene	2.71E-07	=	1.40E-13	+	2.71E-07	+	NA		NA	=	NA	+	NA	+	NA
Chrysene	3.05E-08	=	2.80E-14	+	3.05E-08	+	NA		NA	=	NA	+	NA	+	NA
Dibenzo(a,h)anthracene	***1.40E-04***	=	4.36E-11	+	1.40E-04	+	NA		NA	=	NA	+	NA	+	NA
Dibenzofuran	NA	=	NA	+	NA	+	NA	*Systemic*	***1.47E+00***	=	2.17E-05	+	1.47E+00	+	NA
Fluoranthene	NA	=	NA	+	NA	+	NA	*Systemic, Circulatory*	2.36E-02	=	7.20E-08	+	2.36E-02	+	NA
Fluorene	NA	=	NA	+	NA	+	NA	*Circulatory*	5.08E-02	=	6.93E-07	+	5.08E-02	+	NA
Indeno(1,2,3-cd)pyrene	8.38E-08	=	3.85E-14	+	8.38E-08	+	NA		NA	=	NA	+	NA	+	NA
m & p-Cresols	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Naphthalene	NA	=	NA	+	NA	+	NA	*Respiratory, Systemic*	6.03E-01	=	2.17E-05	+	6.03E-01	+	NA
o-Cresol	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	9.96E-03	=	7.27E-03	+	2.68E-03	+	NA
Phenanthrene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Phenol	NA	=	NA	+	NA	+	NA	*Adrenal*	***2.82E+00***	=	3.86E-03	+	2.82E+00	+	NA
Pyrene	NA	=	NA	+	NA	+	NA	*Systemic*	1.98E-02	=	6.30E-08	+	1.98E-02	+	NA
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	***1.14E+00***	=	1.59E-05	+	1.14E+00	+	NA
Benzene	***1.02E-03***	=	2.31E-07	+	1.02E-03	+	NA	*Circulatory*	***2.71E+01***	=	6.12E-03	+	2.71E+01	+	NA
Ethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, Teratology*	5.19E-01	=	2.36E-05	+	5.19E-01	+	NA
m & p-Xylenes	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	NA	=	NA	+	NA	+	NA
Toluene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	***1.28E+00***	=	9.20E-05	+	1.28E+00	+	NA
Soil CR	***1E-03***	=	2E-07	+	***1E-03***	+	NA	**Soil HI**	***211***	=	7.26E-02	+	***211***	+	NA

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Target Organ HI

Respiratory	5
Circulatory	27
Systemic	176
Adrenal	3.E+00
CNS	2.E+00
Teratology	5.E-01

Attachment I2
Table 24b
Adolescent Wader Risk Summary (Non-linear Low Dose)
Reasonable Maximum Exposure

	Carcinogenic Risk							Target Organs	Noncarcinogenic Hazard						
Equation	CR	=	Ingestion	+	Dermal	+	Inhalation		HQ	=	Ingestion	+	Dermal	+	Inhalation
Units	unitless		unitless		unitless		unitless		unitless		unitless		unitless		unitless
Cyanides	NA	=	NA	+	NA	+	NA	*Thyroid, Systemic*	1.14E-05	=	1.68E-08	+	1.14E-05	+	NA
Iron	NA	=	NA	+	NA	+	NA		NA	=	1.03E-08	+	NA	+	NA
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA	*Respiratory*	***4.86E+00***	=	8.60E-05	+	4.86E+00	+	NA
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA	*Systemic*	***1.71E+02***	=	5.51E-02	+	1.71E+02	+	NA
Acenaphthylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Anthracene	NA	=	NA	+	NA	+	NA	*NOAEL*	2.55E-04	=	2.02E-09	+	2.55E-04	+	NA
Benzo(a)pyrene	***5.47E-05***	=	2.84E-11	+	5.47E-05	+	NA		NA	=	NA	+	NA	+	NA
Benzo(b)fluoranthene	5.17E-06	=	2.63E-12	+	5.17E-06	+	NA		NA	=	NA	+	NA	+	NA
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Benzo(k)fluoranthene	2.71E-07	=	1.40E-13	+	2.71E-07	+	NA		NA	=	NA	+	NA	+	NA
Chrysene	3.05E-08	=	2.80E-14	+	3.05E-08	+	NA		NA	=	NA	+	NA	+	NA
Dibenzo(a,h)anthracene	***1.40E-04***	=	4.36E-11	+	1.40E-04	+	NA		NA	=	NA	+	NA	+	NA
Dibenzofuran	NA	=	NA	+	NA	+	NA	*Systemic*	***1.47E+00***	=	2.17E-05	+	1.47E+00	+	NA
Fluoranthene	NA	=	NA	+	NA	+	NA	*Systemic, Circulatory*	2.36E-02	=	7.20E-08	+	2.36E-02	+	NA
Fluorene	NA	=	NA	+	NA	+	NA	*Circulatory*	5.08E-02	=	6.93E-07	+	5.08E-02	+	NA
Indeno(1,2,3-cd)pyrene	8.38E-08	=	3.85E-14	+	8.38E-08	+	NA		NA	=	NA	+	NA	+	NA
m & p-Cresols	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Naphthalene	NA	=	NA	+	NA	+	NA	*Respiratory, Systemic*	6.03E-01	=	2.17E-05	+	6.03E-01	+	NA
o-Cresol	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	9.96E-03	=	7.27E-03	+	2.68E-03	+	NA
Phenanthrene	NA	=	NA	+	NA	+	NA		NA	=	NA	+	NA	+	NA
Phenol	NA	=	NA	+	NA	+	NA	*Adrenal*	***2.82E+00***	=	3.86E-03	+	2.82E+00	+	NA
Pyrene	NA	=	NA	+	NA	+	NA	*Systemic*	1.98E-02	=	6.30E-08	+	1.98E-02	+	NA
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	***1.14E+00***	=	1.59E-05	+	1.14E+00	+	NA
Benzene	***1.02E-03***	=	2.31E-07	+	1.02E-03	+	NA	*Circulatory*	***2.71E+01***	=	6.12E-03	+	2.71E+01	+	NA
Ethylbenzene	NA	=	NA	+	NA	+	NA	*Systemic, Teratology*	5.19E-01	=	2.36E-05	+	5.19E-01	+	NA
m & p-Xylenes	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	NA	=	NA	+	NA	+	NA
Toluene	NA	=	NA	+	NA	+	NA	*Systemic, CNS*	***1.28E+00***	=	9.20E-05	+	1.28E+00	+	NA
Soil CR	***1E-03***	=	2E-07	+	***1E-03***	+	NA	**Soil HI**	***211***	=	7.26E-02	+	***211***	+	NA

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Target Organ HI

Respiratory	5
Circulatory	27
Systemic	176
Adrenal	3.E+00
CNS	2.E+00
Teratology	5.E-01

Attachment I2

Table 25
Exposure Parameters – Construction Worker

Exposure Pathway	Parameter	Description	Exposure Parameters			
			CTE	Source	RME	Source
Incidental Soil Ingestion	IR	Soil Ingestion Rate (mg/day)	100	(a)	330	(b)
	EF	Exposure Frequency (days/year)	219	(c)	250	(d)
	ED	Exposure Duration (years)	1	(e)	0.5	(e)
	FI	Fraction Ingested (unitless)	1	(f)	1	(f)
	BW	Body Weight (kg)	70	(g,h,i)	70	(g,h,i)
	ATnc	Averaging Time for Noncarcinogenic Effects (days)	365	(j)	183	(j)
	ATc	Averaging Time for Carcinogenic Effects (days)	25,550	(g,h,i)	25,550	(g,h,i)
Dermal Contact with Soil	SA	Skin Surface Area Exposed (cm^2)	1,930	(k)	3,300	(k)
	SSAF	Soil-to-Skin Adherence Factor (mg/cm^2)	0.1	(l)	0.3	(l)
	CF	Conversion Factor (kg/mg)	1E-06	–	1E-06	–
	EF	Exposure Frequency (days/year)	219	(c)	250	(d)
	ED	Exposure Duration (years)	1	(e)	0.5	(e)
	EV	Event Frequency (events/day)	1	(m)	1	(m)
	BW	Body Weight (kg)	70	(g,h,i)	70	(g,h,i)
	ATnc	Averaging Time for Noncarcinogenic Effects (days)	365	(j)	183	(j)
	ATc	Averaging Time for Carcinogenic Effects (days)	25,550	(g,h,i)	25,550	(g,h,i)
Inhalation of Soil Derived Chemicals or Groundwater VOCs	IR	Inhalation Rate (m^3/hour)	1.3	(n)	2.5	(o)
	ET	Exposure Time (hour/day)	8	(p)	8	(p)
	EF	Exposure Frequency (days/year)	219	(c)	250	(d)
	ED	Exposure Duration (years)	1	(e)	1	(e)
	BW	Body Weight (kg)	70	(g,h,i)	70	(g,h,i)
	PEF	Particulate Emission Factor (m^3/kg)	1.32E+09	See Table 21e	1.32E+09	See Table 21e
	VF	Volatilization Factor (m^3/kg)	Calculated	See Table 21c	Calculated	See Table 21c
	ATnc	Averaging Time for Noncarcinogenic Effects (days)	365	(j)	183	(j)
	ATc	Averaging Time for Carcinogenic Effects (days)	25,550	(g,h,i)	25,550	(g,h,i)

Notes:
CTE - Central Tendency Evaluation
RME - Reasonable Maximum Exposure.

(a) US EPA, 2002. Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites, Exhibit 1-2. Value for outdoor workers.
(b) US EPA, 2002, Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites, Exhibit 1-2. Recommended ingestion rate for construction workers.
(c) In the absence of Site-specific information regarding future construction activities, the default industrial worker exposure frequency was used.
(d) In the absence of Site-specific information regarding future construction activities, the default industrial worker exposure frequency was used.
(e) Construction activities are assumed to occur over a 1 year period.
(f) Based on information provided in the HHRA completed by SEH (SEH, 1998) an FI of 1 was selected as the fraction ingested based on the percentage of chemical detections in subsurface soil.
(g) US EPA, 1991. Human Health Evaluation Manual, Supplemental Guidance, Standard Default Exposure Factors.
(h) US EPA, 1989. RAGS, Volume I, Human Health Evaluation Manual (Part A).
(i) 70 kg body weight and 70 year lifetime are used to be consistent with the development of cancer slope factors.
(j) US EPA, 1989. RAGS, Part A. Averaging Time for noncarcinogens is equal to ED (year) × 365 days/year.
(k) Suggested value represents the total skin surface area for head and hands, assuming that a worker wears long sleeve shirts, long pants and shoes. This value may be adjusted based on the following body part-specific surface area (mean, in cm^2), as provided in Table 6-4 of the Exposure Factors Handbook (US EPA, 1997). The skin surface area of 3,300 cm^2 is recommended by USEPA for industrial workers (Exhibit 3-5, RAGS, Part E, USEPA, 2004).

	Men	Women
Head	1,180	1,100
Hands	840	746
Forearms	1,140	1,360
Lower Legs	2,070	1,940
Feet	1,120	975

(l) USEPA, 2004. RAGS Part E, Exhibit 3-3. Recommended default values for a construction worker.
(m) USEPA, 2004. RAGS Part E, Exhibit 3-5. Recommended RME and CTE parameters for industrial scenario.
(n) US EPA, 1997. Exposure Factors Handbook, Volume 1, Table 5-23. Short-term exposures for outdoor workers, moderate activity.
(o) US EPA, 1997. Exposure Factors Handbook, Volume 1, Table 5-23. Hourly average for short-term exposures for outdoor workers.
(p) US EPA, 1997. Exposure Factors Handbook, Table 15-68. Represents the 50th percentile value for time spent at work (males and females, all ages).
(q) Chemical-specific PEF calculated using methodology. Calculated PEFs for construction workers are presented on Table 21e.

Attachment I2

Table 26
Risk Calculations
Construction Worker: Dermal Contact with Ground Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year)

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SA \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SA	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	1.92E-07	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Iron	NA	= (	1.76E-06	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	8.22E-03	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
2,4 Dimethylphenol	NA	= (	1.45E-01	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	1.97E-03	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Anthracene	NA	= (	3.23E-05	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	1.77E-05	= (	1.05E-05	×	1	×	0.5	×	250	×	3,300	×	7.30E+00	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	1.67E-06	= (	9.91E-06	×	1	×	0.5	×	250	×	3,300	×	7.30E-01	) ÷ (	70	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	3.55E-06	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	8.77E-08	= (	5.21E-06	×	1	×	0.5	×	250	×	3,300	×	7.30E-02	) ÷ (	70	×	25,550	)
Chrysene	1.07E-08	= (	6.36E-06	×	1	×	0.5	×	250	×	3,300	×	7.30E-03	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	4.20E-05	= (	2.50E-05	×	1	×	0.5	×	250	×	3,300	×	7.30E+00	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	1.24E-03	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	3.98E-04	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	8.58E-04	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	2.56E-08	= (	1.52E-07	×	1	×	0.5	×	250	×	3,300	×	7.30E-01	) ÷ (	70	×	25,550	)
m & p-Cresols	NA	= (	8.36E-05	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	5.09E-03	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
o-Cresol	NA	= (	3.51E-01	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Phenanthrene	NA	= (	1.12E-03	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Phenol	NA	= (	3.57E-01	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	2.51E-04	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	2.40E-02	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)

Attachment I2

Table 26
Risk Calculations
Construction Worker: Dermal Contact with Ground Water (Linear Low-Dose) – Carcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year)

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SA \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SA	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Benzene	5.80E-04	= (	4.57E-02	×	1	×	0.5	×	250	×	3,300	×	5.50E-02	) ÷ (	70	×	25,550	)
Ethylbenzene	NA	= (	2.19E-02	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
m & p-Xylenes	NA	= (	3.53E-02	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Toluene	NA	= (	4.33E-02	×	1	×	0.5	×	250	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Total CR	***6.42E-04***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (calculated using chemical-specific solubility)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 27
Risk Calculations
Construction Worker: Dermal Contact with Ground Water – Noncarcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year)

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SA)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SA	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
Cyanides	3.10E-04	= (	1.92E-07	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	2.00E-02	)
Iron	NA	= (	1.76E-06	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
2-Methylnaphthalene	6.64E+01	= (	8.22E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	4.00E-03	)
2,4 Dimethylphenol	2.33E+03	= (	1.45E-01	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	2.00E-03	)
Acenaphthylene	NA	= (	1.97E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Anthracene	3.48E-03	= (	3.23E-05	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	1.05E-05	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Benzo(b)fluoranthene	NA	= (	9.91E-06	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Benzo(g,h,i)perylene	NA	= (	3.55E-06	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Benzo(k)fluoranthene	NA	= (	5.21E-06	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Chrysene	NA	= (	6.36E-06	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.50E-05	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Dibenzofuran	2.01E+01	= (	1.24E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	2.00E-03	)
Fluoranthene	3.21E-01	= (	3.98E-04	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	4.00E-02	)
Fluorene	6.93E-01	= (	8.58E-04	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.52E-07	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
m & p-Cresols	NA	= (	8.36E-05	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Naphthalene	8.22E+00	= (	5.09E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	2.00E-02	)
o-Cresol	**2.26E+02**	= (	3.51E-01	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	5.00E-02	)
Phenanthrene	NA	= (	1.12E-03	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Phenol	3.84E+01	= (	3.57E-01	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	3.00E-01	)
Pyrene	2.70E-01	= (	2.51E-04	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	3.00E-02	)

Attachment I2

Table 27
Risk Calculations
Construction Worker: Dermal Contact with Ground Water – Noncarcinogenic Effects
NSP Ashland
(Exposure Frequency = 250 Days/Year)

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SA)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SA	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
1,2,4-Trimethylbenzene	1.55E+01	= (	2.40E-02	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	5.00E-02	)
Benzene	3.69E+02	= (	4.57E-02	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	4.00E-03	)
Ethylbenzene	7.08E+00	= (	2.19E-02	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	1.00E-01	)
m & p-Xylenes	NA	= (	3.53E-02	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	NV	)
Toluene	1.75E+01	= (	4.33E-02	×	1	×	0.5	×	250	×	3,300	) ÷ (	70	×	183	×	8.00E-02	)
Total HI	***3.10E+03***																	

Notes:

Derm-HQ – Dermal Contact with Water Pathway Hazard Quotient
DA_{event} – Absorbed Dose per Event (calculated using chemical-specific solubility)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDabs – Absorbed Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2
Table 28
Construction Worker Risk Summary
Reasonable Maximum Exposure

	Carcinogenic Risk								Target Organs	Noncarcinogenic Hazard							
Equation	CR	=	Ingestion	+	Dermal	+	Inhalation			HQ	=	Ingestion	+	Dermal	+	Inhalation	
Units	unitless		unitless		unitless		unitless			unitless		unitless		unitless		unitless	
Cyanides	NA	=	NA	+	NA	+	NA			3.10E-04	=	NA	+	3.10E-04	+	NA	
Iron	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA			6.64E+01	=	NA	+	6.64E+01	+	NA	
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA			2.33E+03	=	NA	+	2.33E+03	+	NA	
Acenaphthylene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Anthracene	NA	=	NA	+	NA	+	NA			3.48E-03	=	NA	+	3.48E-03	+	NA	
Benzo(a)pyrene	1.77E-05	=	NA	+	1.77E-05	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(b)fluoranthene	1.67E-06	=	NA	+	1.67E-06	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(k)fluoranthene	8.77E-08	=	NA	+	8.77E-08	+	NA			NA	=	NA	+	NA	+	NA	
Chrysene	1.07E-08	=	NA	+	1.07E-08	+	NA			NA	=	NA	+	NA	+	NA	
Dibenzo(a,h)anthracene	4.20E-05	=	NA	+	4.20E-05	+	NA			NA	=	NA	+	NA	+	NA	
Dibenzofuran	NA	=	NA	+	NA	+	NA			2.01E+01	=	NA	+	2.01E+01	+	NA	
Fluoranthene	NA	=	NA	+	NA	+	NA			3.21E-01	=	NA	+	3.21E-01	+	NA	
Fluorene	NA	=	NA	+	NA	+	NA			6.93E-01	=	NA	+	6.93E-01	+	NA	
Indeno(1,2,3-cd)pyrene	2.56E-08	=	NA	+	2.56E-08	+	NA			NA	=	NA	+	NA	+	NA	
m & p-Cresols	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Naphthalene	NA	=	NA	+	NA	+	NA			8.22E+00	=	NA	+	8.22E+00	+	NA	
o-Cresol	NA	=	NA	+	NA	+	NA			2.26E+02	=	NA	+	2.26E+02	+	NA	
Phenanthrene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Phenol	NA	=	NA	+	NA	+	NA			3.84E+01	=	NA	+	3.84E+01	+	NA	
Pyrene	NA	=	NA	+	NA	+	NA			2.70E-01	=	NA	+	2.70E-01	+	NA	
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA			1.55E+01	=	NA	+	1.55E+01	+	NA	
Benzene	5.80E-04	=	NA	+	5.80E-04	+	NA			3.69E+02	=	NA	+	3.69E+02	+	NA	
Ethylbenzene	NA	=	NA	+	NA	+	NA			7.08E+00	=	NA	+	7.08E+00	+	NA	
m & p-Xylenes	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Toluene	NA	=	NA	+	NA	+	NA			1.75E+01	=	NA	+	1.75E+01	+	NA	
Soil CR	***6E-04***	=	NA	+	***6E-04***	+	NA		**Soil HI**	***3104***	=	NA	+	***3104***	+	NA	

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Attachment I2

Table 29
Risk Calculations
Construction Worker: Dermal Contact with Ground Water (Linear-Low Dose) – Carcinogenic Effects
NSP Ashland
(Exposure Frequency = 1 Day/Year))

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SA \times SFabs)}{(BW \times ATc)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SA	×	SFabs	) ÷ (	BW	×	ATc	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg-day/mg		kg		days	
Cyanides	NA	= (	1.92E-07	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Iron	NA	= (	1.76E-06	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
2-Methylnaphthalene	NA	= (	8.22E-03	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
2,4 Dimethylphenol	NA	= (	1.45E-01	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Acenaphthylene	NA	= (	1.97E-03	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Anthracene	NA	= (	3.23E-05	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Benzo(a)pyrene	7.09E-08	= (	1.05E-05	×	1	×	0.5	×	1	×	3,300	×	7.30E+00	) ÷ (	70	×	25,550	)
Benzo(b)fluoranthene	6.68E-09	= (	9.91E-06	×	1	×	0.5	×	1	×	3,300	×	7.30E-01	) ÷ (	70	×	25,550	)
Benzo(g,h,i)perylene	NA	= (	3.55E-06	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Benzo(k)fluoranthene	3.51E-10	= (	5.21E-06	×	1	×	0.5	×	1	×	3,300	×	7.30E-02	) ÷ (	70	×	25,550	)
Chrysene	4.28E-11	= (	6.36E-06	×	1	×	0.5	×	1	×	3,300	×	7.30E-03	) ÷ (	70	×	25,550	)
Dibenzo(a,h)anthracene	1.68E-07	= (	2.50E-05	×	1	×	0.5	×	1	×	3,300	×	7.30E+00	) ÷ (	70	×	25,550	)
Dibenzofuran	NA	= (	1.24E-03	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Fluoranthene	NA	= (	3.98E-04	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Fluorene	NA	= (	8.58E-04	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Indeno(1,2,3-cd)pyrene	1.02E-10	= (	1.52E-07	×	1	×	0.5	×	1	×	3,300	×	7.30E-01	) ÷ (	70	×	25,550	)
m & p-Cresols	NA	= (	8.36E-05	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Naphthalene	NA	= (	5.09E-03	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
o-Cresol	NA	= (	3.51E-01	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Phenanthrene	NA	= (	1.12E-03	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Phenol	NA	= (	3.57E-01	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Pyrene	NA	= (	2.51E-04	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
1,2,4-Trimethylbenzene	NA	= (	2.40E-02	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Benzene	2.32E-06	= (	4.57E-02	×	1	×	0.5	×	1	×	3,300	×	5.50E-02	) ÷ (	70	×	25,550	)
Ethylbenzene	NA	= (	2.19E-02	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)

Attachment I2

Table 29
Risk Calculations
Construction Worker: Dermal Contact with Ground Water (Linear-Low Dose) – Carcinogenic Effects
NSP Ashland
(Exposure Frequency = 1 Day/Year))

$$\text{Derm-Risk} = \frac{(DA_{event} \times EV \times ED \times EF \times SA \times SFabs)}{(BW \times ATc)}$$

Equation / Units	Derm-Risk = unitless		DA_{event} mg/cm²-event		EV events/day		ED years		EF days/year		SA cm²		SFabs kg-day/mg		BW kg		ATc days	
m & p-Xylenes	NA	= (	3.53E-02	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Toluene	NA	= (	4.33E-02	×	1	×	0.5	×	1	×	3,300	×	NV	) ÷ (	70	×	25,550	)
Total CR	***2.57E-06***																	

Notes:

Derm-Risk – Carcinogenic Risk Dermal Contact with Water Pathway
DA_{event} – Absorbed Dose per Event (calculated using chemical-specific solubility)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
SFabs – Absorbed Slope Factor
BW – Body Weight
ATc – Averaging Time for Carcinogens
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2

Table 30
Risk Calculations
Construction Worker: Dermal Contact with Ground Water – Noncarcinogenic Effects
NSP Ashland
(Exposure Frequency = 1 Day/Year)

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SA)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SA	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
Cyanides	1.24E-06	= (	1.92E-07	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	2.00E-02	)
Iron	NA	= (	1.76E-06	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
2-Methylnaphthalene	2.65E-01	= (	8.22E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	4.00E-03	)
2,4 Dimethylphenol	9.34E+00	= (	1.45E-01	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	2.00E-03	)
Acenaphthylene	NA	= (	1.97E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Anthracene	1.39E-05	= (	3.23E-05	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	3.00E-01	)
Benzo(a)pyrene	NA	= (	1.05E-05	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Benzo(b)fluoranthene	NA	= (	9.91E-06	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Benzo(g,h,i)perylene	NA	= (	3.55E-06	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Benzo(k)fluoranthene	NA	= (	5.21E-06	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Chrysene	NA	= (	6.36E-06	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Dibenzo(a,h)anthracene	NA	= (	2.50E-05	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Dibenzofuran	8.02E-02	= (	1.24E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	2.00E-03	)
Fluoranthene	1.29E-03	= (	3.98E-04	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	4.00E-02	)
Fluorene	2.77E-03	= (	8.58E-04	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	4.00E-02	)
Indeno(1,2,3-cd)pyrene	NA	= (	1.52E-07	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
m & p-Cresols	NA	= (	8.36E-05	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Naphthalene	3.29E-02	= (	5.09E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	2.00E-02	)
o-Cresol	9.06E-01	= (	3.51E-01	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	5.00E-02	)
Phenanthrene	NA	= (	1.12E-03	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Phenol	1.54E-01	= (	3.57E-01	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	3.00E-01	)
Pyrene	1.08E-03	= (	2.51E-04	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	3.00E-02	)

Attachment I2

Table 30
Risk Calculations
Construction Worker: Dermal Contact with Ground Water – Noncarcinogenic Effects
NSP Ashland
(Exposure Frequency = 1 Day/Year)

$$\text{Derm-HQ} = \frac{(DA_{event} \times EV \times ED \times EF \times SA)}{(BW \times ATn \times RfDabs)}$$

Equation	Derm-Risk	= (	DA_{event}	×	EV	×	ED	×	EF	×	SA	) ÷ (	BW	×	ATn	×	RfDabs	)
Units	unitless		mg/cm²-event		events/day		years		days/year		cm²		kg		days		mg/kg-day	
1,2,4-Trimethylbenzene	6.21E-02	= (	2.40E-02	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	5.00E-02	)
Benzene	1.48E+00	= (	4.57E-02	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	4.00E-03	)
Ethylbenzene	2.83E-02	= (	2.19E-02	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	1.00E-01	)
m & p-Xylenes	NA	= (	3.53E-02	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	NV	)
Toluene	6.99E-02	= (	4.33E-02	×	1	×	0.5	×	1	×	3,300	) ÷ (	70	×	183	×	8.00E-02	)
Total HI	***1.24E+01***																	

Notes:

Derm-HQ – Dermal Contact with Water Pathway Hazard Quotient
DA_{event} – Absorbed Dose per Event (calculated using chemical-specific solubility)
EV – Event Frequency
ED – Exposure Duration
EF – Exposure Frequency
SA – Skin Surface Area Available for Contact
BW – Body Weight
ATn – Averaging Time for Noncarcinogens
RfDabs – Absorbed Reference Dose
NA – Not Applicable
NV – No toxicity value available for this pathway.

Attachment I2
Table 31
Construction Worker Risk Summary
Reasonable Maximum Exposure

	Carcinogenic Risk								Target Organs	Noncarcinogenic Hazard							
Equation Units	CR unitless	=	Ingestion unitless	+	Dermal unitless	+	Inhalation unitless			HQ unitless	=	Ingestion unitless	+	Dermal unitless	+	Inhalation unitless	
Cyanides	NA	=	NA	+	NA	+	NA		*Thyroid, Systemic*	1.24E-06	=	NA	+	1.24E-06	+	NA	
Iron	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
2-Methylnaphthalene	NA	=	NA	+	NA	+	NA		*Respiratory*	2.65E-01	=	NA	+	2.65E-01	+	NA	
2,4 Dimethylphenol	NA	=	NA	+	NA	+	NA		*Systemic*	***9.34E+00***	=	NA	+	9.34E+00	+	NA	
Acenaphthylene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Anthracene	NA	=	NA	+	NA	+	NA		*NOAEL*	1.39E-05	=	NA	+	1.39E-05	+	NA	
Benzo(a)pyrene	7.09E-08	=	NA	+	7.09E-08	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(b)fluoranthene	6.68E-09	=	NA	+	6.68E-09	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(g,h,i)perylene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Benzo(k)fluoranthene	3.51E-10	=	NA	+	3.51E-10	+	NA			NA	=	NA	+	NA	+	NA	
Chrysene	4.28E-11	=	NA	+	4.28E-11	+	NA			NA	=	NA	+	NA	+	NA	
Dibenzo(a,h)anthracene	1.68E-07	=	NA	+	1.68E-07	+	NA			NA	=	NA	+	NA	+	NA	
Dibenzofuran	NA	=	NA	+	NA	+	NA		*Systemic*	8.02E-02	=	NA	+	8.02E-02	+	NA	
Fluoranthene	NA	=	NA	+	NA	+	NA		*Systemic, Circulatory*	1.29E-03	=	NA	+	1.29E-03	+	NA	
Fluorene	NA	=	NA	+	NA	+	NA		*Circulatory*	2.77E-03	=	NA	+	2.77E-03	+	NA	
Indeno(1,2,3-cd)pyrene	1.02E-10	=	NA	+	1.02E-10	+	NA			NA	=	NA	+	NA	+	NA	
m & p-Cresols	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Naphthalene	NA	=	NA	+	NA	+	NA		*Respiratory, Systemic*	3.29E-02	=	NA	+	3.29E-02	+	NA	
o-Cresol	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	9.06E-01	=	NA	+	9.06E-01	+	NA	
Phenanthrene	NA	=	NA	+	NA	+	NA			NA	=	NA	+	NA	+	NA	
Phenol	NA	=	NA	+	NA	+	NA		*Adrenal*	1.54E-01	=	NA	+	1.54E-01	+	NA	
Pyrene	NA	=	NA	+	NA	+	NA		*Systemic*	1.08E-03	=	NA	+	1.08E-03	+	NA	
1,2,4-Trimethylbenzene	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	6.21E-02	=	NA	+	6.21E-02	+	NA	
Benzene	2.32E-06	=	NA	+	2.32E-06	+	NA		*Circulatory*	***1.48E+00***	=	NA	+	1.48E+00	+	NA	
Ethylbenzene	NA	=	NA	+	NA	+	NA		*Systemic, Teratology*	2.83E-02	=	NA	+	2.83E-02	+	NA	
m & p-Xylenes	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	NA	=	NA	+	NA	+	NA	
Toluene	NA	=	NA	+	NA	+	NA		*Systemic, CNS*	6.99E-02	=	NA	+	6.99E-02	+	NA	
Soil CR	**3E-06**	=	NA	+	3E-06	+	NA		**Soil HI**	***12.42***	=	NA	+	***12.42***	+	NA	

Notes:

NA – Not Applicable
CR – Cancer Risk
HQ – Hazard Quotient
HI – Hazard Index
CNS – Central Nervous System

Attachment I2

Table 32
DNAPL Laboratory Data
NSP Ashland

PARAMETER	Units	Result	conversion factor	Final Result	Solubility in Water	Units
Flashpoint	degrees F	100				
pH	-	7.2				
Alkalinity, bircarb, as HCO3	mg/L	570	1.00E-03	0.57	NA	mg/cm^3
Alkalinity, total as CaCO3 (unfiltered)	mg/L	470	1.00E-03	0.47	NA	mg/cm^3
Alkalinity, carbonate CaCO3	mg/L	ND (<2.3)	1.00E-03		NA	mg/cm^3
Calcium, total as Ca	mg/L	100	1.00E-03	0.10	NA	mg/cm^3
Cyanide, total	mg/L	0.024	1.00E-03	2.40E-05	NA	mg/cm^3
Hardness, total as CaCO3 (calc/unfilt)	mg/L	490	1.00E-03	0.49	NA	mg/cm^3
Iron, total	mg/L	0.22	1.00E-03	2.20E-04	NA	mg/cm^3
Magnesium, total as Mg	mg/L	45	1.00E-03	0.05	NA	mg/cm^3
Nitrate	mg/L	0.15	1.00E-03	1.50E-04	NA	mg/cm^3
Solids, total dissolved (TDS)	mg/L	680	1.00E-03	0.68	NA	mg/cm^3
Solids, total suspended (TSS)	mg/L	16	1.00E-03	0.02	NA	mg/cm^3
Sulfate	mg/L	93	1.00E-03	0.09	NA	mg/cm^3
Total Organic Carbon (TOC)	mg/L	250	1.00E-03	0.25	NA	mg/cm^3
VOCs						
Methylene Chloride	ug/L	650	1.00E-06	6.50E-04	1.30E+01	mg/cm^3
Benzene	ug/L	44000	1.00E-06	4.40E-02	1.75E+00	mg/cm^3
Toulene	ug/L	19000	1.00E-06	1.90E-02	5.26E-01	mg/cm^3
Ethylbenzene	ug/L	550	1.00E-06	5.50E-04	1.69E-01	mg/cm^3
m,p-Xylene	ug/L	3200	1.00E-06	3.20E-03	1.85E-01	mg/cm^3
1,2,4-Trimethylbenzene	ug/L	500	1.00E-06	5.00E-04	5.70E-02	mg/cm^3
Naphthalene	ug/L	8000	1.00E-06	8.00E-03	3.10E-02	mg/cm^3
SVOCs						
Acenaphthylene	ug/L	3200	1.00E-06	3.20E-03	4.24E-03	mg/cm3
Antracene	ug/L	1200	1.00E-06	1.20E-03	4.34E-05	mg/cm3
Benzo(a)pyrene	ug/L	400	1.00E-06	4.00E-04	1.62E-06	mg/cm3
Benzo(b)fluoranthene	ug/L	360	1.00E-06	3.60E-04	1.50E-06	mg/cm3
Benzo(g,h,i)perylene	ug/L	180	1.00E-06	1.80E-04	2.60E-07	mg/cm3
Benzo(k)fluoranthene	ug/L	110	1.00E-06	1.10E-04	8.00E-07	mg/cm3
Chrysene	ug/L	391	1.00E-06	3.91E-04	1.60E-06	mg/cm3
Dibenz(a,h)anthracene	ug/L	110	1.00E-06	1.10E-04	2.49E-06	mg/cm3
Dibenzofuran	ug/L	350	1.00E-06	3.50E-04	3.10E-03	mg/cm3
2,4-Dimethylphenol	ug/L	4800	1.00E-06	4.80E-03	7.87E+00	mg/cm3
Fluoranthene	ug/L	1200	1.00E-06	1.20E-03	2.06E-04	mg/cm3
Fluorene	ug/L	1200	1.00E-06	1.20E-03	1.98E-03	mg/cm3
Indeno(1,2,3-cd)pyrene	ug/L	160	1.00E-06	1.60E-04	2.20E-08	mg/cm3
2-Methylnaphthalene	ug/L	12000	1.00E-06	1.20E-02	2.46E-02	mg/cm3
2-Methylphenol	ug/L	4200	1.00E-06	4.20E-03	2.60E+01	mg/cm3
3 & 4-Methylphenol	ug/L	6200	1.00E-06	6.20E-03	2.27E+01	mg/cm3
Naphthalene	ug/L	26000	1.00E-06	2.60E-02	3.10E-02	mg/cm3
Phenanthrene	ug/L	2600	1.00E-06	2.60E-03	1.15E-03	mg/cm3
Phenol	ug/L	1200	1.00E-06	1.20E-03	8.28E+01	mg/cm3
Pyrene	ug/L	2000	1.00E-06	2.00E-03	1.35E-04	mg/cm3

Attachment J

Evaluation of Construction/Excavation Worker Exposure to VOCs in Trench Air

Attachment J

TABLE 1

VALUES USED FOR DAILY INTAKE CALCULATIONS

NSP Ashland

Medium:	Groundwater
Exposure Medium:	Air
Receptor Population:	C
	R = Current or Future Resident
	C = Construction/Utility Worker
	I = Commercial/Industrial Worker
Exposure Route:	Inhalation
Receptor Age:	A
	A = Adult
	C = Child

Intake Equation:
CDI=CA x IF
Intake Factor Equation:
IF=IR-A x EF x ED x ET x 1/BW x 1/AT

Parameter Code	Parameter Definition	Units	VRP Default Value	Rationale/ Reference	User Defined Value	Rationale/ Reference
CA	Chemical Concentration in Air	mg/m^3	(5)			
CDI	Chronic Daily Intake	mg/kg-day				
IR-A	Inhalation Rate	m^3/hour	2.5	EPA, 1991		
EF	Exposure Frequency	days/year	250			
ED	Exposure Duration	years	1			
ET	Exposure Time (Trench)	hours/day	8			
BW	Body Weight	kg	70	EPA, 1991		
AT-C	Averaging Time (Cancer)	days	25,550	EPA, 1989		
AT-N	Averaging Time (Non-Cancer)	days	365	EPA, 1989		
IF-C	Intake Factor (Cancer)	m^3/kg-day	2.80E-03	calculated		
IF-N	Intake Factor (Non-Cancer)	m^3/kg-day	1.96E-01	calculated		

DEQ= VRP Staff Professional Judgement

EPA, 1989= Risk Assessment Guidance for Superfund: Volume I -- Human Health Evaluation Manual (Part A). Office of Emergency and Remedial Response. EPA/540/1-89/002.

EPA, 1991= Human Health Evaluation Manual, Supplemental Guidance: Standard Default Exposure Factors. Office of Solid Waste and Emergency Response. OSWER Directive 9285.6-03

EPA, 1997= Exposure Factors Handbook. Office of Research and Development. EPA/600/P-95/002Fa.

EPA, 1999= EPA Region III Risk-Based Concentration Table: Technical Background Information.

(1) This exposure route should be evaluated for volatile organic compounds (VOC) only.

(2) Foster, S. A and P. C. Chrostowski, 1987, "Inhalation Exposures to Volatile Organic Contaminants in the Shower," for estimating shower air exposures.

(3) See the Johnson and Ettinger Model for estimating building air exposures at restricted use sites. ET = 24 hours for indoor air.

(4) Since children are assumed to bathe rather than shower this exposure route should be evaluated only for volatilization into buildings. See the Johnson & Ettinger model for estimating building air concentrations.

(5) See Section 3.2.1 of the risk assessment guidance.

(6) DEQ recommends consulting the Johnson and Ettinger model for estimating volatilization from groundwater to indoor air. Soil gas concentrations or measured indoor air concentrations may also be used.

Attachment J
TABLE 2A
CONSTRUCTION WORKER - INHALATION OF TRENCH AIR
EXPOSURE TO CHEMICALS VOLATILIZING FROM KREHER PARK GROUNDWATER
NSP Ashland

Kreher Park GW - Maximum Detections Table 10 Exposure-point concentrations (inhalation) for construction/utility workers in a trench: Groundwater less than 15 feet deep Using Spreadsheets Developed by VA DEQ http://www.deq.state.va.us/vrprisk/raguide.html Last Updated: August 18, 2006	CAS No.	Molecular Weight MWi g/mol	Henry's Law Constant Hi atm-m3/mol	Gas-Phase Mass Transfer Coefficient KiG cm/s	Liquid-Phase Mass Transfer Coefficient KiL cm/s	Overall Mass Transfer Coefficient Ki cm/s	Concentration of Contaminant in Groundwater Cgw ug/L	Volatilization Factor VF L/m3	Concentration of Contaminant in Trench Ctrench ug/m3	Concentration of Contaminant in Trench Ctrench mg/m3	Inhalation Intake Cancer IF-C x Ctrench Intake Factor-C = 6.99E-04 m3/kg-day	Inhalation Slope Factor (SFi) I/(mg/kg-day)	Inhalation Cancer Risk Intake-C/SFi	Inhalation Intake Noncancer IF-NC x Ctrench Intake Factor -NC 4.89E-02 m3/kg-day	Inhalation Reference Dose (RfDi) (mg/kg-day)	Inhalation Hazard Quotient Intake-NC * RfDi
Volatile Organic Compounds (VOCs)																
Benzene	71-43-2	78.11	5.55E-03	5.09E-01	1.28E-03	1.27E-03	3.60E+04	9.35E+00	3.36E+05	3.36E+02	2.35E-01	2.73E-02	6.4E-03	1.65E+01	8.57E-03	1.9E+03
Bromodichloromethane	75-27-4	163.83	1.60E-03	3.98E-01	8.84E-04	8.55E-04					NA	NV	NV	NA	NV	NV
Ethylbenzene	100-41-4	106.17	7.88E-03	4.60E-01	1.10E-03	1.09E-03	4.40E+03	8.05E+00	3.54E+04	3.54E+01	2.47E-02	NV	NV	1.73E+00	2.90E-01	6.0E+00
Isopropylbenzene	98-82-8	120.19	1.16E+00	4.41E-01	1.03E-03	1.03E-03	8.40E+01	7.62E+00	6.40E+02	6.40E-01	4.47E-04	NV	NV	3.13E-02	NV	NV
Methyl tert-butyl ether	1634-04-4	88.15	5.87E-04	4.89E-01	1.21E-03	1.09E-03	3.05E+00	8.07E+00	2.46E+01	2.46E-02	1.72E-05	NV	NV	1.20E-03	NV	NV
Styrene	100-42-5	104.15	2.75E-03	4.63E-01	1.11E-03	1.09E-03	1.30E+03	8.01E+00	1.04E+04	1.04E+01	7.28E-03	NV	NV	5.09E-01	8.60E-01	5.9E-01
Toluene	108-88-3	92.14	6.64E-03	4.82E-01	1.18E-03	1.17E-03	1.60E+04	8.62E+00	1.38E+05	1.38E+02	9.64E-02	NV	NV	6.75E+00	2.60E-01	2.6E+01
Total Xylenes	1330-20-7	106.16	5.18E-03	4.60E-01	1.10E-03	1.09E-03	4.30E+03	8.02E+00	3.45E+04	3.45E+01	2.41E-02	NV	NV	1.69E+00	2.86E-02	5.9E+01
n-butylbenzene	104-51-8	134.22	1.59E-02	4.25E-01	9.77E-04	9.73E-04	1.60E+03	7.18E+00	1.15E+04	1.15E+01	8.03E-03	NV	NV	5.62E-01	NV	NV
sec-butylbenzene	135-98-8	134.22	1.76E-02	4.25E-01	9.77E-04	9.73E-04	1.10E+02	7.19E+00	7.90E+02	7.90E-01	5.53E-04	NV	NV	3.87E-02	NV	NV
tert-butylbenzene	98-06-6	134.22	1.32E-02	4.25E-01	9.77E-04	9.72E-04	2.96E+02	7.18E+00	2.12E+03	2.12E+00	1.49E-03	NV	NV	1.04E-01	NV	NV
isopropyltoluene	99-87-6	134.22	1.10E-02	4.25E-01	9.77E-04	9.72E-04	1.80E+02	7.17E+00	1.29E+03	1.29E+00	9.02E-04	NV	NV	6.31E-02	NV	NV
n-propylbenzene	103-65-1	120.19	1.05E-02	4.41E-01	1.03E-03	1.03E-03	7.50E+00	7.58E+00	5.68E+01	5.68E-02	3.97E-05	NV	NV	2.78E-03	NV	NV
1,2,4-trimethylbenzene	95-63-6	120.19	6.16E-03	4.41E-01	1.03E-03	1.02E-03	5.70E+02	7.55E+00	4.30E+03	4.30E+00	3.01E-03	NV	NV	2.10E-01	1.71E-03	1.2E+02
1,3,5-trimethylbenzene	108-67-8	120.19	8.77E-03	4.41E-01	1.03E-03	1.03E-03	1.90E+02	7.57E+00	1.44E+03	1.44E+00	1.01E-03	NV	NV	7.03E-02	1.71E-03	4.1E+01
Semivolatile Organic Compounds (SVOCs)																
Acenaphthene	83-32-9	154.21	1.55E-04	4.06E-01	9.11E-04	6.73E-04	3.69E+04	4.97E+00	1.83E+05	1.83E+02	1.28E-01	NV	NV	8.96E+00	NV	NV
Acenaphthylene	208-96-8	152.19	1.13E-04	4.07E-01	9.17E-04	6.17E-04	3.82E+03	4.55E+00	1.74E+04	1.74E+01	1.22E-02	NV	NV	8.51E-01	NV	NV
Anthracene	120-12-7	178.23	6.50E-05	3.86E-01	8.47E-04	4.65E-04	1.61E+04	3.43E+00	5.52E+04	5.52E+01	3.86E-02	NV	NV	2.70E+00	NV	NV
Benzo(a)anthracene	56-55-3	228.29	3.35E-06	3.56E-01	7.49E-04	4.58E-05	6.80E+03	3.38E-01	2.30E+03	2.30E+00	1.61E-03	NV	NV	1.12E-01	NV	NV
Benzo(a)pyrene	50-32-8	252.31	1.13E-06	3.44E-01	7.12E-04	1.56E-05	7.75E+03	1.15E-01	8.91E+02	8.91E-01	6.23E-04	3.08E+00	1.9E-03	4.35E-02	NV	NV
Benzo(b)fluoranthene	205-99-2	252.31	1.11E-04	3.44E-01	7.12E-04	4.89E-04	6.26E+03	3.61E+00	2.26E+04	2.26E+01	1.58E-02	NV	NV	1.11E+00	NV	NV
Benzo(g,h,i)perylene	191-24-2	276.33	1.41E-07	3.34E-01	6.81E-04	1.92E-06	4.02E+03	1.42E-02	5.70E+01	5.70E-02	3.98E-05	NV	NV	2.79E-03	NV	NV
Benzo(k)fluoranthene	207-08-9	252.31	8.29E-07	3.44E-01	7.12E-04	1.15E-05	3.07E+03	8.48E-02	2.60E+02	2.60E-01	1.82E-04	NV	NV	1.27E-02	NV	NV
bis-(2-Ethylhexyl)phthalate	117-81-7	390.56	1.02E-07	2.97E-01	5.72E-04	1.24E-06	5.80E+01	9.14E-03	5.30E-01	5.30E-04	3.70E-07	NV	NV	2.59E-05	NV	NV
Butylbenzylphthalate	85-68-7	312.36	1.26E-06	3.20E-01	6.40E-04	1.61E-05					NA	NV	NV	NA	NV	NV
Chrysene	218-01-9	228.29	9.46E-05	3.56E-01	7.49E-04	4.85E-04	7.30E+03	3.58E+00	2.61E+04	2.61E+01	1.83E-02	NV	NV	1.28E+00	NV	NV
Di-n-butylphthalate	84-74-2	278.34	9.38E-10	3.33E-01	6.78E-04	1.28E-08	6.00E+00	9.43E-05	5.66E-04	5.66E-07	3.96E-10	NV	NV	2.77E-08	NV	NV
Dibenzo(a,h)anthracene	53-70-3	278.35	1.47E-08	3.33E-01	6.78E-04	2.00E-07	1.15E+03	1.48E-03	1.70E+00	1.70E-03	1.19E-06	NV	NV	8.31E-05	NV	NV
Dibenzofuran	132-64-9	168.19	1.26E-05	3.94E-01	8.72E-04	1.65E-04	7.20E+00	1.22E+00	8.76E+00	8.76E-03	6.12E-06	NV	NV	4.28E-04	NV	NV
Diethylphthalate	84-66-2	222.24	4.50E-07	3.59E-01	7.59E-04	6.55E-06	3.00E+00	4.84E-02	1.45E-01	1.45E-04	1.01E-07	NV	NV	7.10E-06	NV	NV
2,4-Dimethylphenol	105-67-9	122.16	2.00E-06	4.39E-01	1.02E-03	3.47E-05	1.60E+02	2.56E-01	4.10E+01	4.10E-02	2.86E-05	NV	NV	2.00E-03	NV	NV
Dimethylphthalate	131-11-3	194.18	1.05E-07	3.76E-01	8.12E-04	1.61E-06	1.30E+01	1.19E-02	1.55E-01	1.55E-04	1.08E-07	NV	NV	7.56E-06	NV	NV
Fluoranthene	206-44-0	202.25	1.61E-05	3.70E-01	7.96E-04	1.87E-04	3.24E+04	1.38E+00	4.47E+04	4.47E+01	3.12E-02	NV	NV	2.18E+00	NV	NV
Fluorene	86-73-7	166.22	6.36E-05	3.96E-01	8.78E-04	4.74E-04	2.02E+04	3.50E+00	7.06E+04	7.06E+01	4.94E-02	NV	NV	3.45E+00	NV	NV
Indeno(1,2,3-cd)pyrene	193-39-5	276.33	1.60E-06	3.34E-01	6.81E-04	2.12E-05	3.58E+03	1.56E-01	5.59E+02	5.59E-01	3.91E-04	NV	NV	2.73E-02	NV	NV
2-Methylnaphthalene	91-57-6	142.20	5.18E-04	4.17E-01	9.49E-04	8.57E-04	3.81E+04	6.32E+00	2.41E+05	2.41E+02	1.69E-01	NV	NV	1.18E+01	NV	NV
2-Methylphenol	95-48-7	108.14	1.20E-06	4.57E-01	1.09E-03	2.20E-05	1.50E+03	1.62E-01	2.43E+02	2.43E-01	1.70E-04	NV	NV	1.19E-02	NV	NV
3-Methylphenol	108-39-4	108.14	8.65E-07	4.57E-01	1.09E-03	1.59E-05	2.00E+03	1.18E-01	2.35E+02	2.35E-01	1.64E-04	NV	NV	1.15E-02	NV	NV
4-Methylphenol	106-44-5	108.14	7.92E-07	4.57E-01	1.09E-03	1.46E-05					NA	NV	NV	NA	NV	NV
Naphthalene	91-20-3	128.17	4.83E-04	4.32E-01	9.90E-04	8.95E-04	3.97E+04	6.60E+00	2.62E+05	2.62E+02	1.83E-01	NV	NV	1.28E+01	8.57E-04	1.5E+04
Phenanthrene	85-01-8	178.23	2.33E-05	3.86E-01	8.47E-04	2.57E-04	6.21E+04	1.90E+00	1.18E+05	1.18E+02	8.23E-02	NV	NV	5.76E+00	NV	NV
Phenol	108-95-2	94.11	3.97E-07	4.79E-01	1.17E-03	7.72E-06	2.80E+02	5.70E-02	1.60E+01	1.60E-02	1.12E-05	NV	NV	7.81E-04	NV	NV
Pyrene	129-00-0	202.25	1.10E-05	3.70E-01	7.96E-04	1.38E-04	5.62E+04	1.02E+00	5.72E+04	5.72E+01	4.00E-02	NV	NV	2.80E+00	NV	NV
TOTAL RISK													8.34E-03			1.72E+04

Only evaluated chemicals listed in VaDEQ Table 3.8 and detected in groundwater

GW maximum concentrations from Table 4-7 in June 5, 2006 RI report.

Toxicity values from Table 11a & B of Attachment A, HHRA, January 25, 2007; subchronic values if available for inhalation RfD

Attachment J
TABLE 2B
CONSTRUCTION WORKER - INHALATION OF TRENCH AIR
EXPOSURE TO CHEMICALS VOLATILIZING FROM UPPER BLUFF GROUNDWATER
NSP Ashland

Upper Bluff GW - Maximum Detections Table 12 Exposure-point concentrations (inhalation) for construction/utility workers in a trench: Groundwater less than 15 feet deep Using Spreadsheets Developed by VA DEQ http://www.deq.state.va.us/vrprisk/raguide.html Last Updated: August 18, 2006	CAS No.	Molecular Weight MWi g/mol	Henry's Law Constant Hi atm-m3/mol	Gas-Phase Mass Transfer Coefficient KiG cm/s	Liquid-Phase Mass Transfer Coefficient KiL cm/s	Overall Mass Transfer Coefficient Ki cm/s	Concentration of Contaminant in Groundwater Cgw ug/L	Volatilization Factor VF L/m3	Concentration of Contaminant in Trench Ctrench ug/m3	Concentration of Contaminant in Trench Ctrench mg/m3	Inhalation Intake Cancer IF-C x Ctrench Intake Factor-C = 6.99E-04 m3/kg-day	Inhalation Slope Factor (SFi) 1/(mg/kg-day)	Inhalation Cancer Risk Intake-C/SFi	Inhalation Intake Noncancer IF-NC x Ctrench Intake Factor -NC 4.89E-02 m3/kg-day	Inhalation Reference Dose (RfDi) (mg/kg-day)	Inhalation Hazard Quotient Intake-NC * RfDi
Volatile Organic Compounds (VOCs)																
Benzene	71-43-2	78.11	5.55E-03	5.09E-01	1.28E-03	1.27E-03	1.20E+02	9.35E+00	1.12E+03	1.12E+00	7.84E-04	2.73E-02	2.1E-05	5.48E-02	8.57E-03	6.4E+00
Bromodichloromethane	75-27-4	163.83	1.60E-03	3.98E-01	8.84E-04	8.55E-04	1.30E+00	6.31E+00	8.20E+00	8.20E-03	5.73E-06	NV	NV	4.01E-04	NV	NV
Chloroform	67-66-3	119.38	3.67E-03	4.42E-01	1.04E-03	1.02E-03	4.70E+00	7.53E+00	3.54E+01	3.54E-02	2.47E-05	NV	NV	1.73E-03	NV	NV
Ethylbenzene	100-41-4	106.17	7.88E-03	4.60E-01	1.10E-03	1.09E-03	5.10E-01	8.05E+00	4.10E+00	4.10E-03	2.87E-06	NV	NV	2.01E-04	2.90E-01	6.9E-04
Methyl tert-butyl ether	1634-04-4	88.15	5.87E-04	4.89E-01	1.21E-03	1.09E-03					NA	NV	NV	NA	NV	NV
Styrene	100-42-5	104.15	2.75E-03	4.63E-01	1.11E-03	1.09E-03	8.00E+00	8.01E+00	6.41E+01	6.41E-02	4.48E-05	NV	NV	3.13E-03	8.60E-01	3.6E-03
Toluene	108-88-3	92.14	6.64E-03	4.82E-01	1.18E-03	1.17E-03	8.30E+01	8.62E+00	7.16E+02	7.16E-01	5.00E-04	NV	NV	3.50E-02	2.60E-01	1.3E-01
Total Xylenes	1330-20-7	106.16	5.18E-03	4.60E-01	1.10E-03	1.09E-03	7.00E+01	8.02E+00	5.61E+02	5.61E-01	3.92E-04	NV	NV	2.74E-02	2.86E-02	9.6E-01
n-butylbenzene	104-51-8	134.22	1.59E-02	4.25E-01	9.77E-04	9.73E-04	3.00E+01	7.18E+00	2.16E+02	2.16E-01	1.51E-04	NV	NV	1.05E-02	NV	NV
sec-butylbenzene	135-98-8	134.22	1.76E-02	4.25E-01	9.77E-04	9.73E-04	7.60E+00	7.19E+00	5.46E+01	5.46E-02	3.82E-05	NV	NV	2.67E-03	NV	NV
tert-butylbenzene	98-06-6	134.22	1.32E-02	4.25E-01	9.77E-04	9.72E-04					NA	NV	NV	NA	NV	NV
isopropyltoluene	99-87-6	134.22	1.10E-02	4.25E-01	9.77E-04	9.72E-04	1.90E+00	7.17E+00	1.36E+01	1.36E-02	9.53E-06	NV	NV	6.66E-04	NV	NV
n-propylbenzene	103-65-1	120.19	1.05E-02	4.41E-01	1.03E-03	1.03E-03					NA	NV	NV	NA	NV	NV
1,1,1,2-tetrachloroethane	630-20-6	167.85	2.42E-03	3.94E-01	8.73E-04	8.54E-04					NA	NV	NV	NA	NV	NV
1,2,4-trimethylbenzene	95-63-6	120.19	6.16E-03	4.41E-01	1.03E-03	1.02E-03	1.80E+01	7.55E+00	1.36E+02	1.36E-01	9.50E-05	NV	NV	6.64E-03	1.71E-03	3.9E+00
1,3,5-trimethylbenzene	108-67-8	120.19	8.77E-03	4.41E-01	1.03E-03	1.03E-03	9.80E+00	7.57E+00	7.42E+01	7.42E-02	5.18E-05	NV	NV	3.63E-03	1.71E-03	2.1E+00
Semivolatile Organic Compounds (SVOCs)																
Acenaphthene	83-32-9	154.21	1.55E-04	4.06E-01	9.11E-04	6.73E-04	5.80E+00	4.97E+00	2.88E+01	2.88E-02	2.01E-05	NV	NV	1.41E-03	NV	NV
Acenaphthylene	208-96-8	152.19	1.13E-04	4.07E-01	9.17E-04	6.17E-04	4.80E+01	4.55E+00	2.19E+02	2.19E-01	1.53E-04	NV	NV	1.07E-02	NV	NV
Anthracene	120-12-7	178.23	6.50E-05	3.86E-01	8.47E-04	4.65E-04	4.00E+00	3.43E+00	1.37E+01	1.37E-02	9.59E-06	NV	NV	6.71E-04	NV	NV
Benzo(a)anthracene	56-55-3	228.29	3.35E-06	3.56E-01	7.49E-04	4.58E-05					NA	NV	NV	NA	NV	NV
Benzo(a)pyrene	50-32-8	252.31	1.13E-06	3.44E-01	7.12E-04	1.56E-05	2.30E-01	1.15E-01	2.64E-02	2.64E-05	1.85E-08	3.08E+00	5.7E-08	1.29E-06	NV	NV
Benzo(b)fluoranthene	205-99-2	252.31	1.11E-04	3.44E-01	7.12E-04	4.89E-04	1.20E-01	3.61E+00	4.33E-01	4.33E-04	3.03E-07	NV	NV	2.12E-05	NV	NV
Benzo(g,h,i)perylene	191-24-2	276.33	1.41E-07	3.34E-01	6.81E-04	1.92E-06	1.60E-01	1.42E-02	2.27E-03	2.27E-06	1.58E-09	NV	NV	1.11E-07	NV	NV
Benzo(k)fluoranthene	207-08-9	252.31	8.29E-07	3.44E-01	7.12E-04	1.15E-05	5.70E-02	8.48E-02	4.83E-03	4.83E-06	3.38E-09	NV	NV	2.36E-07	NV	NV
bis-(2-Ethylhexyl)phthalate	117-81-7	390.56	1.02E-07	2.97E-01	5.72E-04	1.24E-06	7.00E+00	9.14E-03	6.40E-02	6.40E-05	4.47E-08	NV	NV	3.13E-06	NV	NV
Butylbenzylphthalate	85-68-7	312.36	1.26E-06	3.20E-01	6.40E-04	1.61E-05					NA	NV	NV	NA	NV	NV
Chrysene	218-01-9	228.29	9.46E-05	3.56E-01	7.49E-04	4.85E-04					NA	NV	NV	NA	NV	NV
Di-n-butylphthalate	84-74-2	278.34	9.38E-10	3.33E-01	6.78E-04	1.28E-08	3.50E+00	9.43E-05	3.30E-04	3.30E-07	2.31E-10	NV	NV	1.61E-08	NV	NV
Dibenzo(a,h)anthracene	53-70-3	278.35	1.47E-08	3.33E-01	6.78E-04	2.00E-07	1.30E-01	1.48E-03	1.92E-04	1.92E-07	1.34E-10	NV	NV	9.39E-09	NV	NV
Dibenzofuran	132-64-9	168.19	1.26E-05	3.94E-01	8.72E-04	1.65E-04	4.30E+00	1.22E+00	5.23E+00	5.23E-03	3.66E-06	NV	NV	2.56E-04	NV	NV
Fluoranthene	206-44-0	202.25	1.61E-05	3.70E-01	7.96E-04	1.87E-04	2.60E+00	1.38E+00	3.58E+00	3.58E-03	2.51E-06	NV	NV	1.75E-04	NV	NV
Fluorene	86-73-7	166.22	6.36E-05	3.96E-01	8.78E-04	4.74E-04	1.70E+01	3.50E+00	5.95E+01	5.95E-02	4.16E-05	NV	NV	2.91E-03	NV	NV
Indeno(1,2,3-cd)pyrene	193-39-5	276.33	1.60E-06	3.34E-01	6.81E-04	2.12E-05	3.50E-01	1.56E-01	5.47E-02	5.47E-05	3.82E-08	NV	NV	2.67E-06	NV	NV
2-Methylnaphthalene	91-57-6	142.20	5.18E-04	4.17E-01	9.49E-04	8.57E-04	8.30E+01	6.32E+00	5.25E+02	5.25E-01	3.67E-04	NV	NV	2.57E-02	NV	NV
2-Methylphenol	95-48-7	108.14	1.20E-06	4.57E-01	1.09E-03	2.20E-05					NA	NV	NV	NA	NV	NV
3-Methylphenol	108-39-4	108.14	8.65E-07	4.57E-01	1.09E-03	1.59E-05					NA	NV	NV	NA	NV	NV
4-Methylphenol	106-44-5	108.14	7.92E-07	4.57E-01	1.09E-03	1.46E-05					NA	NV	NV	NA	NV	NV
Naphthalene	91-20-3	128.17	4.83E-04	4.32E-01	9.99E-04	8.95E-04	5.70E+02	6.60E+00	3.76E+03	3.76E+00	2.63E-03	NV	NV	1.84E-01	8.57E-04	2.1E+02
Pentachlorophenol	87-86-5	266.34	2.44E-08	3.38E-01	6.93E-04	3.37E-07					NA	NV	NV	NA	NV	NV
Phenanthrene	85-01-8	178.23	2.33E-05	3.86E-01	8.47E-04	2.57E-04	6.60E+01	1.90E+00	1.25E+02	1.25E-01	8.75E-05	NV	NV	6.12E-03	NV	NV
Phenol	108-95-2	94.11	3.97E-07	4.79E-01	1.17E-03	7.72E-06	5.60E+00	5.70E-02	3.19E-01	3.19E-04	2.23E-07	NV	NV	1.56E-05	NV	NV
Pyrene	129-00-0	202.25	1.10E-05	3.70E-01	7.96E-04	1.38E-04	4.30E+00	1.02E+00	4.38E+00	4.38E-03	3.06E-06	NV	NV	2.14E-04	NV	NV
TOTAL RISK													2.15E-05			2.28E+02

Only evaluated chemicals listed in VaDEQ Table 3.8 and detected in groundwater

GW maximum concentrations from Table 4-7 in June 5, 2006 RI report.

Toxicity values from Table 11a & B of Attachment A, HHRA, January 25, 2007; subchronic values if available for inhalation RfD

Attachment J
TABLE 2C
CONSTRUCTION WORKER - INHALATION OF TRENCH AIR
EXPOSURE TO CHEMICALS VOLATILIZING FROM FILLED RAVINE GROUNDWATER
NSP Ashland

Filled Ravine GW - Maximum Detections Table 11 Exposure-point concentrations *(inhalation) for construction/utility workers* in a trench: Groundwater less than 15 feet deep Using Spreadsheets Developed by VA DEQ http://www.deq.state.va.us/vrprisk/raguide.html Last Updated: August 18, 2006	CAS No.	Molecular Weight MWi g/mol	Henry's Law Constant Hi atm-m3/mol	Gas-Phase Mass Transfer Coefficient KiG cm/s	Liquid-Phase Mass Transfer Coefficient KiL cm/s	Overall Mass Transfer Coefficient Ki cm/s	Concentration of Contaminant in Groundwater Cgw ug/L	Volatilization Factor VF L/m3	Concentration of Contaminant in Trench Ctrench ug/m3	Concentration of Contaminant in Trench Ctrench mg/m3	Inhalation Intake (mg/kg-day) Cancer IF-C x Ctrench Intake Factor-C = 6.99E-04 m3/kg-day	Inhalation Slope Factor (SFi) 1/(mg/kg-day)	Inhalation Cancer Risk Intake-C/SFi	Inhalation Intake Noncancer IF-NC x Ctrench Intake Factor -NC 4.89E-02 m3/kg-day	Inhalation Reference Dose (RfDi) (mg/kg-day)	Inhalation Hazard Quotient Intake-NC * RfDi
Volatile Organic Compounds (VOCs)																
Benzene	71-43-2	78.11	5.55E-03	5.09E-01	1.28E-03	1.27E-03	8.60E+04	9.35E+00	8.04E+05	8.04E+02	5.62E-01	2.73E-02	1.5E-02	3.93E+01	8.57E-03	4.6E+03
Ethylbenzene	100-41-4	106.17	7.88E-03	4.60E-01	1.10E-03	1.09E-03	3.40E+03	8.05E+00	2.74E+04	2.74E+01	1.91E-02	NV	NV	1.34E+00	2.90E-01	4.6E+00
Methyl tert-butyl ether	1634-04-4	88.15	5.87E-04	4.89E-01	1.21E-03	1.09E-03	3.50E+00	8.07E+00	2.82E+01	2.82E-02	1.97E-05	NV	NV	1.38E-03	NV	NV
Styrene	100-42-5	104.15	2.75E-03	4.63E-01	1.11E-03	1.09E-03	6.00E+02	8.01E+00	4.81E+03	4.81E+00	3.36E-03	NV	NV	2.35E-01	8.60E-01	2.7E-01
Toluene	108-88-3	92.14	6.64E-03	4.82E-01	1.18E-03	1.17E-03	3.60E+04	8.62E+00	3.10E+05	3.10E+02	2.17E-01	NV	NV	1.52E+01	2.60E-01	5.8E+01
Total Xylenes	1330-20-7	106.16	5.18E-03	4.60E-01	1.10E-03	1.09E-03	1.00E+04	8.02E+00	8.02E+04	8.02E+01	5.60E-02	NV	NV	3.92E+00	2.86E-02	1.4E+02
n-butylbenzene	104-51-8	134.22	1.59E-02	4.25E-01	9.77E-04	9.73E-04	6.52E+02	7.18E+00	4.68E+03	4.68E+00	3.27E-03	NV	NV	2.29E-01	NV	NV
sec-butylbenzene	135-98-8	134.22	1.76E-02	4.25E-01	9.77E-04	9.73E-04	9.70E+02	7.19E+00	6.97E+03	6.97E+00	4.87E-03	NV	NV	3.41E-01	NV	NV
tert-butylbenzene	98-06-6	134.22	1.32E-02	4.25E-01	9.77E-04	9.72E-04	6.00E+02	7.18E+00	4.31E+03	4.31E+00	3.01E-03	NV	NV	2.11E-01	NV	NV
isopropyltoluene	99-87-6	134.22	1.10E-02	4.25E-01	9.77E-04	9.72E-04	5.80E+01	7.17E+00	4.16E+02	4.16E-01	2.91E-04	NV	NV	2.03E-02	NV	NV
n-propylbenzene	103-65-1	120.19	1.05E-02	4.41E-01	1.03E-03	1.03E-03	7.00E+01	7.58E+00	5.30E+02	5.30E-01	3.71E-04	NV	NV	2.59E-02	NV	NV
1,2,4-trimethylbenzene	95-63-6	120.19	6.16E-03	4.41E-01	1.03E-03	1.02E-03	9.00E+02	7.55E+00	6.79E+03	6.79E+00	4.75E-03	NV	NV	3.32E-01	1.71E-03	1.9E+02
1,3,5-trimethylbenzene	108-67-8	120.19	8.77E-03	4.41E-01	1.03E-03	1.03E-03	5.00E+03	7.57E+00	3.78E+04	3.78E+01	2.65E-02	NV	NV	1.85E+00	1.71E-03	1.1E+03
Semivolatile Organic Compounds (SVOCs)																
Acenaphthene	83-32-9	154.21	1.55E-04	4.06E-01	9.11E-04	6.73E-04	1.40E+05	4.97E+00	6.95E+05	6.95E+02	4.86E-01	NV	NV	3.40E+01	NV	NV
Acenaphthylene	208-96-8	152.19	1.13E-04	4.07E-01	9.17E-04	6.17E-04	1.40E+05	4.55E+00	6.37E+05	6.37E+02	4.46E-01	NV	NV	3.12E+01	NV	NV
Anthracene	120-12-7	178.23	6.50E-05	3.86E-01	8.47E-04	4.65E-04	1.20E+05	3.43E+00	4.11E+05	4.11E+02	2.88E-01	NV	NV	2.01E+01	NV	NV
Benzo(a)anthracene	56-55-3	228.29	3.35E-06	3.56E-01	7.49E-04	4.58E-05	6.40E+05	3.38E-01	2.16E+05	2.16E+02	1.51E-01	NV	NV	1.06E+01	NV	NV
Benzo(a)pyrene	50-32-8	252.31	1.13E-06	3.44E-01	7.12E-04	1.56E-05	7.10E+04	1.15E-01	8.15E+03	8.15E+00	5.70E-03	3.08E+00	1.8E-02	3.99E-01	NV	NV
Benzo(b)fluoranthene	205-99-2	252.31	1.11E-04	3.44E-01	7.12E-04	4.89E-04	3.10E+04	3.61E+00	1.12E+05	1.12E+02	7.83E-02	NV	NV	5.47E+00	NV	NV
Benzo(g,h,i)perylene	191-24-2	276.33	1.41E-07	3.34E-01	6.81E-04	1.92E-06	3.10E+04	1.42E-02	4.39E+02	4.39E-01	3.07E-04	NV	NV	2.15E-02	NV	NV
Benzo(k)fluoranthene	207-08-9	252.31	8.29E-07	3.44E-01	7.12E-04	1.15E-05	3.60E+04	8.48E-02	3.05E+03	3.05E+00	2.13E-03	NV	NV	1.49E-01	NV	NV
Butylbenzylphthalate	85-68-7	312.36	1.26E-06	3.20E-01	6.40E-04	1.61E-05	3.20E+00	1.19E-01	3.80E-01	3.80E-04	2.66E-07	NV	NV	1.86E-05	NV	NV
Chrysene	218-01-9	228.29	9.46E-05	3.56E-01	7.49E-04	4.85E-04	6.60E+04	3.58E+00	2.36E+05	2.36E+02	1.65E-01	NV	NV	1.16E+01	NV	NV
Di-n-butylphthalate	84-74-2	278.34	9.38E-10	3.33E-01	6.78E-04	1.28E-08	7.70E+01	9.43E-05	7.26E-03	7.26E-06	5.08E-09	NV	NV	3.55E-07	NV	NV
Dibenzo(a,h)anthracene	53-70-3	278.35	1.47E-08	3.33E-01	6.78E-04	2.00E-07	1.20E+03	1.48E-03	1.77E+00	1.77E-03	1.24E-06	NV	NV	8.67E-05	NV	NV
Dibenzofuran	132-64-9	168.19	1.26E-05	3.94E-01	8.72E-04	1.65E-04	4.50E+02	1.22E+00	5.47E+02	5.47E-01	3.83E-04	NV	NV	2.68E-02	NV	NV
2,4-Dimethylphenol	105-67-9	122.16	2.00E-06	4.39E-01	1.02E-03	3.47E-05	3.40E+03	2.56E-01	8.70E+02	8.70E-01	6.08E-04	NV	NV	4.26E-02	NV	NV
Fluoranthene	206-44-0	202.25	1.61E-05	3.70E-01	7.96E-04	1.87E-04	1.40E+05	1.38E+00	1.93E+05	1.93E+02	1.35E-01	NV	NV	9.44E+00	NV	NV
Fluorene	86-73-7	166.22	6.36E-05	3.96E-01	8.78E-04	4.74E-04	1.50E+05	3.50E+00	5.25E+05	5.25E+02	3.67E-01	NV	NV	2.57E+01	NV	NV
Indeno(1,2,3-cd)pyrene	193-39-5	276.33	1.60E-06	3.34E-01	6.81E-04	2.12E-05	2.60E+04	1.56E-01	4.06E+03	4.06E+00	2.84E-03	NV	NV	1.99E-01	NV	NV
2-Methylnaphthalene	91-57-6	142.20	5.18E-04	4.17E-01	9.49E-04	8.57E-04	6.40E+05	6.32E+00	4.05E+06	4.05E+03	2.83E+00	NV	NV	1.98E+02	NV	NV
2-Methylphenol	95-48-7	108.14	1.20E-06	4.57E-01	1.09E-03	2.20E-05	2.80E+03	1.62E-01	4.54E+02	4.54E-01	3.18E-04	NV	NV	2.22E-02	NV	NV
3-Methylphenol	108-39-4	108.14	8.65E-07	4.57E-01	1.09E-03	1.59E-05	6.30E+03	1.18E-01	7.41E+02	7.41E-01	5.18E-04	NV	NV	3.62E-02	NV	NV
4-Methylphenol	106-44-5	108.14	7.92E-07	4.57E-01	1.09E-03	1.46E-05	9.20E+02	1.08E-01	9.92E+01	9.92E-02	6.93E-05	NV	NV	4.85E-03	NV	NV
Naphthalene	91-20-3	128.17	4.83E-04	4.32E-01	9.99E-04	8.95E-04	1.70E+06	6.60E+00	1.12E+07	1.12E+04	7.85E+00	NV	NV	5.49E+02	8.57E-04	6.4E+05
Pentachlorophenol	87-86-5	266.34	2.44E-08	3.38E-01	6.93E-04	3.37E-07	7.60E+01	2.49E-03	1.89E-01	1.89E-04	1.32E-07	NV	NV	9.25E-06	NV	NV
Phenanthrene	85-01-8	178.23	2.33E-05	3.86E-01	8.47E-04	2.57E-04	3.90E+05	1.90E+00	7.39E+05	7.39E+02	5.17E-01	NV	NV	3.62E+01	NV	NV
Phenol	108-95-2	94.11	3.97E-07	4.79E-01	1.17E-03	7.72E-06	4.50E+03	5.70E-02	2.57E+02	2.57E-01	1.79E-04	NV	NV	1.25E-02	NV	NV
Pyrene	129-00-0	202.25	1.10E-05	3.70E-01	7.96E-04	1.38E-04	1.80E+05	1.02E+00	1.83E+05	1.83E+02	1.28E-01	NV	NV	8.96E+00	NV	NV
TOTAL RISK														3.29E-02		6.47E+05

Only evaluated chemicals listed in VaDEQ Table 3.8 and detected in groundwater

GW maximum concentrations from Table 4-7 in June 5, 2006 RI report.

Toxicity values from Table 11a & B of Attachment A, HHRA, January 25, 2007; subchronic values if available for inhalation RfD

Attachment K

Evaluation of Recreational Swimmers and Waders to Site-related Chemicals in Surface Water Using 1998 Baseline HHRA Data

Attachment K
Table 1
Dermal Contact with Surface Water or Groundwater While Wading, Swimming and Trench Construction
Reasonable Maximum Exposure
Ashland Lakefront Site, Ashland, WI

Parameter		Swim		Wading	
		Adult	Adolescent	Adult	Adolescent
Concentration in Water	CW (mg/L)	(a)	(a)	(a)	(a)
Unit Conversion Factor	CF	1.0E-03	1.0E-03	1.0E-03	1.0E-03
Dermal Factor	Z (cm/event)	(b)	(b)	(b)	(b)
Event Frequency	EV (events/day)	1	1	1	1
Exposure Frequency	EF (days/year)	12	12	12	12
Exposure Duration	ED (years)	30	12	30	12
Skin Surface Area	SA (cm^2)	18000	13533	9000	6767
Body Weight	BW (kg)	70	47	70	47
Averaging Time- noncancer	AT (noncancer) (days)	10950	4380	10950	4380
Averaging Time - cancer	AT (cancer) (days)	25550	25550	25550	25550
Intake Rate – Noncancer [L-hr/(cm (kg-day))]		8.45E-03	9.47E-03	4.23E-03	4.73E-03
Intake Rate – Cancer [L-hr/(cm (kg-day))]		3.62E-03	1.62E-03	1.81E-03	8.11E-04

(a) Maximum Surface Water Concentrations from Table 4-11 of Jan 2007 RI Report

(b) The calculation of Z was performed in accordance with Supplemental RAGS Guidance (Part E) (EPA, 2004). The calculated values for Z are presented in Attachment J Table 3.

Attachment K
Table 2
Calculation of Dermal Factors
Potential Dermal Contact with COPCs in Surface Water
Ashland Lakefront

COPCs in Groundwater and Surface Water	Kp[a] (cm/hr)	Swimming Contact t_{event} =1 Z[b] (cm/event)	Wading Contact t_{event} =2 Z[b] (cm/event)	FA[a] dimensionless	$t^{*(a)}$ (hr)	τ^{a} (hr/event)	B[a] (unitless)
SVOCs							
Benzo(a)anthracene	4.7E-01	1.85E+00	2.62E+00	1.00E+00	8.53E+00	2.03E+00	2.80E+00
Benzo(a)pyrene	7.0E-01	3.18E+00	4.49E+00	1.00E+00	1.17E+01	2.69E+00	4.30E+00
Benzo(b)fluoranthene	7.0E-01	3.23E+00	4.57E+00	1.00E+00	1.20E+01	2.77E+00	4.30E+00
Benzo(k)fluoranthene	7.0E-01	3.23E+00	4.57E+00	1.00E+00	1.20E+01	2.77E+00	4.30E+00
Chrysene	4.7E-01	1.85E+00	2.62E+00	1.00E+00	8.53E+00	2.03E+00	2.80E+00
Indeno(1,2,3-cd)pyrene	1.0E+00	3.22E+00	4.56E+00	6.00E-01	1.68E+01	3.78E+00	6.70E+00

Notes:

a = Chemical-specific values were obtained from Supplemental RAGS Guidance (Part E) (EPA, 2004), Exhibit 3-1 (inorganics) and Exhibit B-3 (organics). Used values for benzo(b)fluoranthene for benzo(k)fluoranthene and values for trans 1,2-DCE for cis -12,-DCE.

[b] The calculation of Z was performed in accordance with Supplemental RAGS Guidance (Part E) (EPA, 2004).

t^{*} - (hr); chemical specific

τ - lag time (hr/event); chemical specificc

FA = Fraction Absorbed; chemical specific

Kp - Dermal Permeability Coefficient (cm/hr); chemical-specific

t_{event} - Duration of Event (hr/event)

Z - Dermal Factor (cm/event)

NA = Not Applicable

Source: EPA, 2004. Risk Assessment Guidance for Superfund Volume 1: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment). Final. July 2004.

If $t_{event} < t^{*}$, Then $Z_{organic}$ =
2 FA x Kp [square root (6 x t x t_{event}/p)]

If $t_{event} > t$, Then $Z_{organic}$ =
$FA * Kp [(t_{event}/1 + B) + 2 t ((1 + 3 B + 3 B^2)/(1 + B)^2)]$

$Z_{inorganic}$ =
Kp x t_{event}

Attachment K
Table 3
Dermal Contact with Surface Water While Wading
Reasonable Maximum Exposure
Ashland Lakefront Site, Ashland, WI

Scenario Timeframe: Current
Receptor Population: Wader
Receptor Age: Adult

Medium	Exposure Medium	Exposure Point	Exposure Route	Chemical of Potential Concern	Maximum Conc		Z	Cancer Risk Calculations					Non-Cancer Hazard Calculations				
					Value	Units	Dermal Factor	Intake/Exposure Concentration		Dermal CSF		Cancer Risk	Intake/Exposure Concentration		RfD		Hazard Quotient
								Value	Units	Value	Units		Value	Units	Value	Units	
Surface Water	Surface Water	Surface Water	Dermal Contact	Benzo(a)anthracene	2.9E-04	mg/L	2.62E+00	1.38E-06	mg/kg-day	7.3E-01	1/mg/kg-day	1.0E-06	3.21E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Benzo(b)fluoranthene	1.7E-04	mg/L	4.49E+00	1.38E-06	mg/kg-day	7.3E-01	1/mg/kg-day	1.0E-06	3.23E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Benzo(a)pyrene	3.3E-04	mg/L	4.57E+00	2.73E-06	mg/kg-day	7.3E+00	1/mg/kg-day	**2.0E-05**	6.37E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Benzo(k)fluoranthene	9.5E-05	mg/L	4.57E+00	7.86E-07	mg/kg-day	7.3E-02	1/mg/kg-day	5.7E-08	1.83E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Dibenz(a,h)anthracene	1.7E-04	mg/L	6.93E+00	2.13E-06	mg/kg-day	7.3E+00	1/mg/kg-day	**1.6E-05**	4.98E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Indeno(1,2,3-cd)pyrene	4.2E-04	mg/L	4.56E+00	3.47E-06	mg/kg-day	7.3E-01	1/mg/kg-day	2.5E-06	8.10E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Chrysene	2.7E-04	mg/L	2.62E+00	1.28E-06	mg/kg-day	7.3E-03	1/mg/kg-day	9.3E-09	2.99E-06	mg/kg-day	NTV	mg/kg/day	NTV
			Exp. Route Total									**4.0E-05**					0.0E+00
		Exposure Point Total										**4.0E-05**					0.0E+00
	Exposure Medium Total											**4.0E-05**					0.0E+00

Notes:
Bolded Chemicals and Bold/Underlined Risks = Exceeds a cancer risk of 1E-05.
CSF = Cancer Slope Factor
EPC = Exposure Point Concentration
NC = Not classified as a carcinogen
NE = Not evaluated as a volatile chemical
NTV = No Toxicity Value Available
RfD = Noncancer Reference Dose
Maximum surface water concentrations from Table 4-11 of Jan 2007 RI Report. Values represent the 1998 SEH surface water concentrations, which were not confirmed during the 2005 sampling ever
Toxicity values from Table 11a and 11b of Attachment A of HHRA, (Appendix H)

Attachment K
Table 4
Dermal Contact with Surface Water While Wading
Reasonable Maximum Exposure
Ashland Lakefront Site, Ashland, WI

Scenario Timeframe: Current
Receptor Population: Wader
Receptor Age: Adolescent

Medium	Exposure Medium	Exposure Point	Exposure Route	Chemical of Potential Concern	Maximum Conc		Z	Cancer Risk Calculations					Non-Cancer Hazard Calculations				
					Value	Units	Dermal Factor	Intake/Exposure Concentration		Dermal CSF		Cancer Risk	Intake/Exposure Concentration		RfD		Hazard Quotient
								Value	Units	Value	Units		Value	Units	Value	Units	
Surface Water	Surface Water	Surface Water	Dermal Contact	Benzo(a)anthracene	2.9E-04	mg/L	2.62E+00	6.16E-07	mg/kg-day	7.3E-01	1/mg/kg-day	4.5E-07	3.59E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Benzo(b)fluoranthene	1.7E-04	mg/L	4.49E+00	6.20E-07	mg/kg-day	7.3E-01	1/mg/kg-day	4.5E-07	3.62E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Benzo(a)pyrene	3.3E-04	mg/L	4.57E+00	1.22E-06	mg/kg-day	7.3E+00	1/mg/kg-day	8.9E-06	7.13E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Benzo(k)fluoranthene	9.5E-05	mg/L	4.57E+00	3.52E-07	mg/kg-day	7.3E-02	1/mg/kg-day	2.6E-08	2.05E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Dibenz(a,h)anthracene	1.7E-04	mg/L	6.93E+00	9.56E-07	mg/kg-day	7.3E+00	1/mg/kg-day	7.0E-06	5.58E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Indeno(1,2,3-cd)pyrene	4.2E-04	mg/L	4.56E+00	1.55E-06	mg/kg-day	7.3E-01	1/mg/kg-day	1.1E-06	9.07E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Chrysene	2.7E-04	mg/L	2.62E+00	5.73E-07	mg/kg-day	7.3E-03	1/mg/kg-day	4.2E-09	3.35E-06	mg/kg-day	NTV	mg/kg/day	NTV
			Exp. Route Total									**1.8E-05**					0.0E+00
		Exposure Point Total										**1.8E-05**					0.0E+00
	Exposure Medium Total											**1.8E-05**					0.0E+00

Notes:
Bolded Chemicals and Bold/Underlined Risks = Exceeds a cancer risk of 1E-05.
CSF = Cancer Slope Factor
EPC = Exposure Point Concentration
NC = Not classified as a carcinogen
NE = Not evaluated as a volatile chemical
NTV = No Toxicity Value Available
RfD = Noncancer Reference Dose
Maximum surface water concentrations from Table 4-11 of Jan 2007 RI Report. Values represent the 1998 SEH surface water concentrations, which were not confirmed during the 2005 sampling event.
Toxicity values from Table 11a and 11b of Attachment A of HHRA, (Appendix H).

Attachment K
Table 5
Dermal Contact with Surface Water While Swimming
Reasonable Maximum Exposure
Ashland Lakefront Site, Ashland, WI

Scenario Timeframe: Current
Receptor Population: Swimmer
Receptor Age: Adult

Medium	Exposure Medium	Exposure Point	Exposure Route	Chemical of Potential Concern	Maximum Conc		Z Dermal Factor	Cancer Risk Calculations					Non-Cancer Hazard Calculations				
					Value	Units		Intake/Exposure Concentration		Dermal CSF		Cancer Risk	Intake/Exposure Concentration		RfD		Hazard Quotient
								Value	Units	Value	Units		Value	Units	Value	Units	
Surface Water	Surface Water	Surface Water	Dermal Contact	Benzo(a)anthracene	2.9E-04	mg/L	1.85E+00	1.94E-06	mg/kg-day	7.3E-01	1/mg/kg-day	**1.4E-06**	4.54E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Benzo(b)fluoranthene	1.7E-04	mg/L	3.18E+00	1.96E-06	mg/kg-day	7.3E-01	1/mg/kg-day	**1.4E-06**	4.57E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Benzo(a)pyrene	3.3E-04	mg/L	3.23E+00	3.86E-06	mg/kg-day	7.3E+00	1/mg/kg-day	**2.8E-05**	9.01E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Benzo(k)fluoranthene	9.5E-05	mg/L	3.23E+00	1.11E-06	mg/kg-day	7.3E-02	1/mg/kg-day	8.1E-08	2.59E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Dibenz(a,h)anthracene	1.7E-04	mg/L	4.90E+00	3.02E-06	mg/kg-day	7.3E+00	1/mg/kg-day	**2.2E-05**	7.04E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Indeno(1,2,3-cd)pyrene	4.2E-04	mg/L	3.22E+00	4.91E-06	mg/kg-day	7.3E-01	1/mg/kg-day	**3.6E-06**	1.14E-05	mg/kg-day	NTV	mg/kg/day	NTV
				Chrysene	2.7E-04	mg/L	1.85E+00	1.81E-06	mg/kg-day	7.3E-03	1/mg/kg-day	1.3E-08	4.22E-06	mg/kg-day	1.0E-02	mg/kg/day	NTV
			Exp. Route Total									**5.7E-05**					0.0E+00
		Exposure Point Total										**5.7E-05**					0.0E+00
	Exposure Medium Total											**5.7E-05**					0.0E+00

Notes:
Bolded Chemicals and Bold/Underlined Risks = *Exceeds a cancer risk of 1E-05.*
CSF = Cancer Slope Factor
EPC = Exposure Point Concentration
NC = Not classified as a carcinogen
NE = Not evaluated as a volatile chemical
NTV = No Toxicity Value Available
RfD = Noncancer Reference Dose
Maximum surface water concentrations from Table 4-11 of Jan 2007 RI Report. Values represent the 1998 SEH surface water concentrations, which were not confirmed during the 2005 sampling event.
Toxicity values from Table 11a and 11b of Attachment A of HHRA, (Appendix H).

Attachment K
Table 2
Dermal Contact with Surface Water While Swimming
Reasonable Maximum Exposure
Ashland Lakefront Site, Ashland, WI

Scenario Timeframe: Current
Receptor Population: Swimmer
Receptor Age: Adolescent

Medium	Medium	Exposure Point	Exposure Route	Chemical of Potential Concern	Maximum Conc		Z	Cancer Risk Calculations					Non-Cancer Hazard Calculations				
					Value	Units	Dermal Factor	Intake/Exposure Concentration		Dermal CSF		Cancer Risk	Intake/Exposure Concentration		RfD		Hazard Quotient
								Value	Units	Value	Units		Value	Units	Value	Units	
Surface Water	Surface Water	Surface Water	Dermal Contact	Benzo(a)anthracene	2.9E-04	mg/L	1.85E+00	8.71E-07	mg/kg-day	7.3E-01	1/mg/kg-day	6.4E-07	5.08E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Benzo(b)fluoranthene	1.7E-04	mg/L	3.18E+00	8.77E-07	mg/kg-day	7.3E-01	1/mg/kg-day	6.4E-07	5.11E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Benzo(a)pyrene	3.3E-04	mg/L	3.23E+00	1.73E-06	mg/kg-day	7.3E+00	1/mg/kg-day	**1.3E-05**	1.01E-05	mg/kg-day	NTV	mg/kg/day	NTV
				Benzo(k)fluoranthene	9.5E-05	mg/L	3.23E+00	4.98E-07	mg/kg-day	7.3E-02	1/mg/kg-day	3.6E-08	2.90E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Dibenz(a,h)anthracene	1.7E-04	mg/L	4.90E+00	1.35E-06	mg/kg-day	7.3E+00	1/mg/kg-day	9.9E-06	7.89E-06	mg/kg-day	NTV	mg/kg/day	NTV
				Indeno(1,2,3-cd)pyrene	4.2E-04	mg/L	3.22E+00	2.20E-06	mg/kg-day	7.3E-01	1/mg/kg-day	1.6E-06	1.28E-05	mg/kg-day	NTV	mg/kg/day	NTV
				Chrysene	2.7E-04	mg/L	1.85E+00	8.11E-07	mg/kg-day	7.3E-03	1/mg/kg-day	5.9E-09	4.73E-06	mg/kg-day	NTV	mg/kg/day	NTV
			Exp. Route Total									**2.5E-05**					0.0E+00
		Exposure Point Total										**2.5E-05**					0.0E+00
	Exposure Medium Total											**2.5E-05**					0.0E+00

Notes:
Bolded Chemicals and Bold/Underlined Risks = Exceeds a cancer risk of 1E-05.
CSF = Cancer Slope Factor
EPC = Exposure Point Concentration
NC = Not classified as a carcinogen
NE = Not evaluated as a volatile chemical
NTV = No Toxicity Value Available
RfD = Noncancer Reference Dose
Maximum surface water concentrations from Table 4-11 of Jan 2007 RI Report. Values represent the 1998 SEH surface water concentrations, which were not confirmed during the 2005 sampling event.
Toxicity values from Table 11a and 11b of Attachment A of HHRA, (Appendix H).