United States Environmental Protection Agency

Assessing Human Exposures for Risk Assessment and Risk Management: A U.S. Perspective

Dr. Valerie Zartarian and Dr. Halûk Özkaynak
U.S. EPA National Exposure Research Laboratory
RTP, NC

Exposure Session of 1st International Conference on Risk Assessment
"Global Risk Assessment Dialogue"
November 13-14, 2008
Brussels, Belgium

Acknowledgments

US Environmental Protection Agency:

Office of Research and Development

Brad Schultz, Nicolle Tulve, Kent Thomas, Roy Fortmann, Ross Highsmith, Susan Pearce, Pamela Williams, Larry Reiter, Linda Sheldon

Office of Prevention, Pesticides, and Toxic Substances

David Miller, David Hrdy, Cathy Fehrenbacher

Office of Air and Radiation

Harvey Richmond, Deirdre Murphy, David Pawel, Mike Boyd, Jerry Puskin

Regional Offices

Marian Olsen

Risk Assessment Forum

Gary Bangs

US Department of Agriculture:

Kerry Dearfield, Eric Ebel

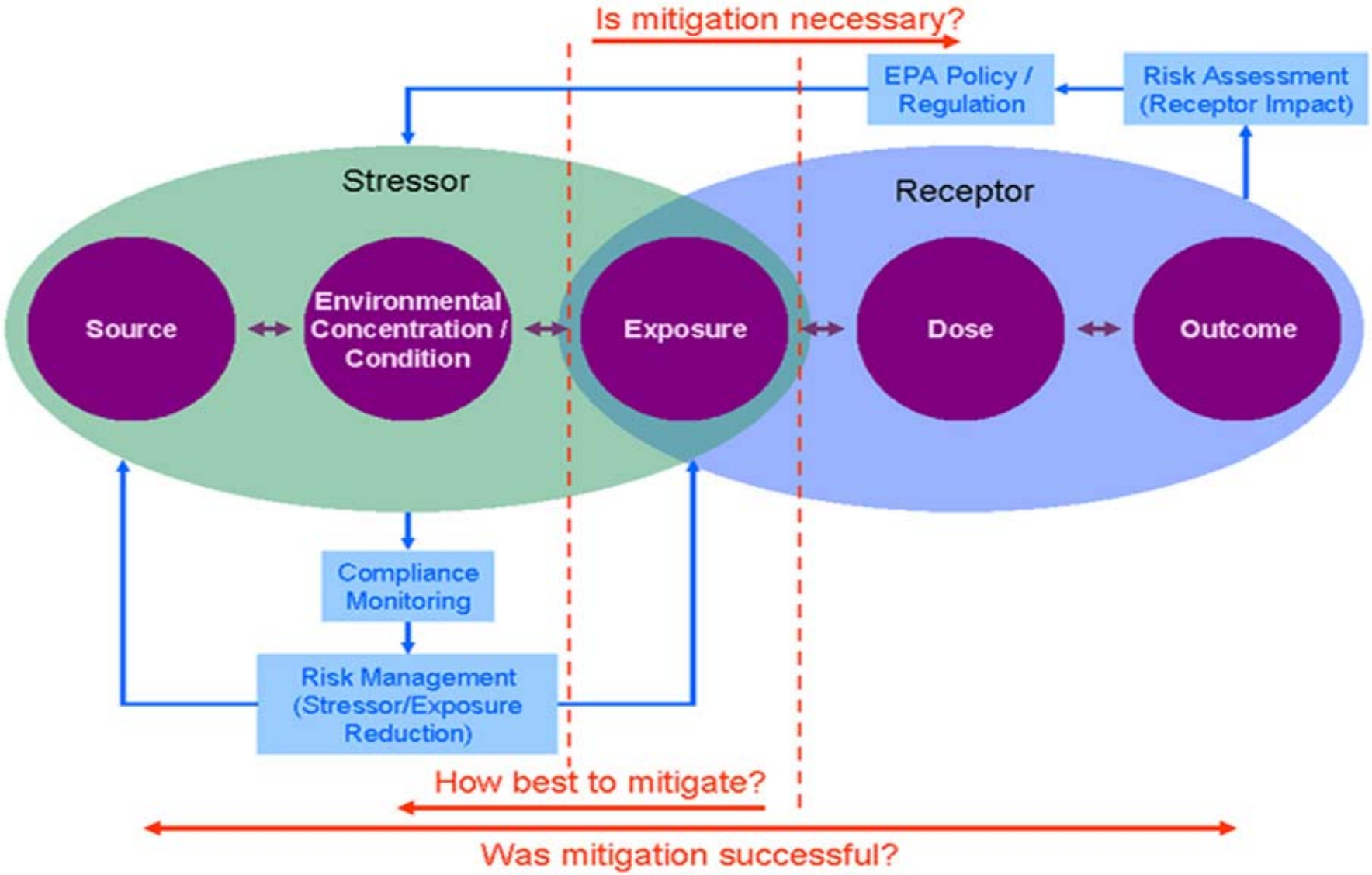
US Consumer Product Safety Commission:

Treye Thomas, Michael Babich

Outline

- Why Is Exposure Important?
- How Do We Currently Address Exposure in the U.S.?
  - Models and measurements
  - Examples: air pollutants, pesticides, other chemicals
- What Are the Issues/Challenges Going Forward?
- Extra Slides with Additional Examples
  - microbials in food, phthalates in toys, hazardous waste, radiation

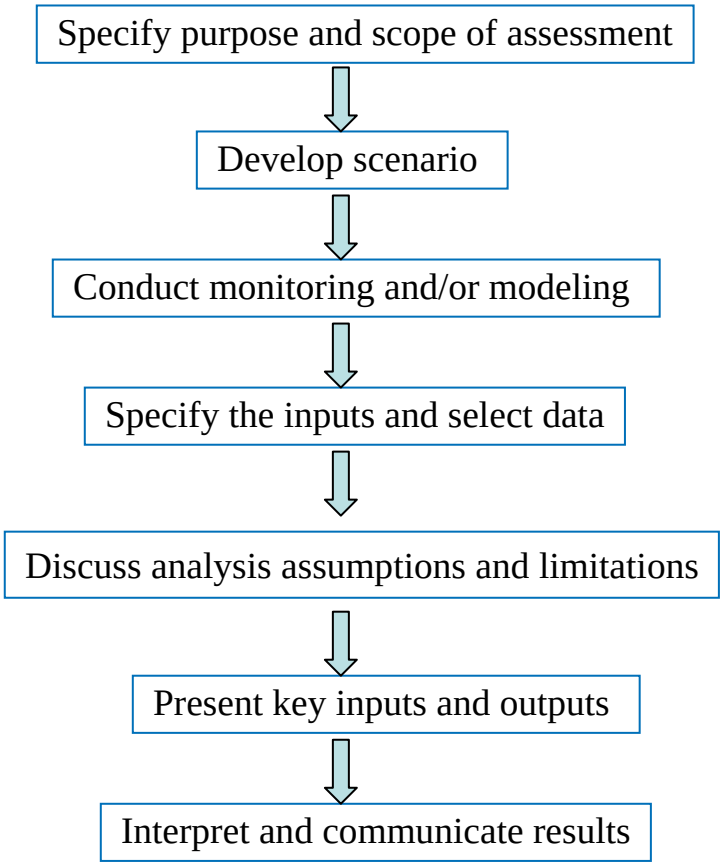
Role of Exposure Research in the Risk Assessment/Risk Management Context



Source: L. Reiter, Exposure Science in the 21st Century, Presented to NAS, October 2008

United States Environmental Protection Agency

Exposure Assessment Steps



Important Exposure Questions

- What are the routes/pathways and factors influencing exposures?
- What is the population distribution of exposure, including high-end exposures to pollutants of health concern?
- What are exposures for susceptible subpopulations, especially children and the elderly?
- Will the exposure cause a health effect?
  - Intensity, duration, frequency, route, timing
- How do we effectively reduce the exposure?
  - Source
  - Route and pathway
- Did we reduce exposure?

Examples of Key Exposure Sources and Pathways

Residential
Outdoor: mobile, commercial, lawn;
Indoor: smoking, cooking, radon, pesticides;
Attached garage

Vehicles
commuting
smoking

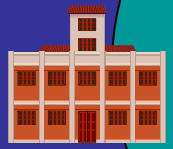
Food

Gas Station
refueling
service

Parking Garage/Lot
outdoor

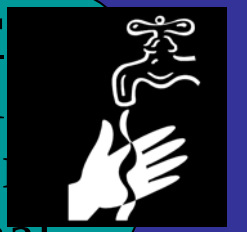
Personal Exposure

Office/School
roadway
other outdoor
indoor sources

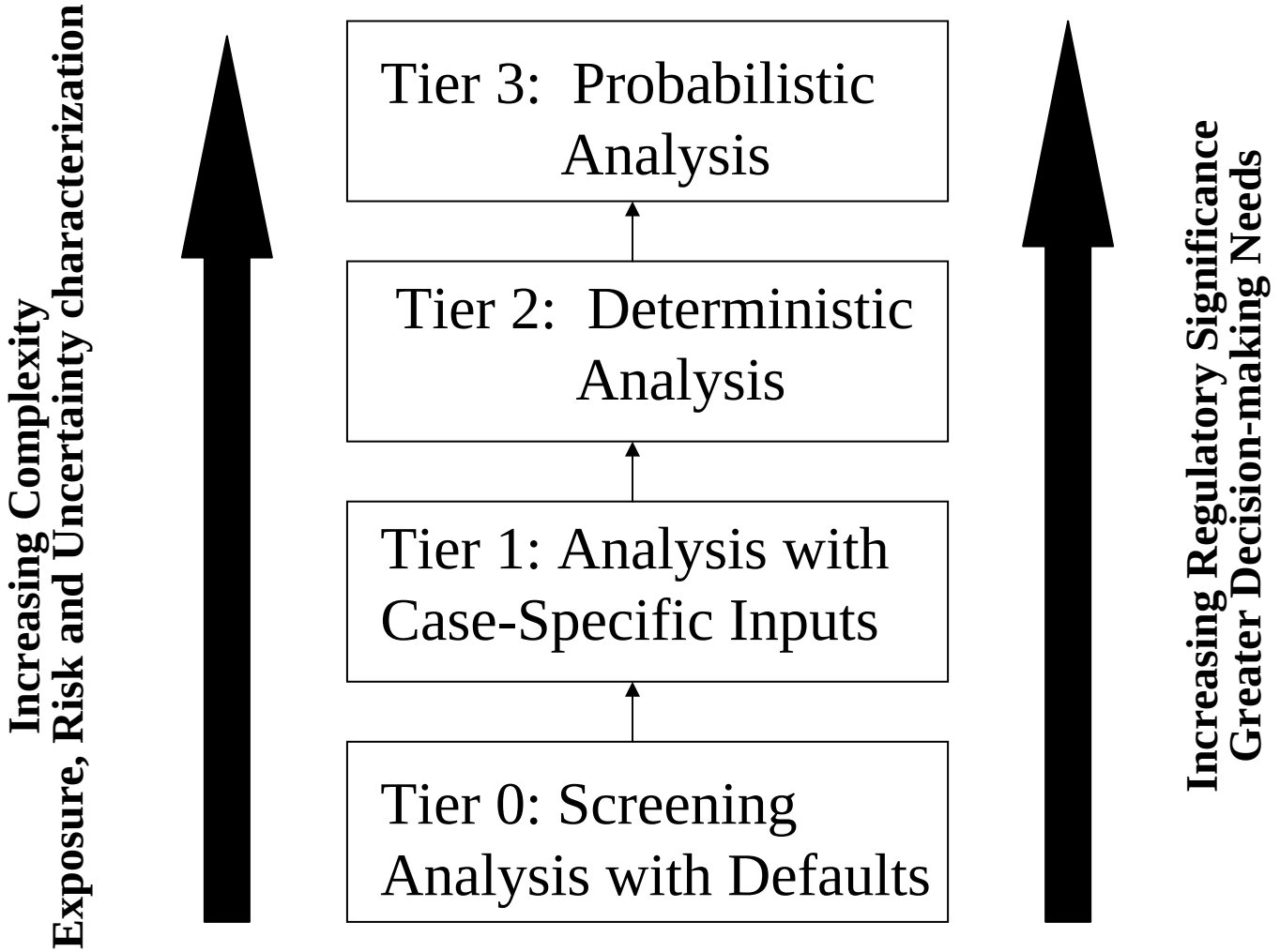


Other Indoor
outdoor
smoking
other sources

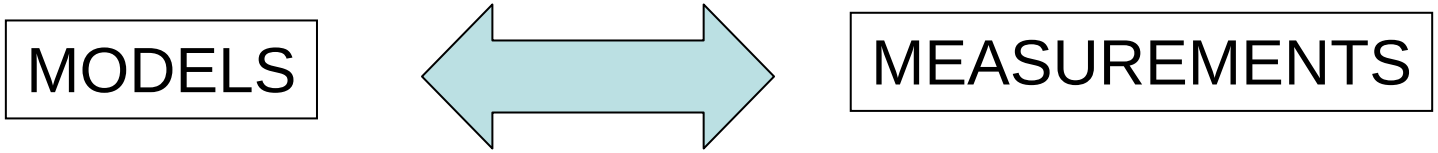
Water
dermal
ingestio
vapor inhal.



Tiered Approach to Exposure and Uncertainty Analysis



United States Environmental Protection Agency



"Models drive measurements, and measurements inform models."

Source: L. Reiter, Exposure Science in the 21st Century, Presented to NAS, October 2008

EXPOSURE MODELS

United States Environmental Protection Agency

Lower Tier

HTM: Exposure Equation and Calculation (Hand-to-Mouth)

ADD *= Average daily dose (mg/kg/day)*

$$ADD = \frac{(DR * SA * FQ * SE * ET)}{BW}$$

Where:

DR *= Dislodgeable Residue (mg/cm²)*

SA *= Surface area of fingers (20 cm²/event)*

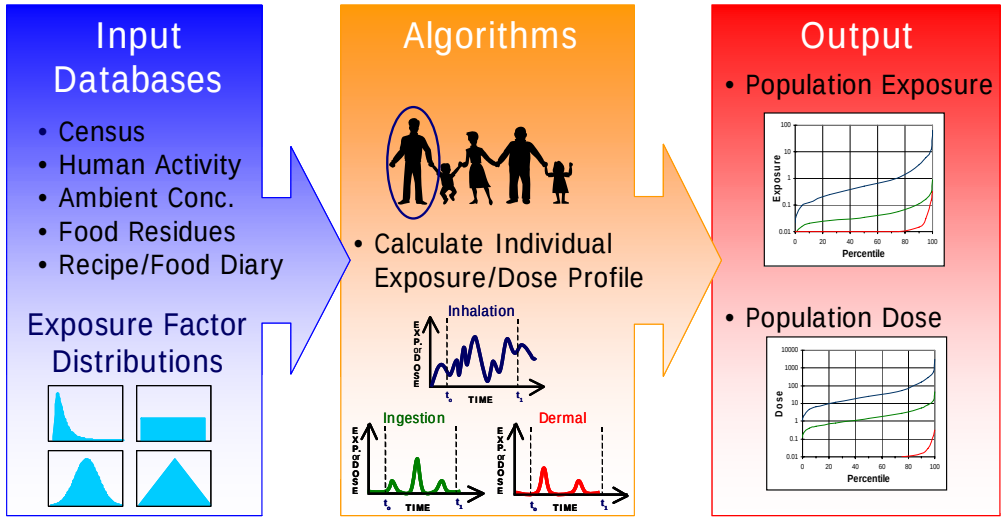
FQ *= Frequency of activity (20/hr)*

SE *= Saliva Extraction factor (50%)*

ET *= Exposure Time (2 hr)*

BW *= Body Weight (15 kg)* Source: EPA/OPP

Higher Tier



Source: EPA/ORD/NERL

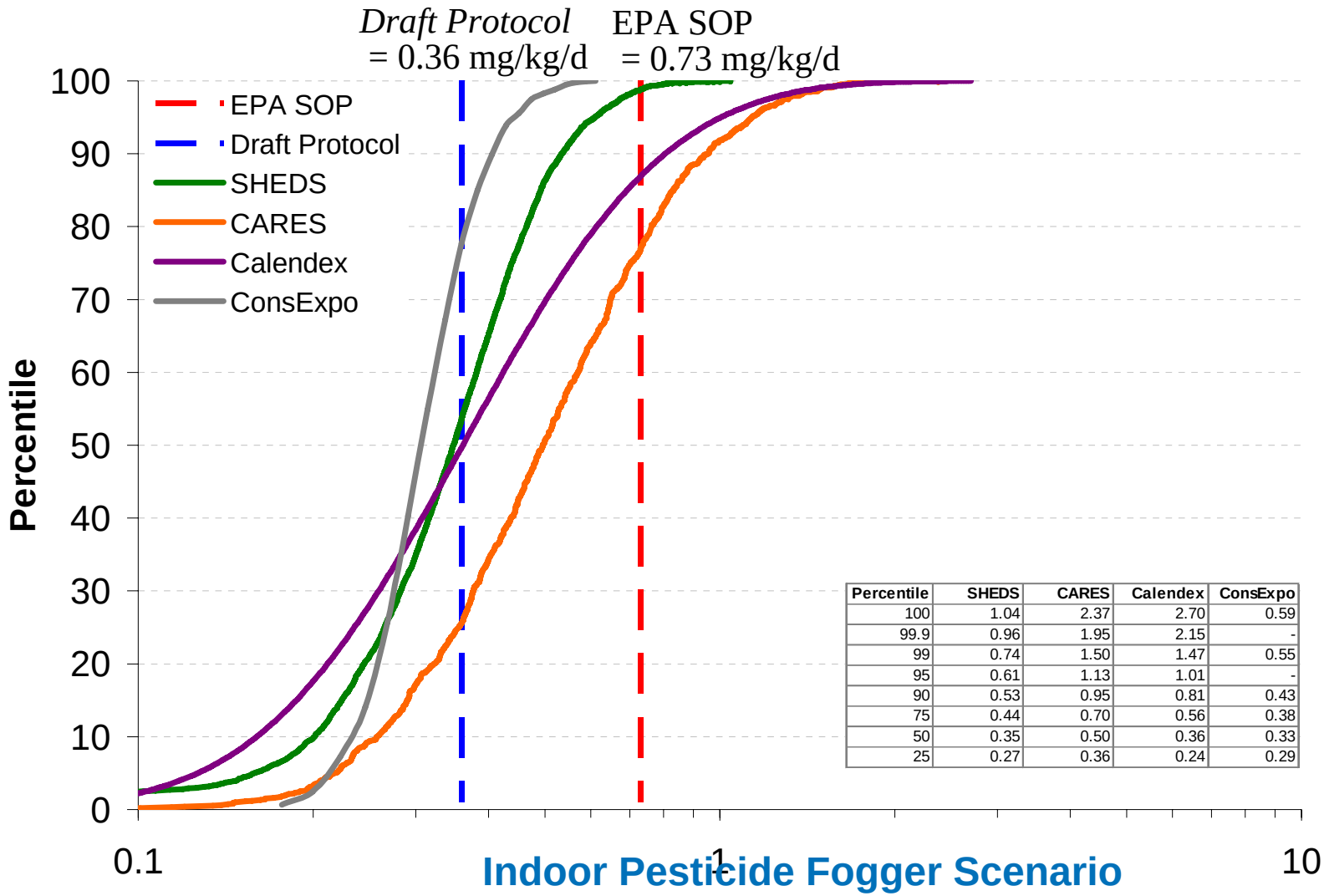
- General information on EPA models and guidance documents at U.S EPA's Council for Regulatory Environmental Modeling (CREM) Knowledge Database:http://cfpub.epa.gov/crem/crem_report.cfm?deid=75916
- Inventory & description of EPA models by CREM: http://cfpub.epa.gov/crem/knowledge_base/crem_results.cfm?Act
- EPA/NERL Center for Exposure Assessment Modeling (CEAM): http://www.epa.gov/ceampubl/
- EPA ORD Exposure Models: http://www.epa.gov/heasd/risk/projects/c1b_exposure_models_development.htm

Application of EPA's Computerized Exposure Assessment Prediction Tools/ Models

Model	Consumer Exposure		General Population Exposure				Agg/Cum Residential Post-Application Exposure	Worker Exposure	Tool Lead
	Dermal	Inhalation	Drinking Water	Dietary	Fish Ingestion	Inhalation			
Priority Setting Tools:									
SRD		❄							OPPT
UCSS								❄	OPPT
Screening Level Tools:									
ChemSTEER								❄	OPPT
SOPs; PIRAT							❄		OPP; OPPT
EFAST	❄	❄	❄		❄	❄			OPPT
Higher Tier Tools:									
IGEMS			❄		❄	❄			OPPT
MCCEM		❄	❄						OPPT
WPEM		❄	❄					❄	OPPT
IAQX						❄			ORD
APEX						❄			OAQPS
HAPEM						❄			OAQPS
SHEDS-ATOX			❄	❄		❄			ORD
SHEDS-Multimedia			❄	❄		❄	❄		ORD
DEEM				❄					OPP

Modified from: http://www.epa.gov/oppt/exposure

COMPARISON OF AGGREGATE RESIDENTIAL HUMAN EXPOSURE MODELS



Percentile	SHEDS	CARES	Calendex	ConsExpo
100	1.04	2.37	2.70	0.59
99.9	0.96	1.95	2.15	-
99	0.74	1.50	1.47	0.55
95	0.61	1.13	1.01	-
90	0.53	0.95	0.81	0.43
75	0.44	0.70	0.56	0.38
50	0.35	0.50	0.36	0.33
25	0.27	0.36	0.24	0.29

Indoor Pesticide Fogger Scenario

Dermal Exposure (mg/kg/d)

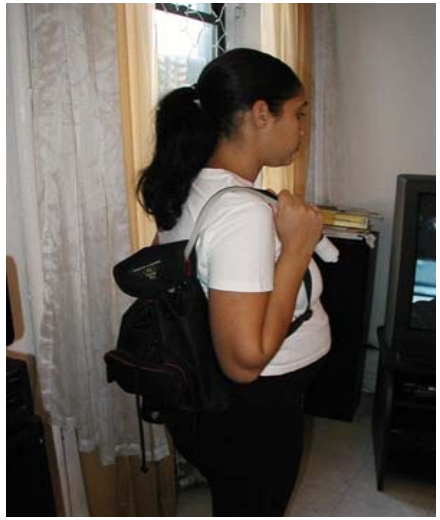
Source: Young et al., 2008 ISEA Conference, Pasadena CA

Assessing Exposures with Surveys and Measurements

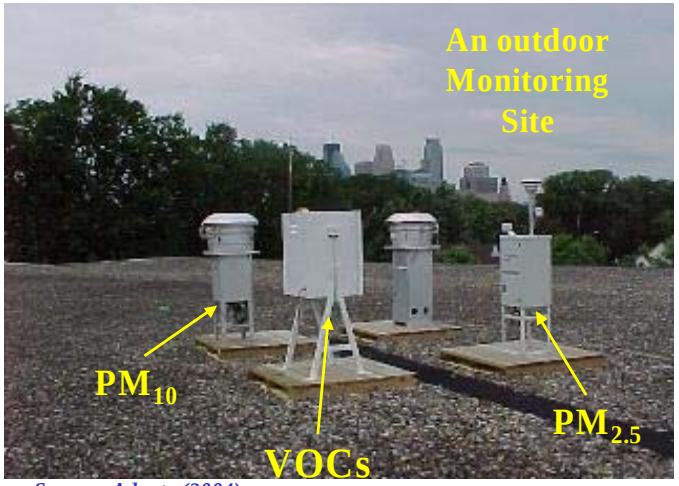
United States Environmental Protection Agency

Questionnaires

Residue Sampling



Personal Monitoring



Source: Adgate (2004)

Ambient Monitoring

Indoor Monitoring

Sources of Data for Exposure Assessments (USA)

United States Environmental Protection Agency

Pollution Source Emissions

Meteorological, Housing & Exposure Factors

Personal Behavior/ Time Activity

- Pollution Source Emissions (Air, Water, Land) (US EPA)
  - Toxic Release Inventory (http://www.epa.gov/tri/)
  - Total Maximum Daily Load Program (http://www.epa.gov/owow/tmdl/intro.html)
  - Water (http://www.epa.gov/ow/)
  - Land (http://www.epa.gov/superfund/)
- Meteorological
  - NOAA's National Weather Service Data (http://www.nws.noaa.gov/)
  - National Climatic Data Center (http://www.ncdc.noaa.gov/oa/ncdc.html)
- Housing Factors
  - Department of Housing and Urban Development Data (http://www.hud.gov/)
- Exposure Factors Data (US EPA)
  - EF and CSEF Handbooks (http://permanent.access.gpo.gov/lps35390/cfpub.epa.gov/ncea/cfm/recordisplay.cfm-deid=55145.htm)
- Time Activity Surveys
  - Consolidated Human Activity Database (http://www.epa.gov/chadnet1/)
  - American Time Use Survey (Bureau of Labor Statistics) (http://www.bls.gov/tus/)
- General: EPA Exposure Assessment Guidelines (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=15263)
- Data may be obtained from many different sources at the federal, state, and local levels

Courtesy: Nicolle Tulve et al., EPA/ORD

Sources of Data for Exposure Assessments (USA)

United States Environmental Protection Agency

Consumer Product Use Data | **Dietary Consumption and Residues** | **Environmental Concentrations**

- Dietary Consumption and Residue Data
  - The Continuing Survey of Food Intakes by Individuals (http://www.ars.usda.gov/Main/site_main.htm?modecode=12-35-50-00)
  - NHANES (http://www.cdc.gov/nchs/nhanes.htm)
  - Total Diet Study (http://www.cfsan.fda.gov/~comm/tds-toc.html)
  - Other Market Basket Surveys (FDA, USDA)
  - Pesticide Data Program (USDA) (http://www.ams.usda.gov/AMSv1.0/ams.fetchTemplateData.do?template=TemplateC&navID=PesticideDataProgram&rightNav1=PesticideDataProgram&topNav=&leftNav=ScienceandLaboratories&page=PesticideDataProgram&r)

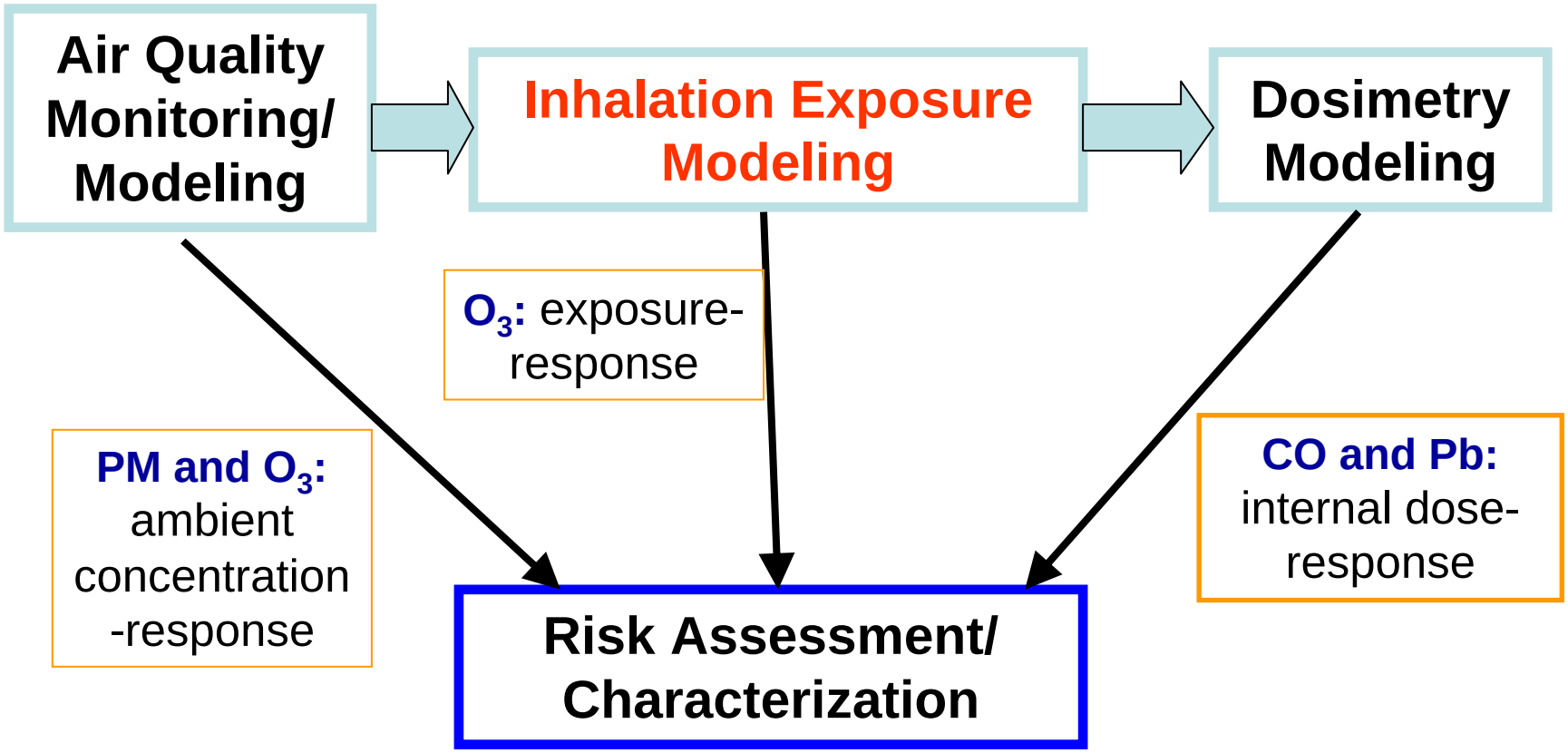
- Consumer Product Use Data
  - Consumer Product Safety Commission Data (http://www.cpsc.gov/)
  - US EPA data
- Environmental Concentrations
  - US EPA Reports (EPA/600/R-07/013)
  - Human Exposure Database System (http://oaspub.epa.gov/heds/study_list_frame)
  - Water, air and ecological data sources (USGS, Fish and Wildlife Service)
- Biomonitoring (for surveillance and model evaluation)
  - CDC NHANES (http://www.cdc.gov/nchs/nhanes.htm)

- Data may be obtained from many different sources at the federal, state, and local levels

Courtesy: Nicolle Tulve et al., EPA/ORD

United States Environmental Protection Agency

EXAMPLE #1:
EPA Office of Air Quality Planning and Standards
Use of Exposure Assessment in NAAQS RA Process



Courtesy: Deirdre Murphy and Harvey Richmond, EPA/OAQPS

Example #2: EPA Office of Pesticide Programs Role of Exposure in Pesticide Risk Assessments

Categories of RA to address the Food Quality Protection Act of 1996 (FQPA):

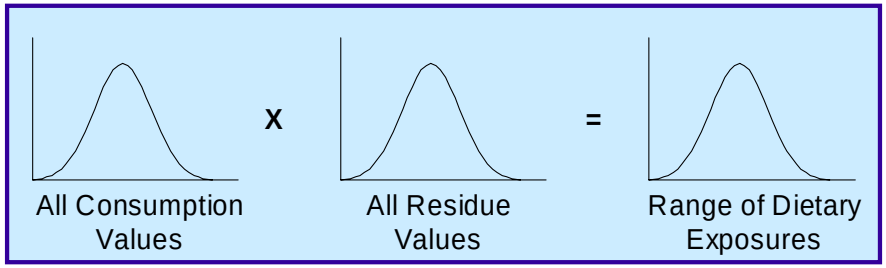
↓ Food

↖ Aggregate (Food, Drinking Water, Residential)

↗ Cumulative

↙ Occupational

- **Dietary exposure estimates are derived from two distinct pieces of information:**
  - USDA's Continuing Survey of Food Intake by Individuals (CSFII)
  - the amount of pesticide in and on food (i.e., pesticide residues) which reflect
    - field trial data
    - monitoring data
      - USDA PDP and FDA
    - market basket survey



- **Degree of tiering depends on:**
  - Available data
  - Type of exposure assessment (acute, chronic)
  - Need for additional refinements

Example #3: EPA Office of Pollution Prevention and Toxics Tiered Exposure Approach for Chemicals of Concern

- OPPT evaluates new and existing chemicals, and finds ways to prevent or reduce pollution
  - addresses Toxic Substances Control Act (TSCA) and the Pollution Prevention Act (PPA)
  - considers what happens to chemicals when used and released to environment; and how workers, public, consumers, aquatic ecosystems may be exposed

- Step 1. Gather Basic Data & Info for a Complete, Transparent Exposure Assessment.
  - Identify all of the manufacturing, processing and use activities for the chemical.
  - Document all measured data, environmental release scenarios, all potentially exposed human populations, exposure scenarios, assumptions and estimation techniques.

- Step 2. Develop a Screening Level Exposure Assessment to Quickly Prioritize Further Work.
  - Use readily available measured data, existing release and exposure estimates.
  - Simple models may be used to fill in gaps.

- Step 3. (If Needed) Develop an Advanced Exposure Assessment
  - For more accurate estimates, focused on higher priorities identified in screening.

Source: http://www.epa.gov/oppt/

Issues and Challenges for Exposure Assessment

United States Environmental Protection Agency

- **Limited mechanistic understanding of source, exposure, dose and effects linkages**
  - Source ⟷ Exposure ⟷ Dose ⟷ Effects
- **Uncertainties in our exposure prediction tools**
  - Age-Specific Exposure Issues
  - Exposures to Multiple Pollutants
  - Exposure or Effect Modifiers (e.g., vulnerability and susceptibility)
  - Tracking Exposures for Long-Latency Outcomes
  - Spatial and Temporal Variations in Sources and Exposures
  - Does the exposure model capture the important exposure routes and pathways?
  - Does the model estimate the exposures properly?
  - How can we verify the results (e.g., the utility of biomarkers for exposure reconstruction)?
- **Adequacy of exposure measurement or modeling estimates**
  - How much measurement data is needed to represent the vulnerable population (e.g., children, elderly)?
  - How do we extrapolate from a relatively small sample or few scenarios to the larger group?
  - Do we have right tools and info to predict cumulative exposures to multiple pollutants or mixtures?
  - How to predict exposure and dose for a large number of compounds based on limited available data?
- **Effectively communicating results to risk assessors and decision makers**
  - Need for easily accessible databases and efficient tools for different applications
  - Providing both outputs and their limitations/uncertainties to the decision-makers
  - Developing accountability indicators for assessing impacts of regulatory or risk management decisions

United States Environmental Protection Agency

Disclaimer

Although this work was reviewed by EPA and approved for presentation, it may not necessarily reflect official Agency policy.

United States Environmental Protection Agency

EXTRA SLIDES: ADDITIONAL EXAMPLES

United States Environmental Protection Agency

EXAMPLE #4: Exposure Assessment
USDA-Food Safety and Inspection Service

- Microbial focus
  - Discrete/integer exposure doses
    - Prevalence [i.e., 1-P(dose=0)] can be important
  - Single-hit dose-response theory
    - Single organism has some probability of causing illness

- Point source focus
  - Product-pathogen pairs
    - e.g., Salmonella sp. in broiler chicken
  - Exposure route: ingestion
  - Begin at live animal or carcass

- Acute illness focus
  - Typically assume exposures are independent and non-cumulative
  - Sequelae to acute illnesses sometimes considered
  - Exposure variability is more influenced by variability in pathogen levels than variability in consumption patterns

Courtesy: Kerry Dearfield, USDA

EXAMPLE #4: Exposure Assessment
USDA-Food Safety and Inspection Service (cont'd)

- Surveillance systems provide hazard data
  - Human health data can calibrate/validate exposure assessments
  - Data document the microbial hazard and can facilitate attribution of those illnesses to general/specific meat products
    - e.g., *E. coli* O157 in beef or ground beef

- Process models in exposure assessments can consider:
  - On-farm epidemiology
  - Slaughter/processing effects
  - Wholesale/retail/consumer storage and handling
  - Food preparation
  - Predictive microbiology
    - Microbial dynamics are functions of environmental conditions

Courtesy: Kerry Dearfield, USDA

EXAMPLE #5: U.S. EPA Superfund Risk Assessment

- Evaluated under current (baseline) and future conditions
- Baseline conditions evaluated in the absence of institutional or other controls
- Goal is health protection under reasonable maximum exposures

Courtesy: Marian Olsen, EPA/Region 2

EXAMPLE #5: U.S. EPA Superfund Risk Assessment (cont'd)

United States Environmental Protection Agency

GROUNDWATER INGESTION

$CDI\ (mg/kg/day) = C_W \times IR_W \times EF \times ED \times 1/BW \times 1/AT$

Adult

IR_W	= 2 liters/day
EF	= 350 days/year
ED	= 30 years
BW	= 70 kg
AT_C	= 25,550 days
AT_N	= 10,950 days

Child

IR_W	= 1 liter/day
EF	= 350 days/year
ED	= 6 years
BW	= 15 kg
AT_C	= 25,550 days
AT_N	= 2,190 days

SOIL INGESTION

$CDI\ (mg/kg/day) = C_S \times IR_S \times FI \times EF \times ED \times CF \times 1/BW \times 1/AT$

Adult

IR_S	= 100 mg/day
FI	= 1
EF	= 350 days/year
ED	= 24 years
CF**	= 1E-06 kg/mg
BW	= 70 kg
AT_C	= 25,550 days
AT_N	= 8,760 days

Child

IR_S	= 200 mg/day
FI	= 1
EF	= 350 days/year
ED	= 6 years
CF**	= 1E-06 kg/mg
BW	= 15 kg
AT_C	= 25,550 days
AT_N	= 2,190 days

Courtesy: Marian Olsen, EPA/Region 2

EXAMPLE #5: U.S. EPA Superfund Risk Assessment (cont'd)

Hazardous Waste Risk Management

- Exposure/risk assessment key source for making risk management decisions for human health and ecological risk assessments
- Risk Management decisions include establishing remediation goals, evaluating remedial options, implementing institutional controls and selecting remedial actions.
- Nine-criteria to assess remediation include:
  - **Threshold Criteria** 1. Overall Protection of Human Health and the Environment and *2*. Compliance with Applicable or Relevant and Appropriate Requirements —i.e., *state and federal regulations*
  - **Balancing Criteria—Must be Considered -** 1. Long-Term Effectiveness and Permanence
  - 2. Reduction of Toxicity, Mobility, and Volume 3. Short-Term Effectiveness 4. Implementability 5. Capital and Operating and Maintenance Cost
  - **Modifying Criteria—Must be Considered** 1. State Acceptance 2. Community Acceptance

Courtesy: Marian Olsen, EPA/Region 2

EXAMPLE #6: Consumer Product Safety Commission Exposure Assessment for Phthalates in Toys

- Independent regulatory agency addressing Federal Hazardous Substances Act
- Products in/around home (not food, drugs, cosmetics, medical devices, pesticides, cars)
- CPSC risk assessment of Diisononyl Phthalate (DINP)
  - DINP has been used to soften some plastic toys and children's products.
  - CPSC concluded that there was little or no risk to children from DINP in teethers and toys, and no regulatory action was taken.
  - Recently, Congress passed the "Consumer Product Safety Improvement Act," which bans 6 phthalates in children's products.
  - The Act also requires CPSC to convene a new Chronic Hazard Advisory Panel to consider the risk to children from total exposure to all phthalates, as well as phthalate substitutes.

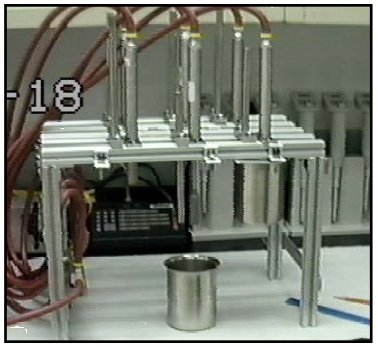


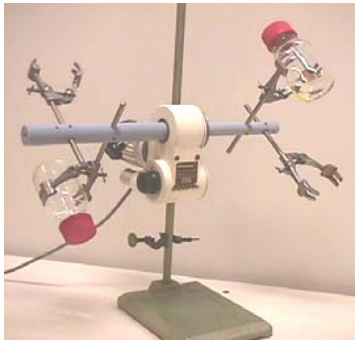

Modified from: Michael Babich, CPSC

EXAMPLE #6: Consumer Product Safety Commission Exposure Assessment for Phthalates in Toys (cont'd)

- Exposure Assessment for Diisononyl Phthalate (DINP)
  - Exposure = Product Migration Rate * Mouthing Time * Exposure Time / BW
  - Observation study, 169 Children 3 to 36 months; objects mouthed, frequency and duration

Product Migration Methods





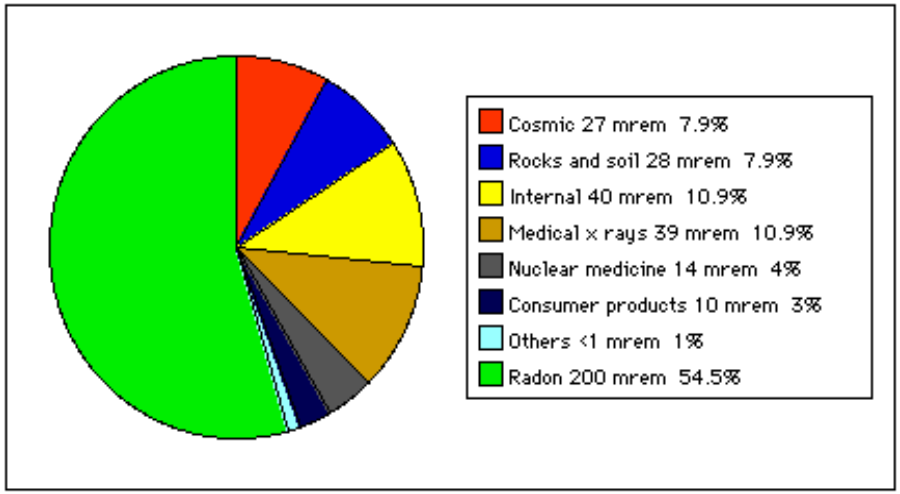
Mouthing Observation Study

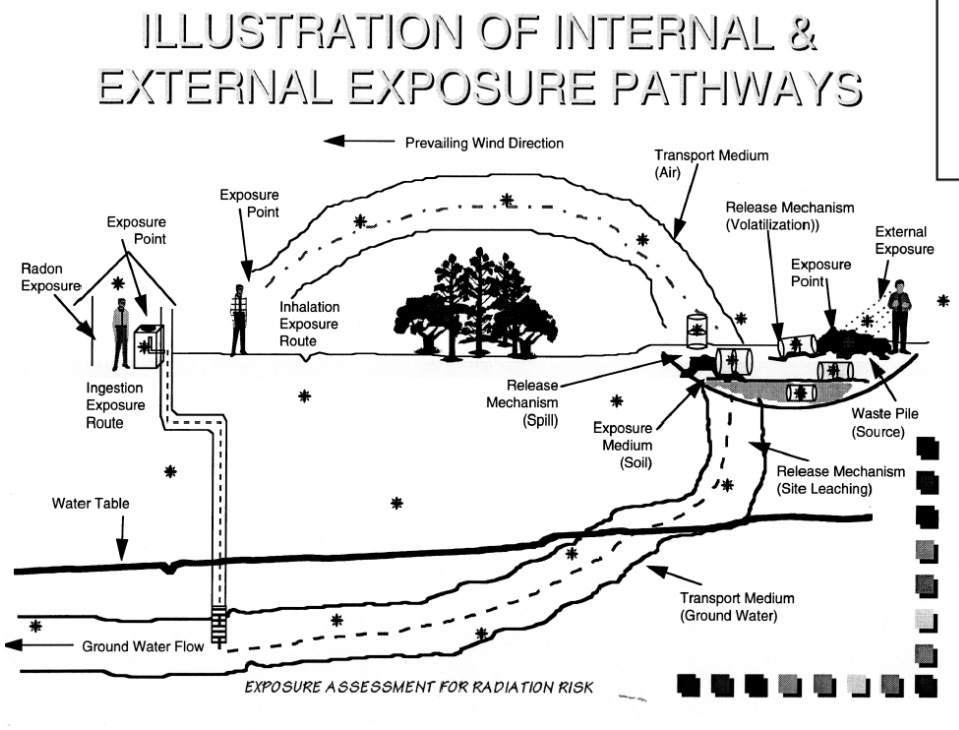
Modified from: Michael Babich, CPSC

EXAMPLE #7: U.S. EPA Radiation Protection Division Exposure Assessment for Radiation Risk

United States Environmental Protection Agency

Sources and Pathways of Radiation Exposure





Courtesy: David Pawel, Mike Boyd, EPA/OAR

EXAMPLE #7: U.S. EPA Radiation Protection Division Exposure Assessment for Radiation Risk

COMPARISON OF RADIATION AND CHEMICAL RISK ASSESSMENT: EXPOSURE ASSESSMENT

Item	Radiation Risk Assessment	Chemical Risk Assessment
Exposure	Intake/External Exposure = Internal and External Exposure Pathways	Intake = Internal Exposure Pathways
External Exposure	Gamma and x-rays	--
Unit	Activity (Bq or Ci or pCi) or pCi-yr/g for external	mg/kg/day
Fate and Transport	Radioactive decay and ingrowth	Chemical or biological degradation
Intake/External Exposure	Intake/External Source Intake = C × CR × EF × ED External Exposure = C × ED	Intake = C × CR × EF × ED / (BW × AT)

Courtesy: Mike Boyd, EPA/OAR