UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

November 25, 2008

MEMORANDUM

SUBJECT: Summary of Human Health Effects Data for the Mineral Acids Registration Review Decision Document.

DP Barcode: 358834 **Case No.:** 4064
PC Codes: 045901, 076001, 073201, and 078001
CAS#: 7647-01-0, 7664-38-2, 7681-38-1, and 7664-93-9

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Introduction

The Antimicrobial Division (AD) Registration Review Team has evaluated the status of the human health assessments for mineral acids (RED case 4064). The mineral acids case includes four active ingredients: hydrogen chloride (PC Code 045901), phosphoric acid (PC Code 076001), sodium bisulfate (PC Code 073201), and sulfuric acid (PC Code 021801). Mineral acids are antimicrobial pesticides used on indoor food, indoor medical, indoor residential, aquatic nonfood industrial, indoor residential and indoor non-food as a sanitizer, disinfectant, viricide, disinfectant, microbiocide/microbiostat, and fungicide. Registered uses include eating establishments, eating establishment equipment/utensils, food processing plant equipment, animals premises treatment, bathroom premises/hard surfaces, refuse/solid waste sites, toilet bowls, urinals, a variety of disinfectant uses (hospital, agricultural, and dairy) and mushroom houses. The mineral acid active ingredients are formulated as emulsifiable concentrates, soluble concentrates/liquids, and liquid ready to use products. The team looked at the hazard and exposure databases for mineral acids and attempted to determine whether changes in science policy or deficiencies in the databases materially affected the overall risk picture. Mineral acids were first registered as a pesticide in the early 1970's. A Reregistration Eligibility Decision (RED) was conducted for mineral acids in December 1993. According to Agency data in OPPIN, there are currently 41 labeled hydrochloric acid products, 55 labeled phosphoric acid products, 2 labeled sodium bisulfate products, and 7 labeled sulfuric acid products.

The primary source of information for this assessment is the most recent mineral acids RED (1993). No new toxicity data for mineral acids have been submitted to the Agency since reregistration. The purpose of this screen is to determine whether sufficient data are available to support registration review, report on whether risk assessments have been conducted and to report whether new human health assessments are needed to support the registration review process.

The Food and Drug Administration (FDA) considers these chemicals to be generally recognized as safe (GRAS) for use in foods. The mineral acids are strongly acid, release hydrogen and dissociate in water and decrease the pH. The extent and duration of the drop will depend on the neutralizing ions, the buffering capacity, and the dilution. Many of the end-use products are significantly diluted and this has a large effect on the overall toxicity of the chemical. Mineral acids are also registered as an inert ingredient in other pesticide products. Table 1 presents the chemical identity of mineral acids.

Section 1. Chemical Identity

Table 1 Chemical Identity	
Common Name	Mineral acids
CAS name	Mineral acids
PC Code	045901 hydrochloric acid 076001 phosphoric acid 073201 sodium bisulfate 021801 sulfuric acid
CAS registry number	7647-01-0 hydrochloric acid 7664-38-2 phosphoric acid 7681-38-1 sodium bisulfate 7664-93-9 sulfuric acid
Registration Review Case No.	4064

Section 2. Toxicology

The Agency has reviewed the existing toxicity assessments and toxicity data for mineral acids and believes that additional toxicity studies for technical chemicals will not be needed. The Agency reviewed the historical toxicological database supporting the original mineral acids RED which was comprised mostly from published and unpublished studies obtained directly from published open literature (Sax and Lewis, 1989). The Agency searched the available literature, registrant submissions and believes that for the most part the existing acute toxicological database and acute toxicity categories from the RED do not need to be updated. Dietary (food and drinking water) exposures of concern are not anticipated for sulfuric acid, phosphoric acid, hydrochloric acid or sodium bisulfate.

The Agency will rely on most of the acute toxicity data submitted at the time of the RED for registration review. In technical form, the RED states that the mineral acids are extremely irritating to the eye (toxicity category I). Additionally, the RED states that in technical form hydrochloric acid, phosphoric acid and sulfuric acid are corrosive to the skin (toxicity category I for dermal irritation). However, sodium bisulfate is not a skin irritant (toxicity category IV).

According to the RED for the acute oral toxicity is moderate (toxicity category III) for all mineral acids except for sulfuric acid which is toxicity category II. Mineral acids have moderate dermal toxicity (acute toxicity category III). Acute inhalation studies for the technical active ingredient were waived in the RED since sulfuric acid; hydrochloric acid and phosphoric acid are corrosive and severely irritating to lung tissue. This waiver is still accurate. The Agency grants acute inhalation toxicity data waivers for chemicals that are corrosive (pH<2) and irritating (USEPA, 2002). The default inhalation toxicity

category would be toxicity category I. Acute oral and inhalation toxicity studies for sodium bisulfate were submitted after the RED and reviewed by the Agency in 1996 (D3223172). Based on the Agency review, the existing inhalation toxicity category for sodium bisulfate was changed to toxicity category IV.

The Agency reviewed the historical data from the RED as well as new subchronic and chronic toxicological from the existing scientific literature. The Agency concluded that no additional sub-chronic, chronic dermal and/or or oral toxicity data will be required for registration review based on the availability of toxicity information in the existing literature for many of the mineral acids. It should be noted that the labeled end-use mineral acids are diluted by more than a factor of 10 to 1, the acids are neutralized in water and would dissociate to salts which are GRAS for use in foods and of low toxicity for oral and dermal when diluted. It should also be noted that technical grade active ingredients (TGAI) are used for subchronic and chronic animal toxicity tests would be expected to be significantly less when end-use products are used. Based on this information, subchronic and/or chronic toxicity data for oral and dermal exposures are not anticipated.

Inhalation Toxicity

As far as inhalation exposure to end-use exposure, the labeled end-use mineral acids are diluted by more than a factor of 10 to 1, the acids will be neutralized in water and dissociate to salts relative to the molar concentrations. However, there is evidence that phosphoric acid, hydrogen chloride, and sulfuric acid are hazardous at higher concentrations through the inhalation route. The Agency will rely on toxicity data presented in the RED and published inhalation toxicity data for phosphoric acid and hydrogen chloride from EPA's Integrated Risk Information System (IRIS) (IRIS, 2008). For sulfuric acid, IRIS toxicity values were not reported. However, there are a limited amount of inhalation toxicity animal studies and human epidemiological data from sources such as the Agency of Toxic Substances and Disease Registry (ATSDR) and other sources. For sodium bisulfate, no subchronic inhalation toxicity data is available. However, and the sulfate and sodium salts would not be an inhalation toxicity concern.

Phosphoric Acid

IRIS developed a reference concentration (RfC) of 1E-2 mg/m^3 for phosphoric acid. The RfC was based on a 13-week rat inhalation study in which the critical effect measured was bronchiolar fibrosis. The principle study identified was a 13-week inhalation study administered to Sprague-Dawley rats (Aranyi et al 1988). The Aranyi et al. study, which occurred in two trials, exposed 40 rats per dose level in 1 cubic meter exposure chambers to aerosolized concentrations of combustion products from burning 95% red phosphorous and 5% butyl rubber. The concentrations of phosphorus acids ranged from 71 to 79%. The first study measured rats after being exposed to air concentrations of 300, 750 and 1500 mg/m^3 and the second study measured rats after being exposed to 50, 180 and 300 mg/m^3 (IRIS, 2008).

Both studies clearly indicated that the terminal bronchioles were the target organ with dose dependent bronchial fibrosis. In the first study, lesions were noted at the two highest

dose levels (750 and 1500 mg/m^3). In the second study, lesions were noted in 4/20 animals at the 180 mg/m^3 dose level which was assigned as the LOAEL . The NOAEL assigned was 50 mg/m^3. IRIS recommended that a benchmark concentration (BMC) analysis was generally a preferable alternative to the NOAEL/LOAEL approach to define a point of departure. Therefore IRIS combined the data from both trials to perform a BMC analysis using both Weibull (non-threshold) and linear models. The Weibull model produced a better goodness-of-fit. The calculated BMC10 from the Weibull model was 100 mg/m^3. The BMC10 was amortized by the exposure time of 2.25 hours per 24 hours day and 4 days per week (2.25 hours/24 hours x 4 days/7 days) or 5.4 mg/ m^3. Additionally, EPA adjusted the BMC10 by the RDDR (regional deposited dose ratio for particulates to account for differences between rats and humans). The RDDR for an effect in the terminal bronchiole is 0.64 and was used to derive a human equivalent concentration (HEC) of 3.4 mg/m^3 (5.4 mg/m^3 x 0.64). It should that hygroscopic particle growth in airways of phosphoric acid is a complex issue and is complicated by the degree of humidification and the transit time of the particle (IRIS, 2008).

When conducting inhalation risk assessments, the magnitude of the UFs applied is dependent on the methodology used to calculate risk. For studies in this risk assessment with inhalation animal data, UFs are based on the RfC methodology developed by the Office of Research and Development (ORD) for the derivation of inhalation reference concentrations (RfCs) and human equivalent concentrations (HECs) for use in margin of exposure (MOE) calculations. Since the RfC methodology takes into consideration the pharmacokinetic (PK) differences <u>but not the pharmacodynamic (PD) differences</u>, the UF for interspecies extrapolation may be reduced to 3X to account for the PD differences.

Hydrogen Chloride

IRIS developed a RfC of 1E-2 mg/m^3 for hydrogen chloride. The RfC was based on a study conducted by (Albert et. al 1982) in which one hundred male Sprague Dawley rats were exposed to 10 ppm hydrogen chloride for 6 hours/day, 5 days/week for their lifetime. Based on adjusting by the exposure duration the concentration would be 2.5 mg/cm^3. The critical effect was hyperplasia of nasal mucosa larynx and trachea. It should be noted that IRIS reported that there was low confidence in this data because the study was limited to one dose and had limited toxicological measurements (IRIS, 2008).

When conducting inhalation risk assessments, the magnitude of the UFs applied is dependent on the methodology used to calculate risk. For studies in this risk assessment with inhalation animal data, UFs are based on the RfC methodology developed by the Office of Research and Development (ORD) for the derivation of inhalation reference concentrations (RfCs) and human equivalent concentrations (HECs) for use in margin of exposure (MOE) calculations. Since the RfC methodology takes into consideration the pharmacokinetic (PK) differences <u>but not the pharmacodynamic (PD) differences</u>, the UF for interspecies extrapolation may be reduced to 3X (to account for the PD differences).

Sulfuric Acid

An RfC was not developed in the IRIS database nor has an HEC been developed in any other peer reviewed literature (e.g ATSDR) for sulfuric acid. ATSDR, 1998 reported

a number of respiratory effects to occupational workers overexposed to sulfuric acid. A limited amount of animal studies also is available. However these studies are primarily acute inhalation studies. For example, Stengel et al 1993 reported in a guinea pig study that animals suffered labored breathing and 6% death as a result of 1-hour nose-only exposures to 52-61 mg/m^3 sulfuric acid aerosols in the size range of 0.8-1.2 µm. In addition, Wolff et al. 1979 reported labored breathing and hyperinflated lungs from guinea pigs exposed to sulfuric acid aerosols for 8 hours. The effects were observed after at 17.4 mg/m3 for aerosols with an MMAD of 0.8 µm and 37.3 mg/m3 for aerosols with a MMAD of 0.4 µm.

A TLV-TWA of 0.2 mg/m^3 is assigned to sulfuric acid mist by ACGIH. This TLV is assigned to "protect against central airway effects (i.e., clearance and pulmonary function changes) as well as the laryngeal cancer associated with exposure to sulfuric acid mists." www.acgih.gov

Existing literature for sulfuric acid indicates that "in numerous repeated studies with sulfuric acid aerosol, toxicity was confined to changes in the structure and function of the respiratory tract, suggesting that it has a local effect and no systemic effects. The observed properties are related to the irritant properties and are most likely due to the H+ ions."
http://www.inchem.org/documents/sids/sids/7664939.pdf

Section 3. Dietary Assessment

Both sulfuric acid and phosphoric acid are exempt from the requirement of a tolerance for active and inert ingredients for use in antimicrobial formulations (dairy processing equipment, and food-processing equipment and utensils). When diluted these acids dissociate into sulfate and phosphate salts and FDA assigns all of the mineral acids as GRAS. EPA agrees with the conclusion presented in the individual FDA GRAS reports.

Dietary (food and drinking water) exposures of concern are not anticipated for sulfuric acid. The FDA considers sulfuric acid generally GRAS for use in foods under 21 CFR 184.1095.
According to the FDA website http://www.cfsan.fda.gov/~dms/opascogd.html

> *Sulfates are natural constituents of foods and normal products of sulfur metabolism in animals. … There is no evidence in the available information on sulfuric acid, and on ammonium, calcium, potassium, and sodium sulfates that demonstrates, or suggests reasonable grounds to suspect, a hazard to the public when they are used at levels that are now current or that might reasonably be expected in future.*

Dietary (food and drinking water) exposures of concern are not anticipated for sulfuric acid. The FDA considers phosphoric acid GRAS for use in foods under 21 CFR 182.1073. According to the FDA website http://www.cfsan.fda.gov/~dms/opascogd.html

> *There is no evidence in the available information on phosphate salts that demonstrates or suggests reasonable grounds to suspect a hazard to the public when they are used at levels that are now current or might reasonably be expected in the future.*

Dietary (food and drinking water) exposures of concern are not anticipated for hydrochloric acid. The FDA considers hydrochloric acid as GRAS when used as a buffer and neutralizing agent in accordance with good manufacturing or feeding practice (21 CFR 582.1057). According to the FDA website http://www.cfsan.fda.gov/~dms/opascogd.html

> *Hydrochloric acid in concentrated form is a strongly corrosive agent and the consequences of exposure to it are well known. However, as it is used in food processing, or as a food additive to adjust the pH, hydrochloric acid is neutralized or buffered by the food to which it is added. Thus, human consumption is not of the acid, but of the chloride ion in the salts formed in the neutralization process. The small amounts of hydrochloric acid that may persist in foods or drinks, would, in turn, be neutralized and buffered during ingestion and digestion, or after absorption. Hydrochloric acid is also a natural secretory product of the stomach of animals, including man (about 0.5 percent concentration in the gastric juice). The normal production of hydrochloric acid by the stomach exceeds many fold the amounts that could be derived from foods. Animal experiments have not revealed untoward effects of hydrochloric acid consumption in amounts greatly exceeding those that can be reasonably expected to result from consumption of foods treated with hydrochloric acid. Based on these considerations, the Select Committee concludes that: There is no evidence in the available information on hydrochloric acid that demonstrates or suggests reasonable grounds to suspect a hazard to the public when it is used at levels that are now current or that might reasonably be expected in the future.*

Dietary (food and drinking water) exposures of concern are not anticipated for mineral acids because concentrations are significantly diluted, dissociate in water to salts, and there are no oral toxicity issues. The use of mineral acids as a food surface sanitizer may be expected to result in the introduction of low concentrations of mineral acids into drinking water and food supply. However, taking into account the low toxicity of mineral acids, the already insignificant risk from food sources, and the existing tolerance exemptions, exposure via food or drinking water consumption is not of concern.

Section 4. Aggregate and Cumulative Exposure

In examining aggregate exposure, EPA takes into account the available and reliable information concerning exposures to pesticide residues in food and drinking water, and non-occupational pesticide exposures. Dietary (food and drinking water) exposures of concern are not anticipated for mineral acids because concentrations are significantly diluted, dissociate to salts in water and there are no oral toxicity issues. FDA considers sulfuric and phosphoric acid GRAS for use in foods and drinking water Risks associated with mineral acids exposures are expected to be minimal based on limited evidence of any subchronic or chronic systemic effects through the oral route of exposure.

Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." EPA has not yet determined

whether mineral acids have a common mechanism with other compounds, consequently a cumulative assessment will not be performed.

Section 5. Occupational/Residential Exposure

An occupational and/or residential exposure assessment is required for an active ingredient if (1) certain toxicological criteria are triggered and (2) there is potential exposure to handlers (mixers, loaders, applicators, etc.) during use or to persons entering treated sites after application is complete. For mineral acids, the toxicological criteria are not triggered for dermal or oral. Therefore, new dermal and incidental ingestion occupational and residential risk assessments are not required for registration review.

For inhalation exposure, certain toxicological triggers are not met for sodium bisulfate. However, for sulfuric acid phosphoric acid and hydrogen chloride (e.g., hydrochloric acid), an inhalation toxicological endpoint has been developed. The Agency may have potential exposures concerns based on the fact that the product may be introduced in specific situations as an aerosolized spray. The paragraphs below summarize why in some cases risk assessments may be appropriate or not appropriate for specific mineral acids.

Sodium Bisulfate

Based on the Agency review, the sodium bisulfate does not trigger toxicological concerns; therefore a risk assessment for sodium bisulfate is not required.

Sulfuric Acid

Based on review of the available labels sulfuric acid, EPA expects inhalation exposures will likely be minimized based on the label use directions and there is little potential for to generate aerosolized spray. There are inhalation sub-chronic and chronic toxicological concerns for sulfuric acid.

Currently sulfuric acid is used in only one label (EPA Reg # 4959-41) as a sanitizer in a mixture with several other active ingredients for circulate-in-place (CIP) uses for food processing and dairy equipment. According to this label, only 1 ounce of product containing 9.5% active ingredient is mixed with 6 gallons of water. Since very low amounts of liquid concentrate are used, the mixing/loading process would not be expected to result in significant amounts of aerosolized spray, and the process is likely to be enclosed, there would be minimal dermal and/or inhalation exposure concerns for workers and therefore a risk assessment would not be anticipated for sulfuric acid. However, the Agency would require exposure data on product use information on this chemical.

Phosphoric Acid

Based on review of the available labels for phosphoric acid, EPA expects inhalation exposures will likely be minimized based on the label use directions, but for registration

review EPA will need to conduct a risk assessment based on: 1) noted toxicological concerns of bronchial fibrosis in the lung of rats during a 13-week study which was reported in the recent IRIS database literature for phosphoric acid and 2) potential occupational and residential handler inhalation exposure concerns to aerosolized spray mist when using this spray as a sanitizer or disinfectant.

Potential exposure pathways to occupational workers for phosphoric acid include mixer/loader exposure for circulate-in-place (CIP) uses for dairy processing equipment or utensils. Labels indicate that the chemicals are usually significantly diluted (many labels recommend 1 in 500 dilutions and the % ai is significantly lower than 1% ai) during the CIP sanitizing process. Since very low amount of liquid concentrate are used (1 oz) and the process is likely to be enclosed except for minimal exposure mixing/loading, there would be minimal dermal and inhalation exposure concerns and therefore a risk assessment would be required for this scenario.

Occupational and residential mixer/loader/applicator exposures can also occur when phosphoric acid is used as a wipe, mop or spray and would likely pose a greater inhalation concern than the CIP use. Phosphoric acid is used as a disinfectant and sanitizer for treatment in bathrooms (sinks, countertops, floors, etc) and other hard surfaces. For example, in label (EPA Reg 875-97) the product used is less than 20% active ingredient, used in small amounts (1 oz) are diluted (10 gallons) for use. The label recommends that users wear rubber gloves and reduce contact time (e.g., limit contact time to < 10 minutes) in order to minimize exposure. The Agency believes that there are potential inhalation exposure concerns for occupational and residential handler to aerosolized spray mist based on spray applications to countertops; therefore, a risk assessment will be anticipated for this use. It is also anticipated that the duration of exposure could potentially be long if used particularly in medical settings. The Agency would likely need additional product use information as well as inhalation exposure use for this use pattern.

Hydrogen Chloride

Based on review of the available labels for hydrogen chloride, EPA expects exposures will also likely be minimized based on specific label use directions and requirements for the application equipment. Currently hydrogen chloride is used exclusively used to disinfect, sanitize, and deodorize toilet bowls and urinals. Application is exclusively used through a child proof squeeze bottle. For example, a representative label indicates that a user squeezes approximately 4 ounces of cleaner (23% ai) into the toilet bowl or urinal which contains approximately ¾ gallon of water After 10 minutes, the user then scrubs bowl or urinals with a toilet brush and then flushes (EPA Reg 675-1). The labels for these products prohibit the use of the product on wash bowls, floors, countertops and other hard surfaces. The inhalation concern for this scenario is minimal since this chemical is not aerosolized using a squeeze bottle. It is not anticipated that the duration of exposure would be for any extended period.

It should be noted however, that one particular product containing multiple active ingredient which includes hydrogen chloride at 0.66% active ingredient (EPA Reg 74331-2) and marketed in 1 gallon bottles. This product is different in that the

application method is through spray, wipe or immersion. Although the application would likely be only for spot treatments, and is not a continuous exposure a risk assessment would be needed based on the use pattern. The use pattern is different from many of the labels in that the product is used to disinfect hard food and non-food hard surfaces which include residential facilities, animal premises (swine and poultry), and mushroom houses.

Based on review of the available labels for hydrogen chloride, EPA expects inhalation exposures will likely be minimized based on the label use directions, but for registration review EPA will need to conduct a risk assessment based on: 1) noted toxicological concerns of hyperplasia of nasal mucosa larynx and trachea of rats during their lifetime which was reported in the recent IRIS database literature for phosphoric acid and 2) potential occupational and residential mixer/loader/applicators inhalation exposure concerns to aerosolized spray mists (i.e., specific wipe and spray uses on animal premises) . It should be noted that most of the registered products for hydrogen chloride have a very specific use pattern (e.g., toilet bowl and urinals) which would result in minimal exposure concern, however. The Agency would likely need additional product use information as well as inhalation exposure use for this use pattern.

To protect workers mixing concentrated mineral acids present labels require a "Danger" precautionary statement because of acute eye irritation and skin irritation for all mineral acids except sodium bisulfide. To protect the worker, the existing mineral acids labels require personal protective equipment (PPE) including face shields, rubber gloves, goggles, and protective clothing and also advises users to avoid breathing spray mist. Based on this required PPE, worker or residents would be protected from any acute effects (e.g. dermal or eye irritation) from the corrosive active ingredient.

Section 6. Anticipated Data Needs

The Antimicrobial Division (AD) anticipates the need for the following studies to complete risk assessments for the registration review process for hydrogen chloride and phosphoric acid inhalation risk assessments. These studies were not required in the original 1993 RED data call-in (DCI), but this data are now anticipated (refer to Appendix A for justifications):

<u>Occupational and Residential Applicator Exposure Data Needs</u>

- (GLN 875.1400) Inhalation Indoor Exposure
- (GLN 875.1600) Data Reporting and Calculations
- (GLN 875.1700) Product Use Information

Appendix A provide detailed justifications why these studies are required.
The Antimicrobial Division (AD) will not be requiring any further studies for mineral acids for registration review:

Section 7. Tolerances

Sulfuric acid (CAS # 7664-93-9) is exempt from the requirement of a tolerance for active and inert ingredients for use in antimicrobial formulations (dairy processing

equipment, and food-processing equipment and utensils) (40 CFR 180.940). When used for ready to use, the end-use concentration has a limit not to exceed 288 ppm.

Phosphoric acid (CAS# 7664-38-2) is exempt from the requirement of a tolerance for active and inert ingredients for use in antimicrobial formulations (dairy processing equipment, and food-processing equipment and utensils) (40 CFR 180.940). A limit was not specified.

Hydrochloric acid (CAS 7647-01-0) is exempt from the requirement of a tolerance when used as a solvent, neutralizer in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest. 40 CFR 180.910.

Section 8. Overall Conclusions

The Agency reviewed the hazard and exposure databases for mineral acids and anticipates that no additional toxicity data will be required. However addition exposure data will be needed to assess inhalation exposure for registration review. Additionally, the EPA anticipates that additional occupational and residential handler assessments will be needed to ensure that the mineral acids registration review case meets the safety standards established by FFDCA, as amended by FQPA.

Section 9. Reference

- Reregistration Eligibility Decision (RED) Mineral acids, December, 1993. http://www.epa.gov/pesticides/reregistration/status.htm
- Hydrogen Chloride IRIS document. http://www.epa.gov/iris/subst/0396.htm
- Phosphoric Acid IRIS document. http://www.epa.gov/iris/subst/0697.htm
- ATSDR 1998. Toxicological Profile for Sulfuric Trioxide and Sulfuric Acid. US Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry. December 1998.
- USEPA, 2002. “Guidance: Waiver Criteria for Multiple-Exposure Inhalation Toxicity Studies.” Memorandum: From Margaret Stasikowski to Health Effects Division. August 15, 2002.

Appendix A: Exposure Guideline Study Justifications		
875.1400 (Applicator)	Inhalation Indoor Exposure	*Note: Inhalation exposure data are needed for both residential and occupational uses. The selection of an outdoor versus an indoor site is based on the high end exposure scenario (for inhalation the selection is typically indoors). In almost all cases, repeating an exposure study for the same scenario outdoors and indoors is not necessary.* **1) What is the value of the study?** The inhalation exposure route is very important for exposure scenarios such as paint rollers and airless sprayers where aerosols would be generated. In addition, inhalation exposures from liquid pouring are evident in exposure studies in the Pesticide Handlers Exposure Database (PHED). The significance of these exposures is directly affected by the severity of the inhalation toxicological endpoint of concern. At this point in time, no toxicological data are available to assess the inhalation risk. The existing Chemical Manufacturer Association (CMA) data base and PHED for these scenarios are limited in scope for QA/QC and number of monitoring units. EPA presented the need for additional handler exposure data to the January 2007 Science Advisory Panel (SAP) as well as to the April 2007 Human Studies Review Board (HSRB) and both groups agreed that additional data are warranted. **2) How would the data be used?** The inhalation exposure data would be used to assess the occupational and residential short-term exposure of spraying a mineral acids sanitizer or disinfectant on hard surfaces. **3) How could the data affect the risk assessment?** The inhalation exposure data would be used to determine the accuracy of the inhalation risks to both residence and occupational workers. If risks warrant mitigation, the inhalation exposure data would provide the types of mitigation necessary such as respiratory protection from respirators or closed systems for commercial uses to potential removal of uses from the label. **4) What is triggering the need for this data?** The criteria for the inhalation exposure data are based on the potential for respiratory exposure from the labeled uses (e.g., trigger pump sprayers) and evidence of toxicity. If no toxicological endpoints of concern were identified, then the inhalation exposure data would not be needed.

875.1600 (Applicator)	Data Reporting and Calculations	**1) What is the value of the study?** For all exposure studies this data need is needed to facilitate the review of the data. **2) How would the data be used?** The study report and all raw data/calculations would be reviewed for the adequacy of the data. **3) How could the data affect the risk assessment?** The data are needed to interpret the inhalation exposure data collected. **4) What is triggering the need for this data?** This data need is triggered if an exposure study is conducted.
875.1700 (Applicator)	Product Use Information	**1) What is the value of the study?** Product use information is a description of how the product is actually applied; it is not a field study. A description of how this product is used would provide for a comprehensive realistic assessment of its potential applications. **2) How would the data be used?** The description of the application techniques would be used to define the exposure scenarios to be assessed in the risk assessment. **3) How could the data affect the risk assessment?** A complete description of product use would ensure that the risk assessment is inclusive of the types of exposures occurring during residential and occupational use. **4) What is triggering the need for this data?** The need for a risk assessment as needed under Registration Review would require that the risk assessor understands how the product is applied.