An overview of chemical exposures in your environment

Lunch & Learn: EPA Finance Center

5/18/17

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National Center for Environmental Assessment

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Conflict of Interest Statement

- We have no conflicts of interest to disclose.
- The views expressed in this presentation are those of the author and do not necessarily reflect the views or policies of the U.S. EPA.

Everything is a Chemical

- Pesticides/Herbicides
- Nanomaterials
- Perfluorinated Chemicals
- Plastics/Polymers
- Polycyclic Aromatic Hydrocarbons
- Flame Retardants

Chemical Regulation

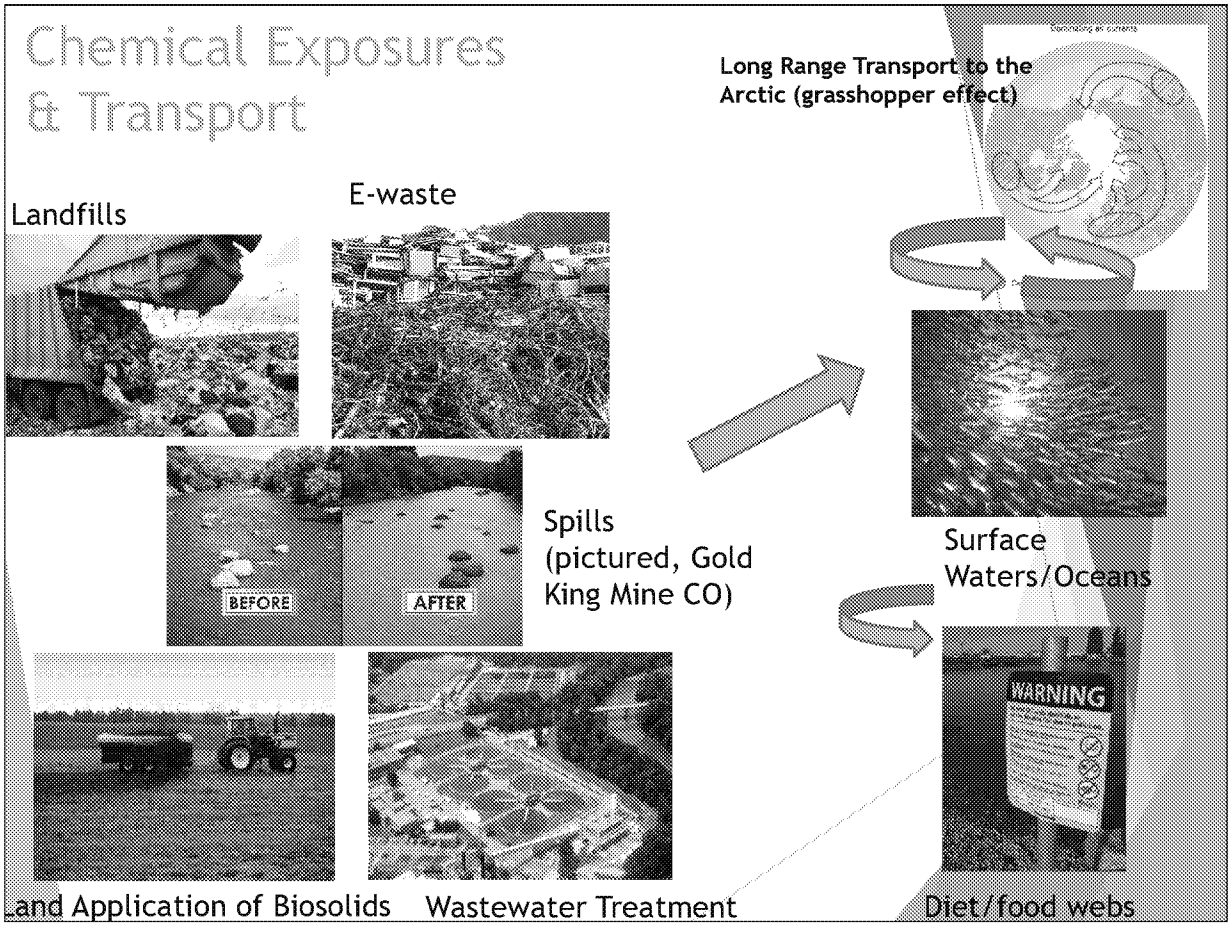
- **Toxic Substances Control Act (TSCA)**
  - "chemicals of commerce"
  - Recently revised in 2015-2016; Lautenburg Act for Chemical Safety
- **Federal Insecticide Fungicide Rodenticide Act (FIFRA)**
  - Herbicides, insecticides, and pesticides
- **Food Drug Administration (FDA)**
  - Drugs, medical devices

Introduction to Toxicology

- Integrative discipline concerned with study of adverse effects of chemicals on living organisms
  - Ecotoxicology, environmental toxicology, human health
- Factors influencing toxicity
  - dosage, acute/chronic exposures, route of exposure, species, age, sex, environment
  - History: "The Dose makes the poison" -*Paracelsus*
- Testing methods
  - Non-human animals
  - Alternative testing methods (high throughput, modeling, etc)

The Chemical Problem

- Too many chemicals, not enough time/resources
  - Estimated 80,000 chemicals registered
  - Current estimates ~30,000 substances in commercial use
- Expense associated with testing
  - EPA guideline study for developmental neurotoxicity can take 1-2 years, cost $1 million
  - Large numbers of chemicals, difficult to test with traditional methods
- Human Health Risk Assessment: function of hazard identification, dose-response relationship, exposure characterization, and risk characterization


Chemical Exposures & Transport
Long Range Transport to the Arctic (grasshopper effect)
Landfills
E-waste
BEFORE
AFTER
Spills (pictured, Gold King Mine CO)
Surface Waters/Oceans
WARNING
and Application of Biosolids
Wastewater Treatment
Diet/food webs

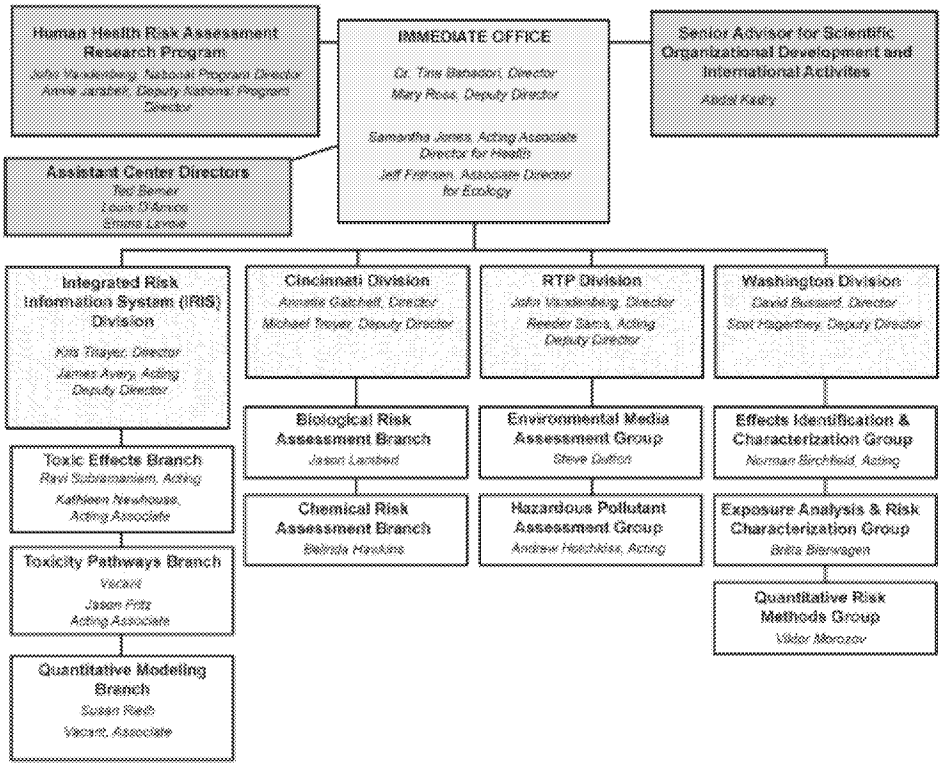
National Center for Environmental Assessment

- Part of the Office of Research & Development
  - Split across multiple divisions: RTP, Cincinnati, Washington
- Diverse Staff
  - Biologists, chemists, ecologists, engineers, epidemiologists, toxicologists, & statisticians
- Guidance Documents / Work Products
  - Guidance documents
  - Criteria documents
  - Risk assessments
  - Risk assessment methodologies
  - Models

National Center for Environmental Assessment

- human health and ecological risk assessment- a robust scientific process used to determine how pollutants or other stressors may impact human health and the environment
  - interacts with other agencies, the scientific community, industry, policy-makers, and the public
  - innovative risk assessment methods and tools that help extrapolate between experimental data and real-world scenarios, improve our understanding of uncertainties, and facilitate careful evaluation of scientific evidence

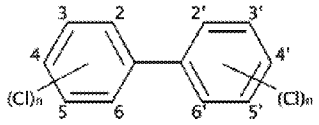
National Center for Environmental Assessment



Toxicology & Risk Assessment

- Systematic review of existing human and animal data on potential health impacts
- When sufficient data exist, development of toxicological reviews that develop recommended levels of exposure that do not come with increase risk of adverse health effects
- Look at a few case example chemicals:
  - Polychlorinated Biphenyls (PCBs)
  - Phthalates

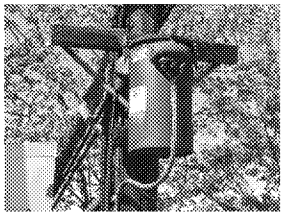
Polychlorinated Biphenyls (PCBs)

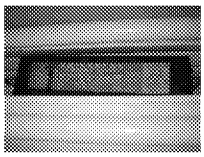


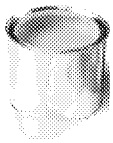
- 209 congeners
- Sold as commercial mixtures (1930-1977)
  - Aroclor (US); Kanechlor (Japan); Clophen (Germany), many other trade names
  - >600 million kg/yr produced in US alone
- Persistent Organic Pollutants
  - banned by TSCA 1979
  - Stockholm Convention's Dirty Dozen 2001
- Not currently in use
  - PCB contamination continues through disposal of PCB-containing products and environmental partitioning
  - Many congeners have long half lives; bioaccumulative/biomagnification

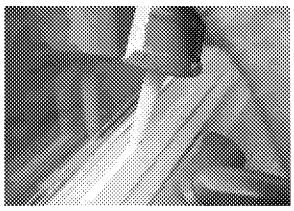
Extensive environmental contamination (ex: Great Lakes; Anniston, AL, NYC's Hudson River, etc.)

Sources of PCB Exposure

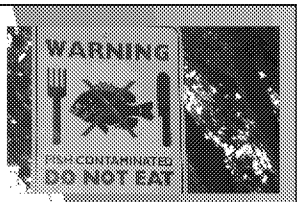


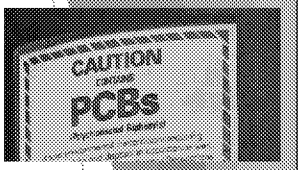






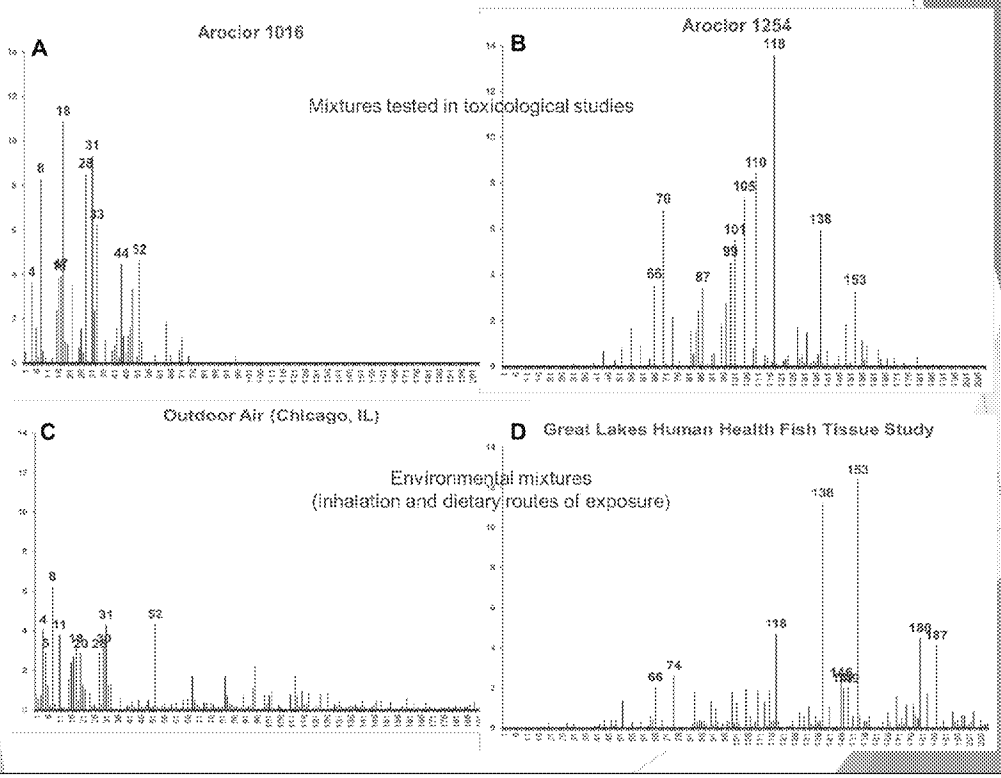
Human Exposure to PCBs





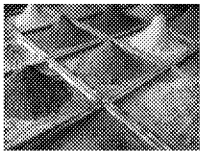
- General population
  - Contaminated food (fish, meat, dairy, others)
  - Inhalation of contaminated air (indoor settings; schools)
  - ~2ng PCB/kg-d (FDA; 2003)
  - Greater Exposures- recreational fishers; native American/subsistence fishers
- Occupational exposures
  - Inhalation and dermal contact in workplaces where PCBs are present
- Childhood Exposures
  - Lactational transfer through breastfeeding
  - Inhalation exposures in schools
- Difficulties with Characterizing PCB Exposures
  - Epidemiological studies use PCB serum levels, breast milk, or adipose tissue (commonly detected congeners: PCB-138, -153, and -180; PCB -28, -118, -180)
  - Exposure data consisting of only a few congeners may not accurately reflect exposures to other PCBs, which may be biologically active

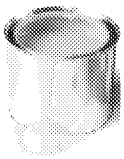
Congener Compositions of Aroclor Mixtures versus Environmental Mixtures

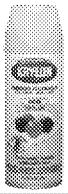


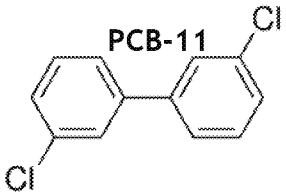
Emerging PCB Sources

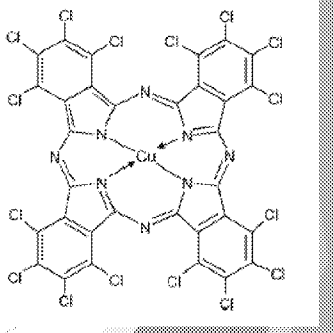
- Manufacturing processes result in inadvertent production of PCBs
  - Pigment production (PCB 11, 28, 52, 77, 209)
  - Paper recycling and colored inks
- Emerging issue, high levels of lower chlorinated congeners observed in water samples; PCB-11 specifically
  - Toxicity of PCB-11 and uptake/accumulation not well understood
  - PCB-11 detected in humans
- Widespread Environmental Distribution
  - Atmospheric transport globally PCB-11
  - point sources and industrial/municipal waste water











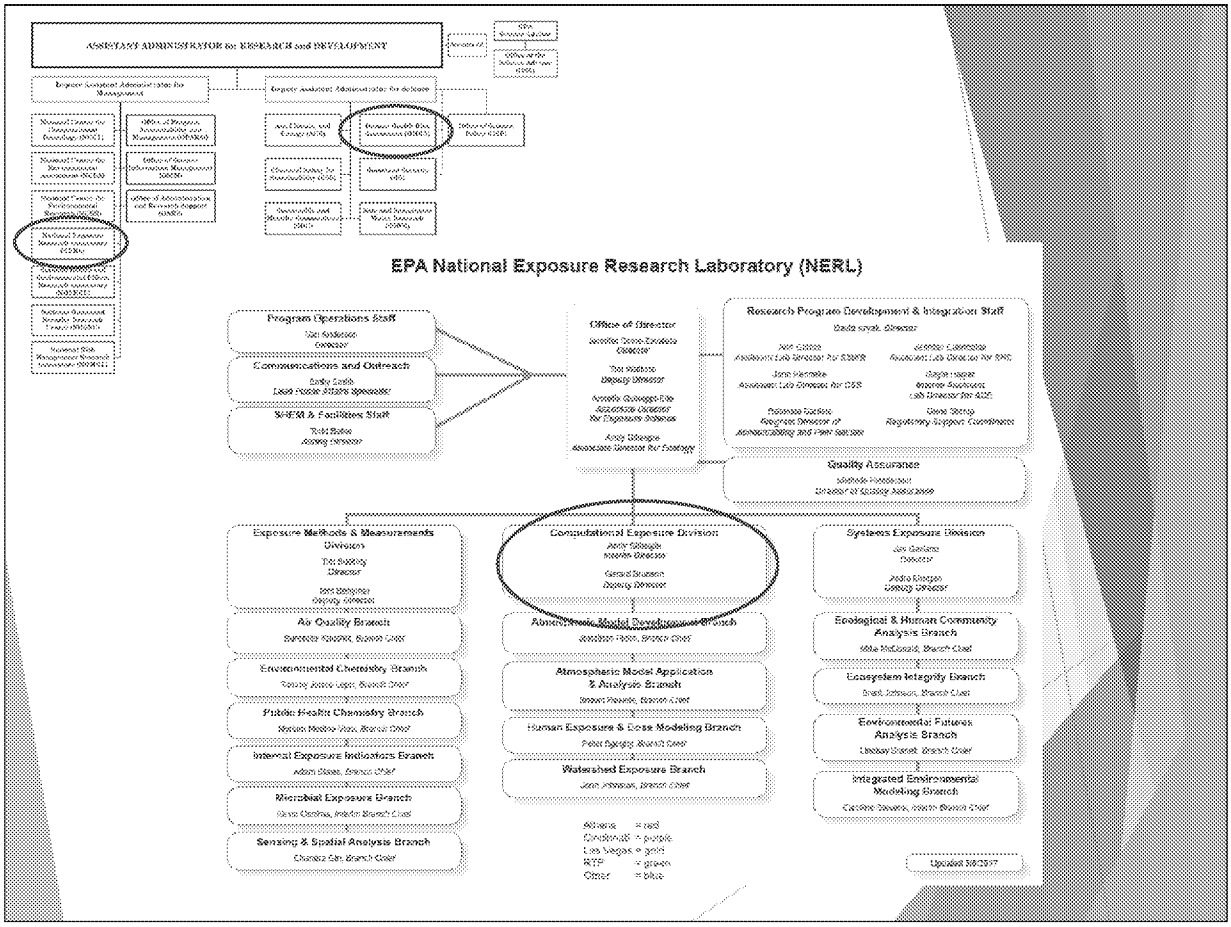
Phthalocyanine green (pigment)

PCB-11 may be a result of direct exposure in humans; currently being evaluated by NTP

PCB Exposure & Health Outcomes

- PCBs have been shown to impact variety of organ systems
- The modes of action are congener-dependent
- Animal Studies evaluating PCB toxicity have observed:
  - Thyroid Effects
  - Neurological effects
  - Immunological effects
  - Reproductive effects
  - Hepatic Effects
  - Developmental Effects
  - Other organ system effects

Currently, IRIS PCB assessment (non-cancer) will consider health effects listed above associated with exposure to PCB mixtures as they are found in the environment.


ASSISTANT ADMINISTRATOR for RESEARCH and DEVELOPMENT
EPA National Exposure Research Laboratory (NERL)
Program Operations Staff
Tim Gleddison
Director
Communications and Outreach
Emily Smith
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Tim Hoffman
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Annette Gallagher-Kile
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Andy Gillespie
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Associate Lab Director for STAR
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Associate Lab Director for CES
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Quality Assurance
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Director of Quality Assurance
Exposure Methods & Measurements Division
Tim Buckley
Director
Jane Mangione
Deputy Director
Air Quality Branch
Surendra Kalagnisi, Branch Chief
Environmental Chemistry Branch
Ronald Jones Lopez, Branch Chief
Public Health Chemistry Branch
Mariam Medina Vera, Branch Chief
Internal Exposure Indicators Branch
Adam Gates, Branch Chief
Microbial Exposure Branch
Steve Dentine, Interim Branch Chief
Sensing & Spatial Analysis Branch
Chandra Sah, Branch Chief
Computational Exposure Division
Andy Gillespie
Interim Director
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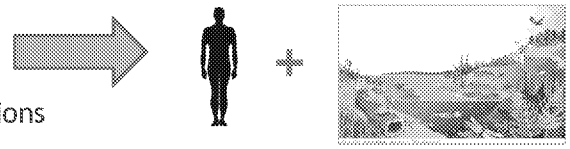
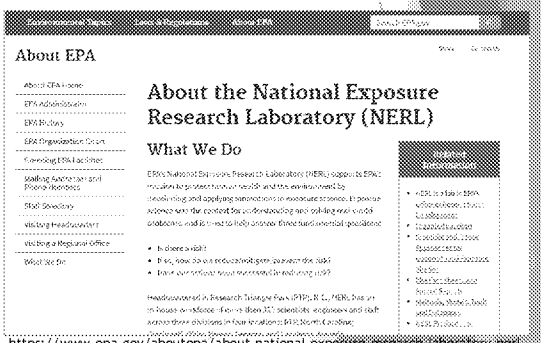
Human Exposure & Dose Modeling Branch
Peter Egeghy, Branch Chief
Watershed Exposure Branch
John Johnson, Branch Chief
Systems Exposure Division
Jon Garland
Director
Andrea Kirkpatrick
Deputy Director
Ecological & Human Community Analysis Branch
Mike McDonald, Branch Chief
Ecosystem Integrity Branch
Brett Johnson, Branch Chief
Environmental Futures Analysis Branch
Lindsay Stanek, Branch Chief
Integrated Environmental Modeling Branch
Caroline Stevens, Interim Branch Chief
Research = red
Cincinnati = purple
Las Vegas = gold
RTP = green
Other = blue
Updated 5/6/2017

National Exposure Research Laboratory

- Exposure science
  - Develops tools and understanding to quantify exposure in:
    - Humans
    - Ecosystems



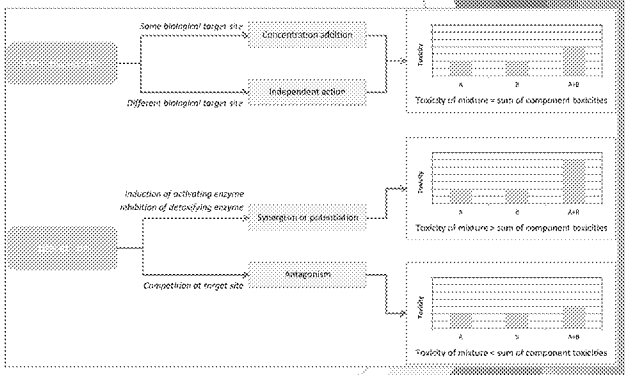
- Answers the questions
  - Determining risk
  - How to reduce or prevent risk
  - Are mitigation strategies successful
- Some of NERL's work is centered around
  - Monitoring methods development
  - Exposure/dose process characterization
  - Decision support tools
  - Predictive modeling
  - Tools for decision making
  - Source apportionment



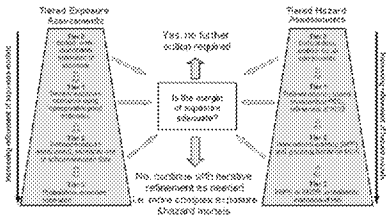
https://www.epa.gov/aboutepa/about-national-exposure-research-laboratory-nerl

Mixtures research and cumulative assessment

- Making all of those (~80,000) chemicals even more complicated…
- Chemical-by-chemical assessment
  - TSCA and REACH do not require consideration of cumulative exposures when determining human health effects
  - Underestimate toxicity
- What happens when we look at chemicals together/jointly?
  - Additive, Synergistic, Antagonistic
- Cumulative assessment
  - WHO



RSC Adv., 2016, 6, 47844. doi: 10.1039/c6ra05406d



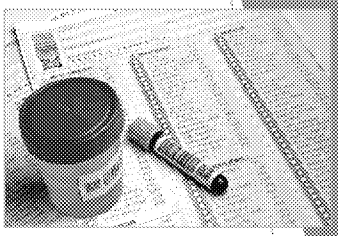
Price et al. Environmental Sciences Europe 2012, 24:26. doi:10.1186/2190-4715-24-26

Rapid Exposure and Dosimetry (RED) project

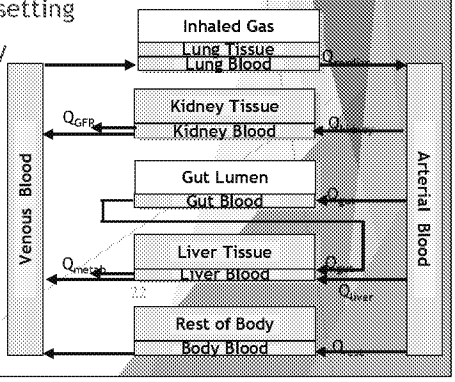
- RED is one of the current Chemical Safety for Sustainability (CSS) projects
  - Research projects (e.g. CSS) extend across labs/centers
- RED group
  - Human and ecological exposures for ***prioritization***
  - develop the data, tools, and evaluation approaches required to generate ***rapid exposure predictions***
  - models of human and ecological exposures, identification or generation of new high-throughput exposure data (e.g., chemical use or property information, consumer product use data, and consumer product and article chemical compositions, and ecological/biological monitoring data)
  - development of innovative ***statistical techniques*** for evaluating exposure predictions against available monitoring data.
  - develop the scientific approaches from *ToxCast* to predicted real world doses.
  - Rapid prediction allows ***prioritization*** based upon risk of adverse outcomes due to ***environmental chemical exposure***

Understanding chemicals and quantifying exposures

- Biomonitoring data (human biological media)
  - Metabolites
  - Blood (serum and plasma), urine exhaled breath, breast milk, hair, teeth, saliva, etc.
- Physiologically Based PharmacoKinetic (PBPK)
  - PK origins in medicine
  - Time and concentration to determine dose
  - Extended to different exposures/ranges in an environ. setting
  - "PB" Based on the body compartments (mathematically modeled) instead of something entirely empirical
  - Body is arranged in a series of "compartments" set up towards a specific tissue
- High Throughput ToxicoKinetic (HTTK)
  - Large number of chemicals
  - Tying HTTK to rapid exposures

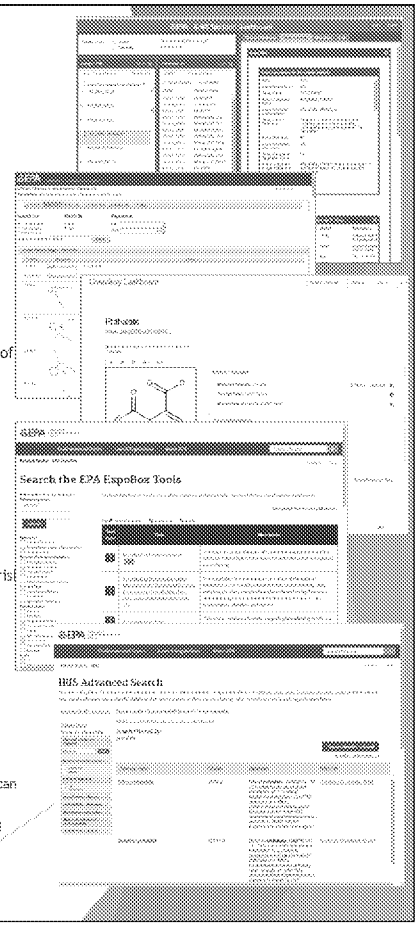


http://www.umweltbundesamt.de/en/topics/health/commission-working-group-human-biomonitoring-commission/reference-hbm-values



EPA databases and models

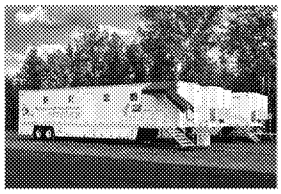
- ToxCast (Toxicity Forecaster)
  - https://actor.epa.gov/dashboard/
  - Over 9,000 chemicals and approximately 1000 assay endpoints
  - explore the data from a chemical or an assay viewpoint, biological activity for the chemical-assay combinations, downloaded by the user.
- CPDat (Chemical and Product Database)
  - https://actor.epa.gov/cpcat/faces/home.xhtml
  - >43,000 chemicals to a set of terms categorizing their usage or function from publically available sources. Unique ***use category*** taxonomies from each source are mapped onto a single common set of ***~800 terms***.
- SHEDS-HT (Stochastic Human Exposure and Dose Simulation High Throughput)
  - https://www.epa.gov/chemical-research/forms/registration-download-and-use-sheds-software
  - probabilistic models that estimate exposures people face from chemicals encountered in everyday activities
- CompTox (Computational Toxicology) Dashboard (AKA the Chemistry Dashboard)
  - https://comptox.epa.gov/dashboard
  - develop innovative methods to change how chemicals are currently evaluated for potential health ris
- ExpoBox (Exposure Toolbox)
  - https://www.epa.gov/expobox
  - exposure assessment tools that links to exposure assessment guidance, databases, models, key references, and related resources
- IRIS (Integrated Risk Information System)
  - https://www.epa.gov/iris
  - identifying and characterizing the health hazards of chemicals found in the environment. Each IRIS assessment can cover a chemical, a group of related chemicals, or a complex mixture
  - an important source of toxicity information used by state and local health agencies, other federal agencies, and international health organizations

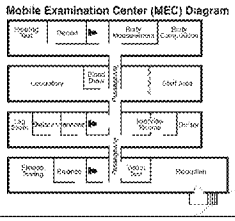


National Health and Nutrition Examination Survey (NHANES)

- A program of studies designed to assess the ***health*** and ***nutritional status*** of adults and children in the United States
- The survey is unique in that it combines ***interviews*** and ***physical examinations***
- Demographics, dietary information, examination data, laboratory data, questionnaire data
- Since 1999, ~5,000 people, once every 2 years,

  100+ chemicals/metabolites



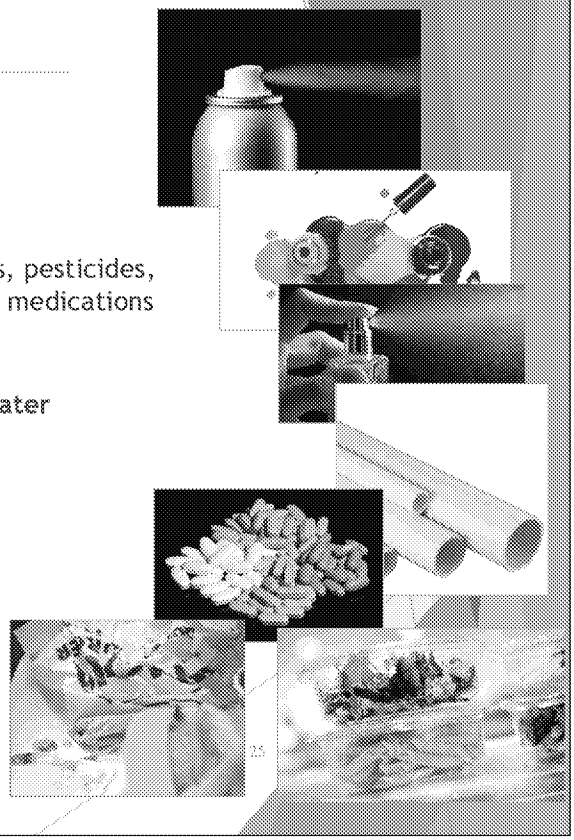


CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

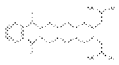
Phthalates

phthal·ate
/ ˈTHa_lāt/

- Phthalates
  - Esters of phthalic acid used as plasticizers
  - Oily liquids are room temperature
- They are in a wide variety of goods
  - Vinyl flooring, tubing and pipes, tablecloths, pesticides, food packaging, cosmetics, skin care, some medications
- Phthalates get into the body by
  - **Ingestion - through food, contaminated water**
  - Skin - application of products on skin
  - Inhalation (from dust)
- Examples: softener for PVC pipes
- **Phthalates are in everyday products**
  - Metabolizes quickly but frequently exposed
  - Exposure in utero

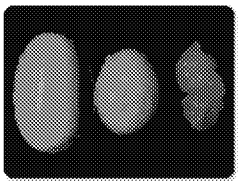


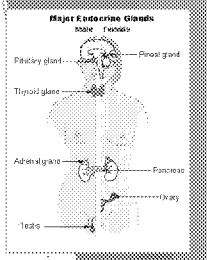
Phthalates

Phthalate	Abbreviation	Uses	Chemical Structures
phthalic acid	---	---	
di-n-butyl phthalate	DBP	Adhesives, caulk, cosmetics, industrial solvent	
diisobutyl phthalate	DIBP	Adhesives, caulk, cosmetics, industrial solvent	
butyl benzyl phthalate	BBP	Vinyl flooring, adhesives, sealants, industrial solvent	
di(2-ethylhexyl) phthalate	DEHP	Soft plastic, including tubing, toys, home products, food containers, food packaging	
diisononyl phthalate	DINP	Vinyl	
diisodecyl phthalate	DIDP	plastic coating, including cook ware, pills, food packaging	

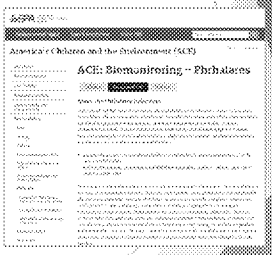
Phthalates

- Some phthalates are endocrine disruptors
  - Rat studies
  - "phthalate syndrome"
    - Infertility, decreased sperm count,
    - changes in reproductive organs





- Phthalate mixture
  - Most of this group (DBP, DIBP, BBP, DINP, DEHP) associated with the "phthalate syndrome"
- How much is manufactured?
  - 90,528 tons DEHP and 2,650 tons DBP in 2012 (Lee et al., Environment International, 2014) and 470 million pounds a year (EPA 2006)
- Which have the highest toxicity of these six phthalates?
  - DBP
- Which can the most frequent exposures?
  - DEHP and DINP
- National Academy of Science 2008 document
  - Cumulative risk assessment
  - investigating mechanism of action to common adverse outcome



- EPA phthalates action plan
  - Several studies have shown associations between phthalate exposures and human health
  - Under TSCA, manufacturers and processors of DPP to notify EPA at least 90 days before starting or resuming new uses of this chemical (DPP in PVC pipe)

Current Phthalates Research

- Current research

Research

Recent Fast Food Consumption and Bisphenol A and Phthalates Exposures among the U.S. Population in NHANES, 2003–2010

Ami R. Zota, Cassandra A. Phillips, and Susanna D. Mitro

Department of Environmental and Occupational Health, Milken Institute School of Public Health, George Washington University, Washington, DC, USA

Paraben Concentrations in Maternal Urine and Breast Milk and Its Association with Personal Care Product Use

Mandy Fisher,[*,†,‡] Susan MacPherson,[*] Joseph M. Braun,[§] Russ Hauser,[§] Mark Walker,[§] Mark Feeley,[‖] Ranjeeta Mallick,[§] René Bérubé,[§] and Tye E. Arbuckle[†]

Mediation of the Relationship between Maternal Phthalate Exposure and Preterm Birth by Oxidative Stress with Repeated Measurements across Pregnancy

Kelly K. Ferguson,[1] Yin-Hsiu Chen,[2] Tyler J. VanderWeele,[3] Thomas F. McElrath,[4] John D. Meeker,[1] and Bhramar Mukherjee[2]

ORIGINAL ARTICLE

Variation in urinary spot sample, 24h samples, and longer-term average urinary concentrations of short-lived environmental chemicals: implications for exposure assessment and reverse dosimetry

Lewis L. Aylward[1], Sean M. Hays[2] and Angelika Zidek[3]

Research | Children's Health

Prenatal Exposure to Phthalates and Anogenital Distance in Male Infants from a Low-Exposed Danish Cohort (2010–2012)

Tina Kold Jensen,[1,2] Henrik Friedenberg,[3] Henriette Boye Kyhl,[3] Tina Hartner Lassen,[3] Eduard H. Swan,[4] Carl-Gustaf Bornehag,[4] Niels E. Bankkeduse,[5] Katharina M. Main,[5] Dorte Vesterholm Lund,[1] Steffen Husby,[2] and Anna-Maria Andersson[3]

Diverging temporal trends of human exposure to bisphenols and plastizisers, such as phthalates, caused by substitution of legacy EDCs?

ORIGINAL ARTICLE

Linking a dermal permeation and an inhalation model to a simple pharmacokinetic model to study airborne exposure to di(n-butyl) phthalate

Non-phthalate plasticizers in German daycare centers and human biomonitoring of DINCH metabolites in children attending the centers (LUPE 3)

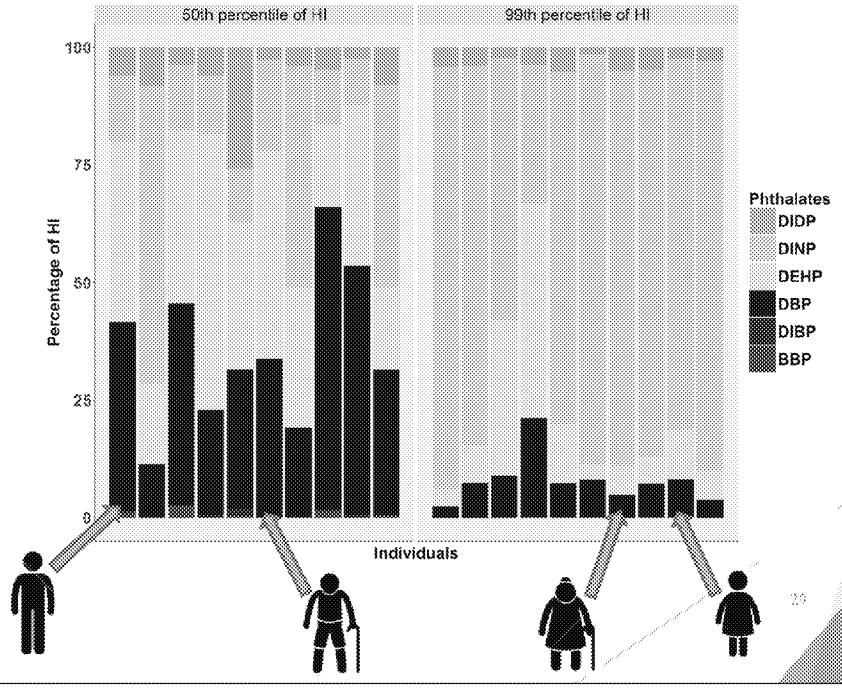
H. Fromme[*,†,‡], A. Schütze[*], T. Lahrz[‡], M. Kraft[*], L. Fembacher[*], S. Siewering[*], R. Burkardt[‡], S. Dietrich[*], H.M. Koch[‡], W. Völkel[‡]

Exposure to di-2-ethylhexyl terephthalate in a convenience sample of U.S. adults from 2000 to 2016

Manori J. Silva[3] · Lee-Yang Wong[1] · Ella Samandar[1] · James L. Preau[1] · Antonia M. Calafat[1] · Xiaoyun Ye[1]

- Differences by age and race
  - Kids (ages 6-10) have higher levels than adolescents (ages 16-17)
  - For years 2005-2008, Mexican-American children had lower levels than White non-Hispanic children and Black non-Hispanic children
  - For years 2005-2008, Black women of child-bearing age had higher concentrations than any other race

Cumulative versus chemical-by-chemical

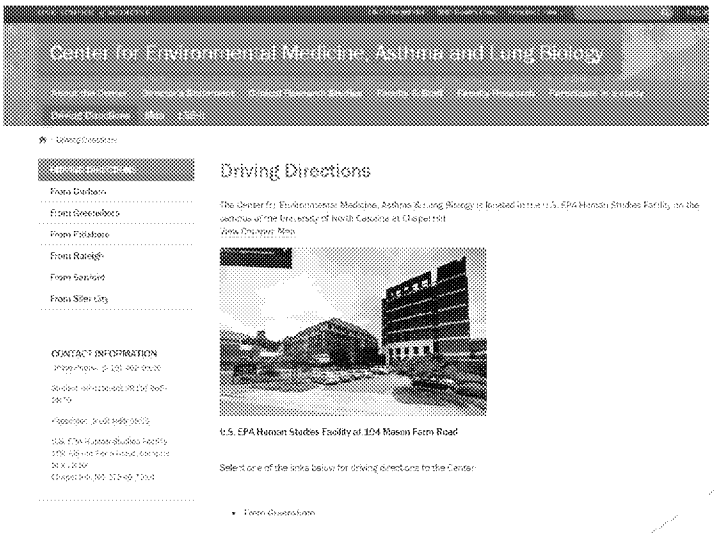


Being An Informed Consumer

- Read labels
- Check your products online- some NGO organizations have developed cosmetic/product database recommendations
- More information: www.ewg.org

Possible to participate

- Support and participate in the science



Questions?

- Acknowledgements: NCEA co-workers
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