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Approaches to Quantifying Exposure

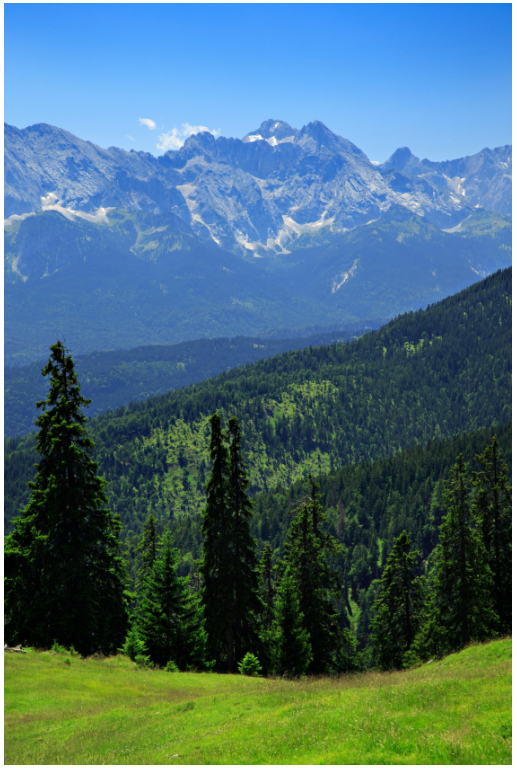


RISK ASSESSMENT TRAINING AND EXPERIENCE
Exposure Assessment Course Series – EXA 402

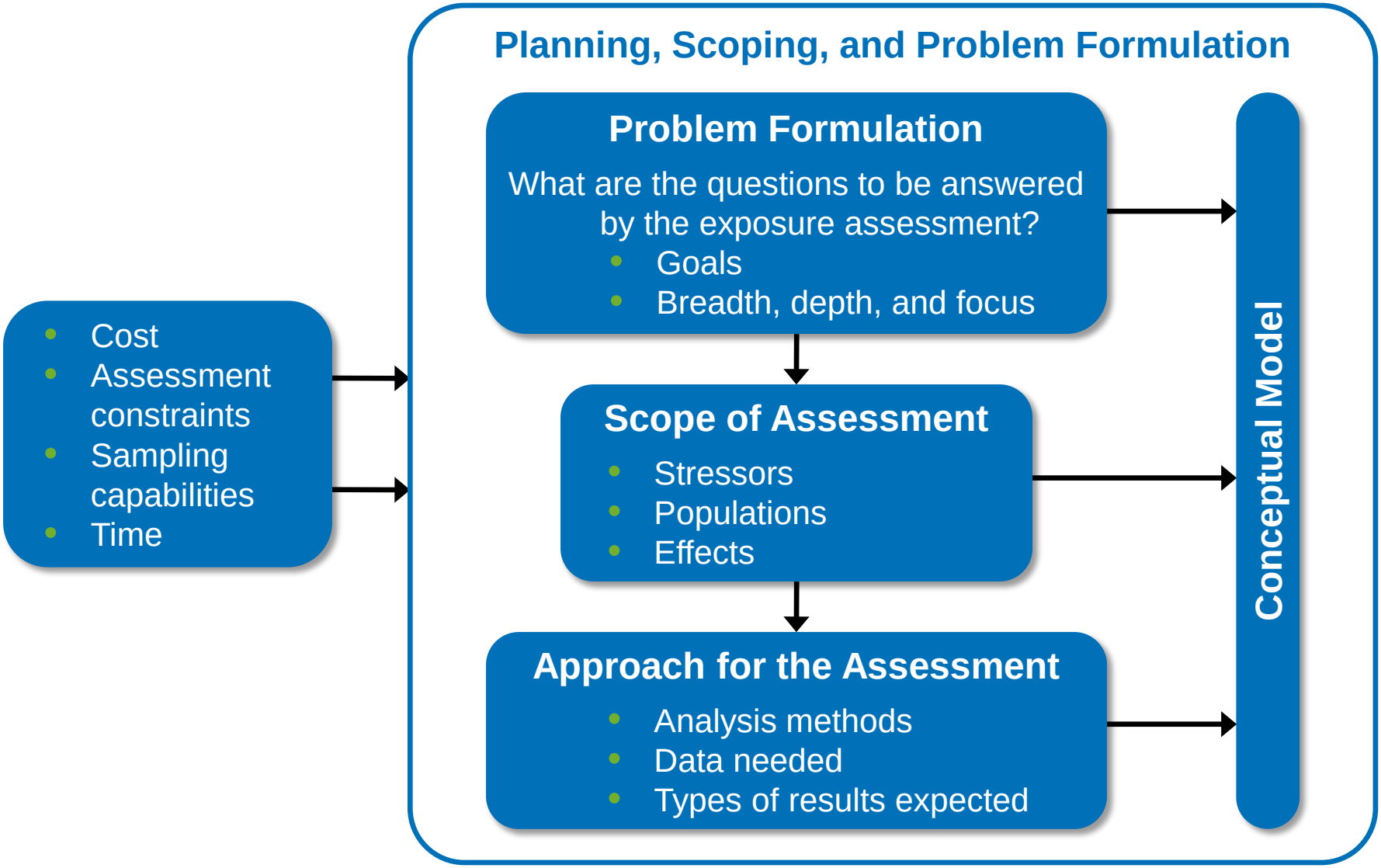
Office of Research and Development
National Center for Environmental Assessment

What You Can Expect to Learn from this Course

- Approaches for quantifying exposure
  - Types of approaches
  - Scope of approach
  - Exposure descriptors
- Methods of quantifying exposure
  - Point-of-contact assessment
  - Scenario evaluation
  - Reconstruction of dose



Preparing to Evaluate Exposure



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SCOPE OF THE EXPOSURE ASSESSMENT

What is the Scope of the Assessment?

"Scoping…involves defining the elements that will or will not be included in the risk assessment. These include the stressors, sources, pathways, routes, populations, and effects or assessment endpoints to be evaluated."

EPA's Framework for Cumulative Risk Assessment, 2003

- **Scope** can be affected by a range of issues

Legal

Environmental

Geographic

Demographic

Stressor

- **Tiered approach** facilitates an iterative evaluation of risk management decisions

What is the Geographic Scale?

INTERNATIONAL

PCBs in wildlife

NATIONAL

Phthalates in plastics

REGIONAL

Problem with all underground storage tanks in an area

LOCAL

Leaking underground storage tank

- Scale also influenced by
  - Cost
  - Receptor population(s)
  - Industries or areas affected
  - Remediation options
  - Legacy or lifetime exposures

Demographics: Who Are the Receptors?

Receptor: Individual or group actually or potentially exposed

EPA's Cumulative Risk Resource Document, 2007

Susceptibility: An increased likelihood of an adverse effect, often discussed in terms of relationship to a factor that can be used to describe a human population (e.g., lifestage, demographic feature, or genetic characteristic)

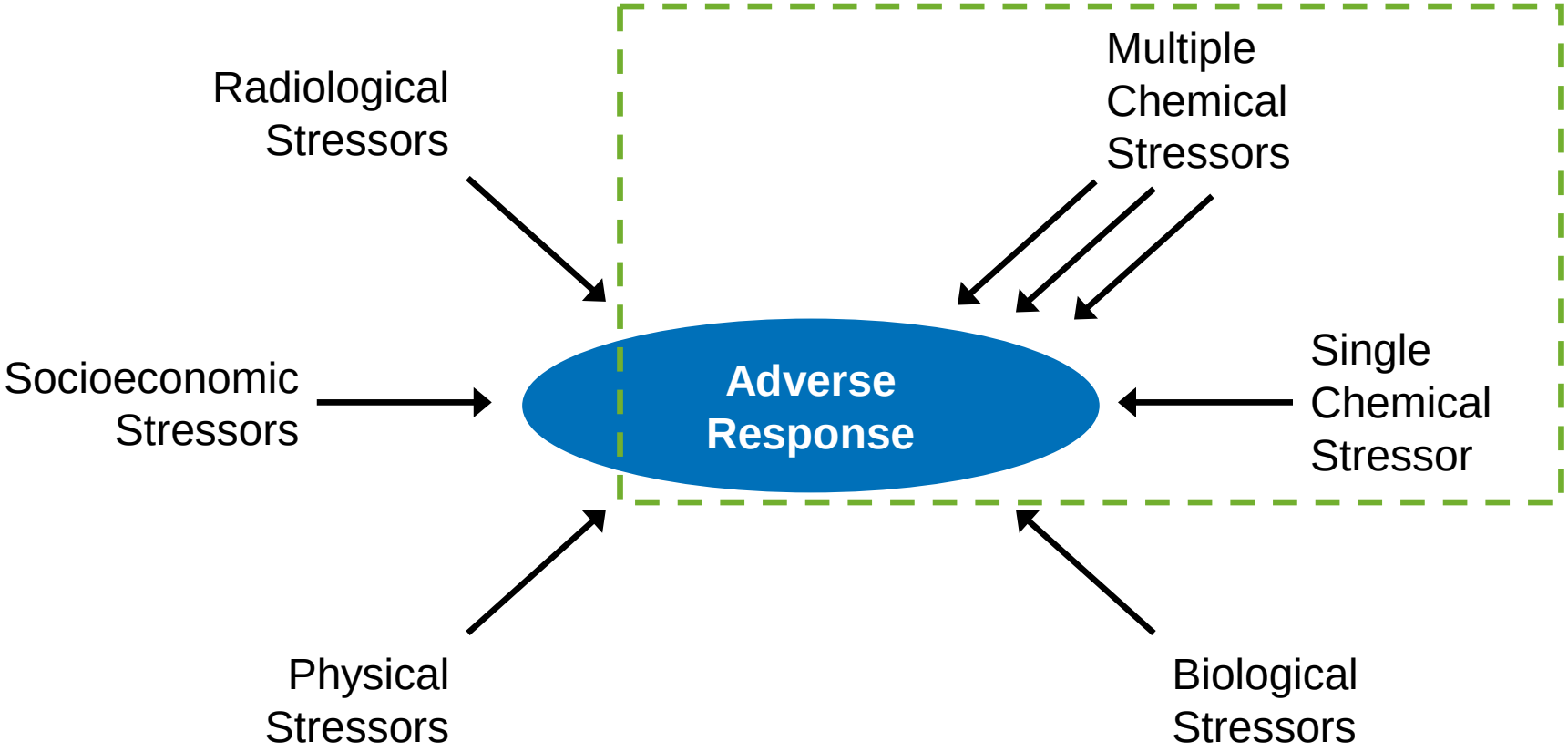
EPA's Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens, 2005

- Potentially susceptible populations
  - Children and the elderly
  - Women of child-bearing age
  - People with compromised immune systems
- Highly exposed populations
  - Individuals who eat fish or produce that is contaminated by the stressor
  - People who are occupationally exposed

Chemicals: What Are the Stressors?

Stressor: Any biological, chemical, or physical entity that can cause or induce an adverse response in a human or ecological receptor

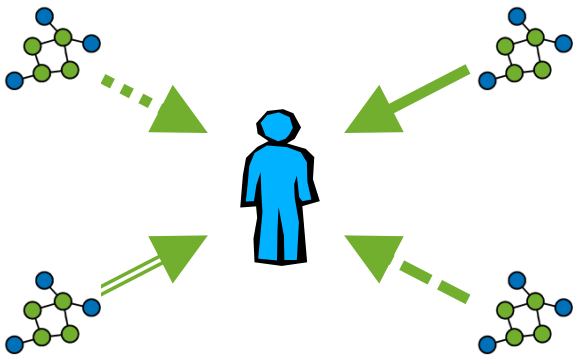
EPA's RAGS Volume III Part A, 2001



Aggregate and Cumulative Exposures

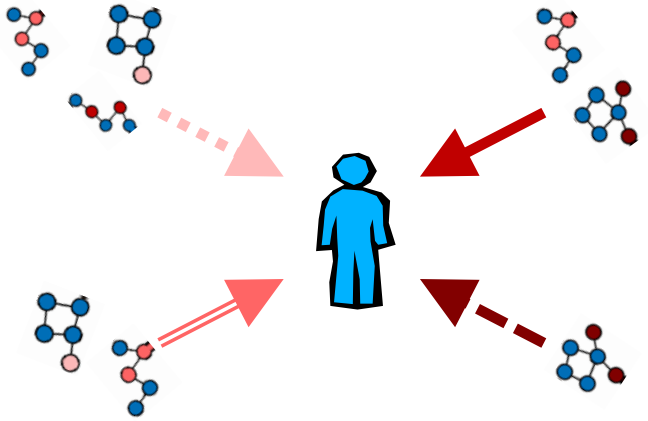
Aggregate exposure

- Exposure to a single chemical from multiple sources and exposure pathways



Cumulative exposure

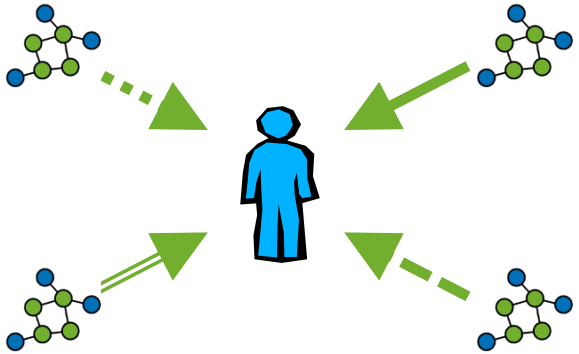
- Exposure to multiple chemicals with similar mechanisms of action from multiple exposure pathways



Assessing Aggregate Exposure

- Aggregate exposure assessments evaluate combined exposure to a **single chemical** across **multiple routes and pathways**

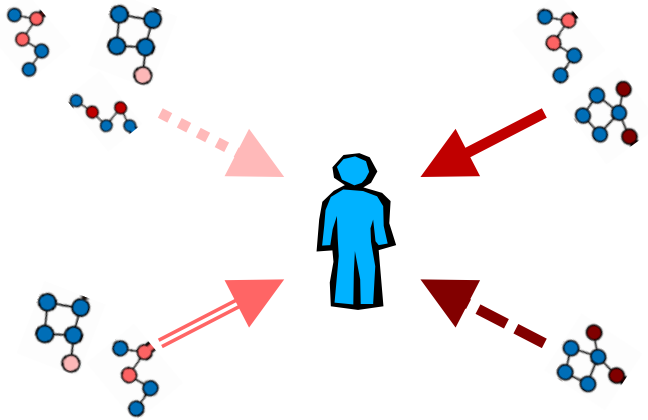
- EPA aggregate exposure assessment for pesticides
  - Acute and chronic exposure to residues in food
  - Residues in water
  - Residential exposures to consumer products



Assessing Cumulative Exposure

- Cumulative exposure assessments evaluate the impact of **multiple chemicals** with **multiple routes and pathways** of exposure and **similar mechanisms** of toxicity
- Not simply a sum of aggregate exposure assessments – individual interactions must be considered

- Examples
  - EPA consideration of exposure to pyrethroid pesticides with same mechanism of action
  - EPA residual risk assessment of air toxics emissions from point sources



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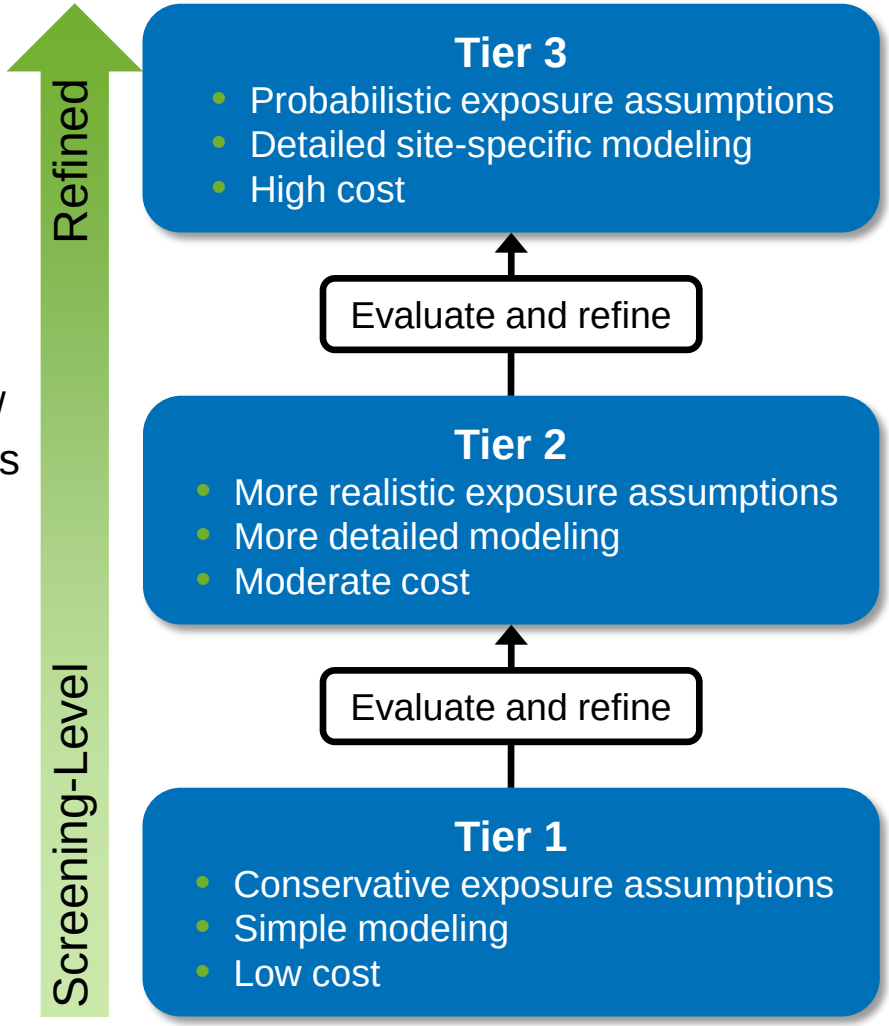
TIERED APPROACH TO EXPOSURE ASSESSMENT

What is the Tiered Approach to Exposure Assessment?

Increasing Complexity/
Resource Requirements
Characterization of
Variability and/or
Uncertainty



Adapted from Figure 31-1, ATRA, Volume 1

Screening-Level Exposure Assessment

- Preliminary evaluation tool
- Produces quantitative, conservative estimates with available data and/or models
- Results useful for general comparisons or prioritization
  - Simple, determines whether or not there may be a concern
- Prevents unnecessary expense

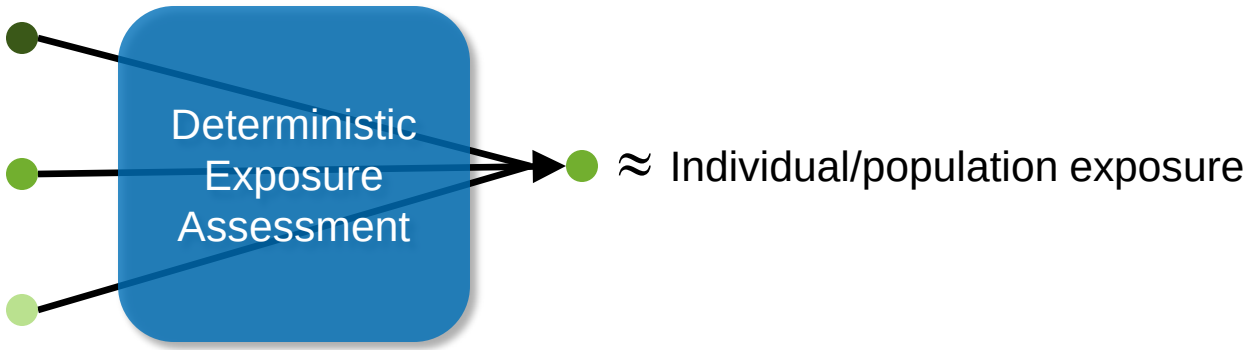
- Example
  - Do children's toys contain phthalates?
  - Screening-level assessment used to determine if more modeling is needed

Refining an Exposure Assessment

	Screening Assessment	Refined Assessment
Measurements	• Readily available measured data • Release estimates based on generic emission factors	• Site-specific measured data • Emissions monitoring data
Inputs	• Generic or conservative model parameterization • Generic conservative exposure assumptions	• Site-specific parameterization
Models	• Simple models	• More complex models

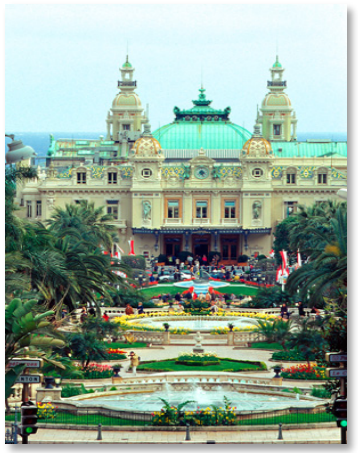
Deterministic Exposure (or Risk) Assessment

- Uses **point estimates** for input parameters to quantify exposure for a population or individual
- Resulting exposure estimate is also a point estimate (e.g., central tendency or reasonable maximum exposure)
- Straightforward and relatively economical
- Limited characterization of uncertainty or variability with multiple deterministic runs



Probabilistic Exposure Assessment

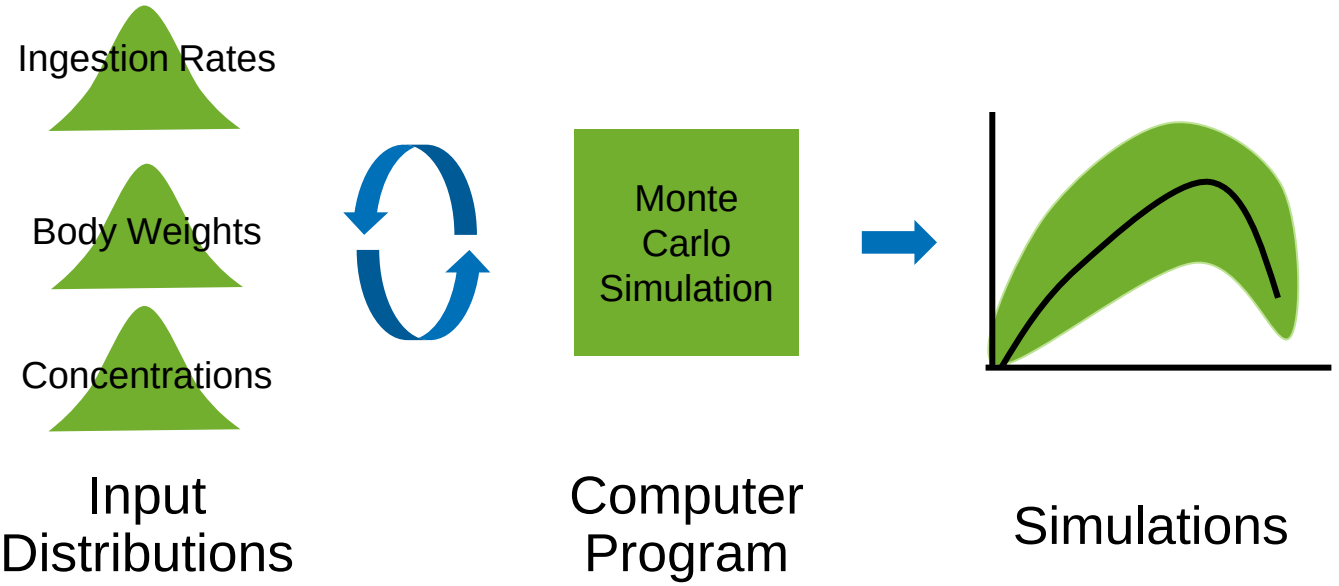
- Uses **probability (frequency) distributions** for certain influential parameters to quantify exposure and account for variability
- Describe the range of values and estimate the likelihood that the values may occur for random variables
- Guidance on conducting probabilistic assessments in EPA RAGS and ATRA
- **Monte Carlo simulation**
  - Common sampling approach to generate probabilistic results



What is a Monte Carlo Simulation?

"A technique for characterizing the uncertainty and variability in risk (or exposure) estimates by repeatedly sampling the probability distributions of the risk equation inputs and using these inputs to calculate a range of risk values."

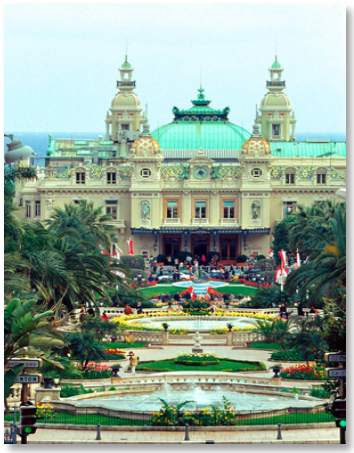
EPA's RAGS Volume III Part A, 2001

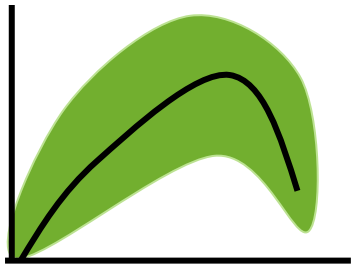


Source: U.S. EPA "Approaches for the Application of Physiologically Based Pharmacokinetic (PBPK) Models and Supporting Data in Risk Assessment National," 2006.

Monte Carlo and Probabilistic Methods

- May require more data than deterministic approaches
- Allow for better estimates of variability in exposure
- Probabilistic methods not always necessary, the extra time and money may not be required, depends on situation
- Even probabilistic methods can be iterative





“Garbage In, Garbage Out”

- Model outputs are only as accurate as the data used to build them
- A great model cannot improve bad data; output is only as good as the input
- Sophisticated models or Monte Carlo simulations cannot transform low-quality data to be more accurate or precise

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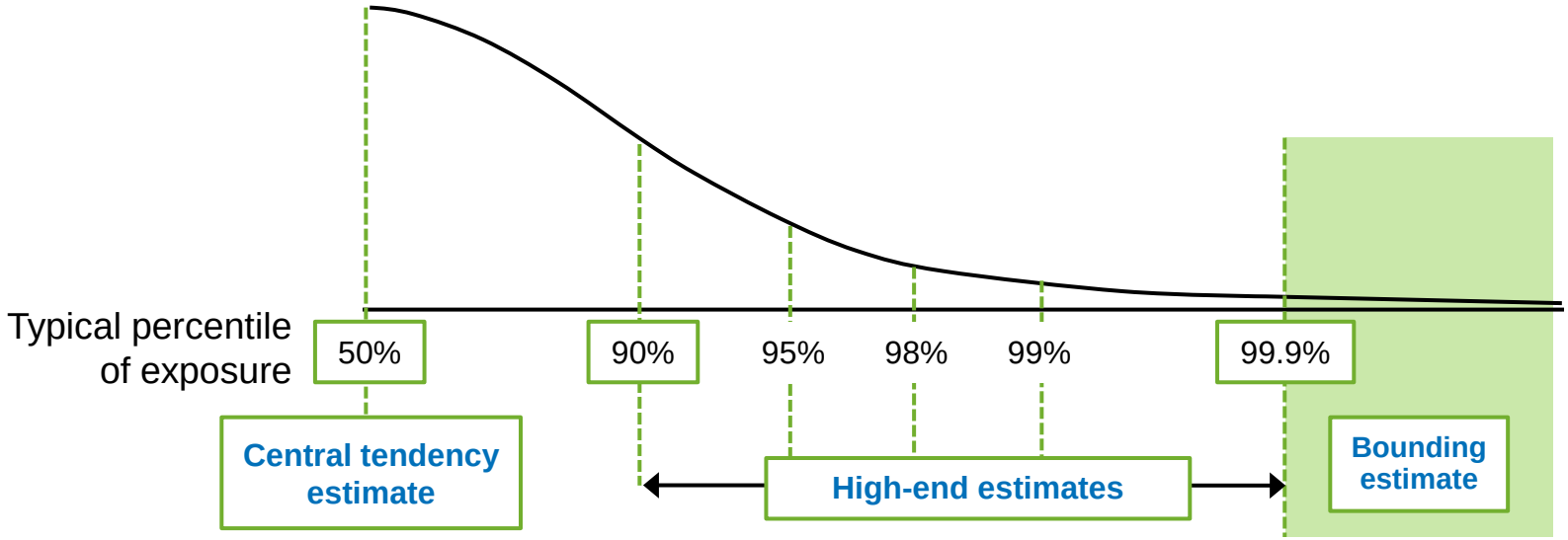
EXPOSURE DESCRIPTORS

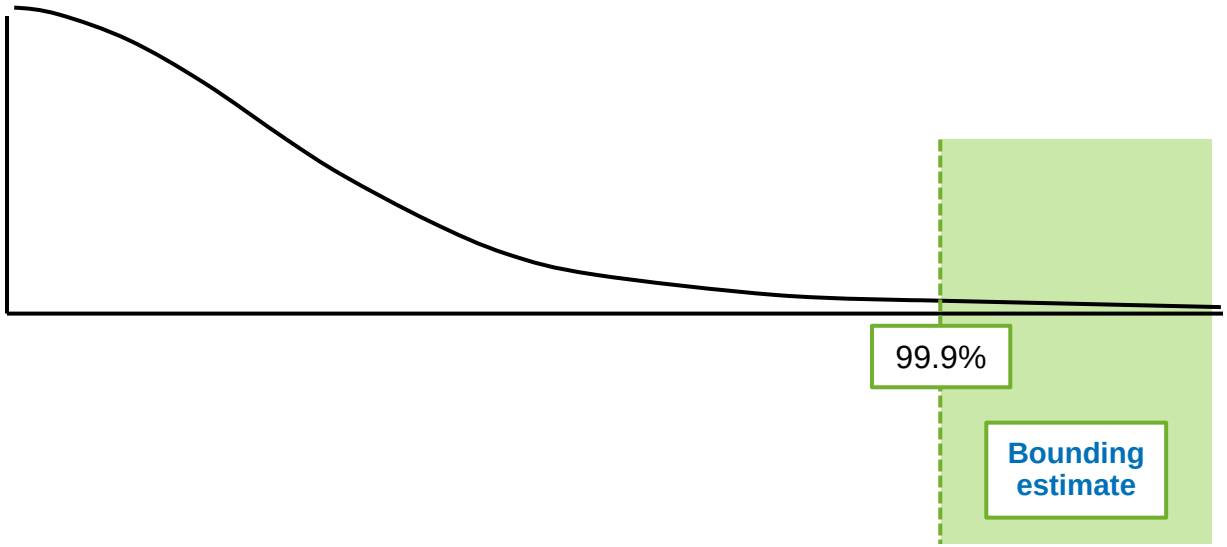
Use of Exposure Descriptors

- **Exposure descriptors** are estimates of specific points on the exposure distribution
  - Based on selected parameter values
  - May be for individual or population exposures
  - Help assessors communicate with risk managers



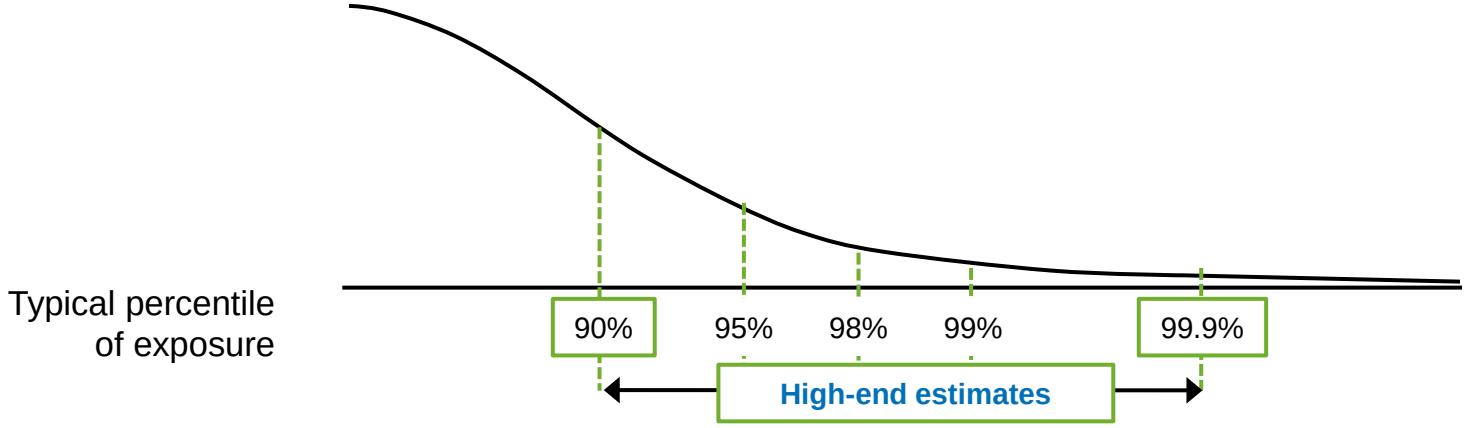
Bounding Estimates

- **Bounding estimates** capture highest possible exposure or theoretical upper bound estimate
  - Useful for rapid screening estimate
  - Uses highest intake rates, exposure frequency and distribution; and average body weights for estimate



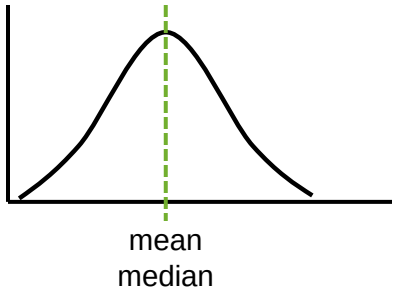
High-End Estimates

- **High-End Estimates** – at or above 90th percentile of population distribution
  - Combination of high and central tendency inputs
  - More realistic than upper bound
- **Reasonable Maximum Exposure** (RME) – from EPA 2001
  - Used in Superfund remedy decisions
  - Highest exposure reasonably likely to occur
  - Generally represents the 90th–99.9th percentile of the exposure distribution estimated from a probabilistic risk assessment
- **Reasonable worst-case exposure** (90th–98th percentile) – from EPA 1992
- **Maximum exposure** (98th percentile) – from EPA 1992
- As exposure estimate moves higher in the range, level of uncertainty rises

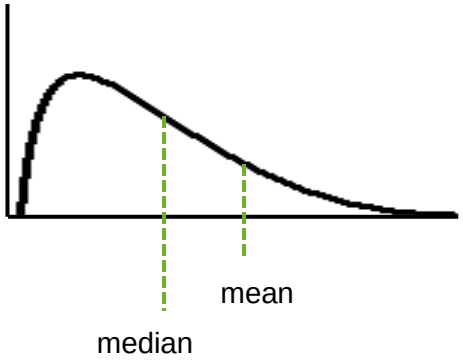


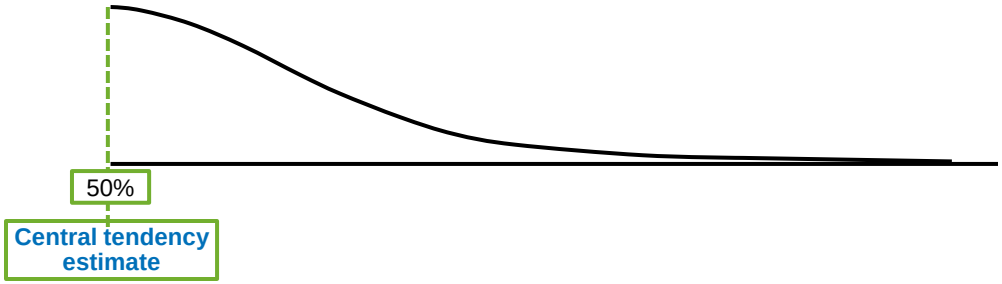
Central Tendency Estimates

- Goal is to provides an **average** or **typical intake** for a population or for a specific scenario. Derived using:
  - **Arithmetic mean**
    - Uses average values for all factors
    - Representative of "average" receptor or group



  - **Median** exposure/dose
    - Corresponds to 50th percentile exposure/dose
    - Useful when data are in a lognormal distribution





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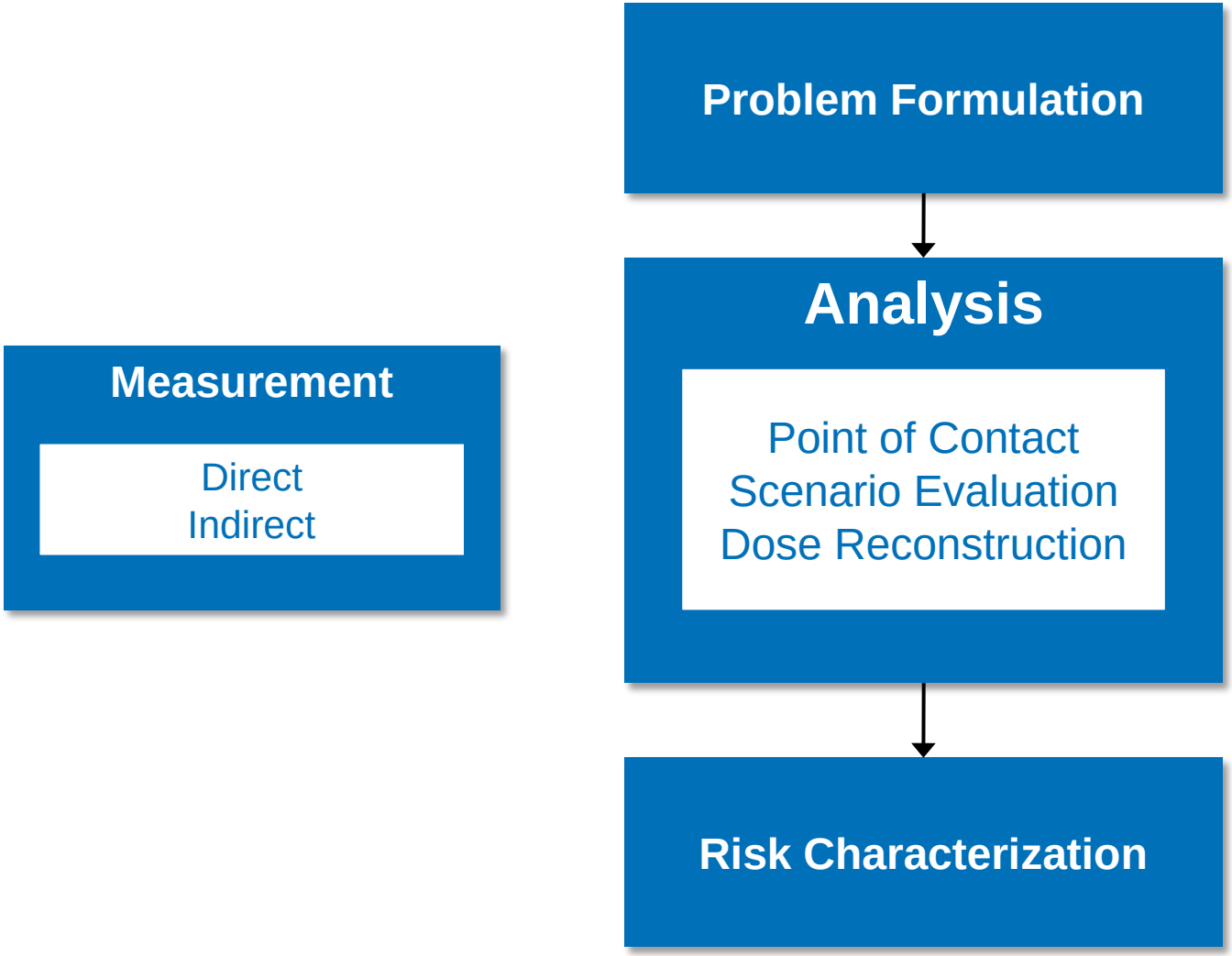
THREE APPROACHES FOR QUANTIFYING EXPOSURE

Approaches to Quantifying Exposure



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POINT OF CONTACT FOR EXPOSURE ASSESSMENT

Point of Contact Exposure Measurement

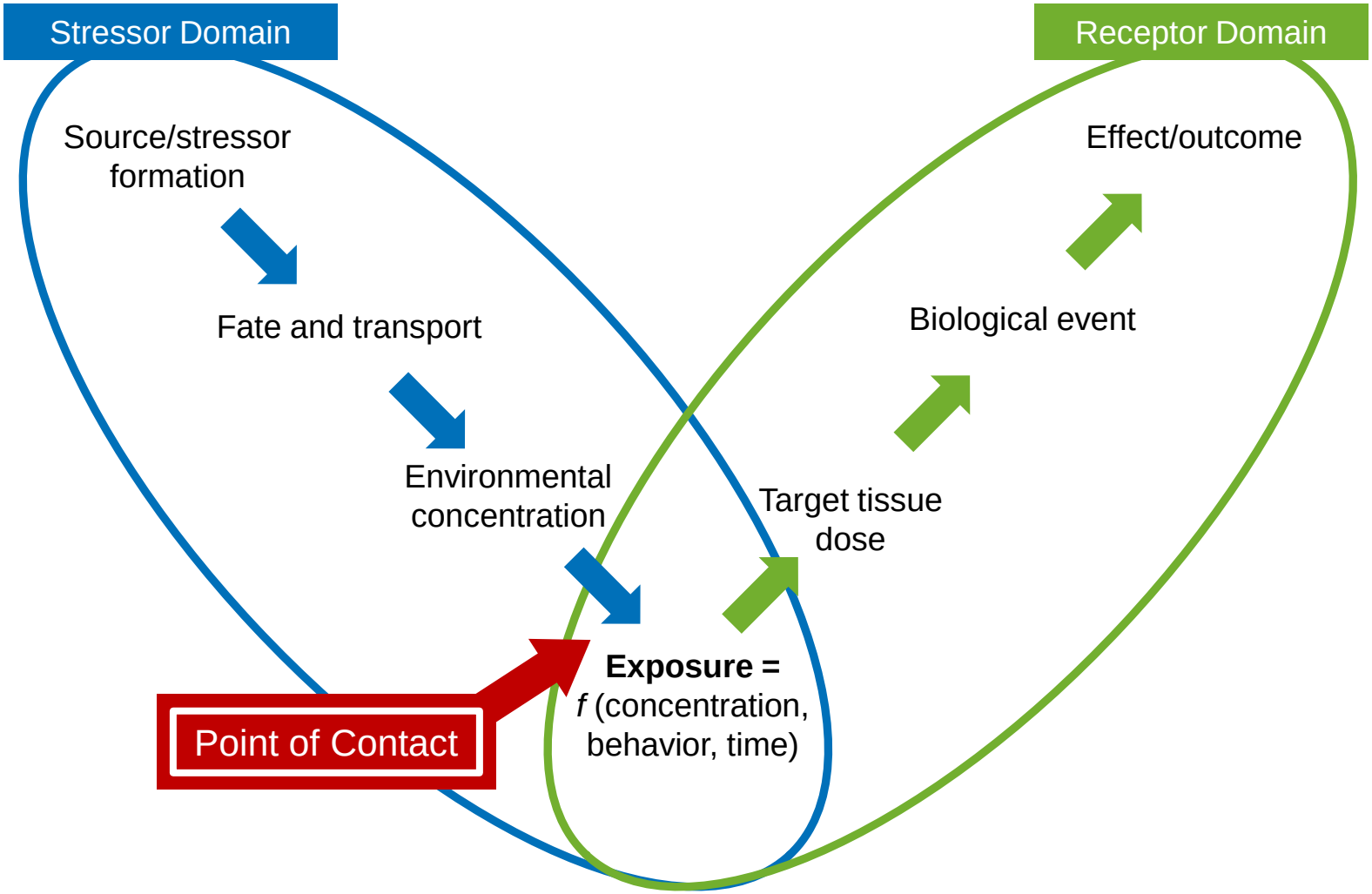
Point of contact exposure measurement evaluates the exposure as it occurs, by measuring the chemical concentrations at the interface between the person and the environment as a function of time, resulting in an exposure profile

EPA's Guidelines for Exposure Assessment,1992

Radiation dosimeters of 1950s – "pocket screamer" and "chirper" from Oak Ridge National Lab

Modern radiation detection devices

Where does Point of Contact Fit?



Point of Contact Strengths and Weaknesses

- **Strengths**
  - Measures exposures directly
  - Representative of individual exposures
  - Most accurate method for quantifying exposure

- **Weaknesses**
  - Expensive
  - Not source-specific
  - Not available for all chemicals
  - Relies on accuracy of the device, the person operating it and the strength of analytical methods

Direct Measurements of Dermal Exposure

- Wide range of methods and devices for measuring dermal exposure
  - **Patches** – used for pesticides, metals, dusts
  - **Whole-body dosimeters** – radiation badges, coveralls, full-length cotton underwear
  - **Removal** – rinsing, wiping, and tape strips to collect contaminants from skin
  - **Optical methods** – fluorescent tracers

Direct Measurements of Oral Exposure Concentrations

- **Duplicate diet studies**
  - Individuals collect duplicate samples of all foods consumed in a given period
  - Samples are evaluated by investigators to determine concentrations of chemicals of concern
  - Provide information on:
    - Concentration of chemical in food
    - Intake rate of chemicals of concern, per bodyweight of participant
    - Total amount of chemical by food type

An EPA Point of Contact Assessment

- **National Human Exposure Assessment Survey**
  - Involved 550 people in several states
  - Began in 1995, data collection finished in 1997 and results were published in 1999
  - Conducted to provide multipathway and multimedia exposure distributions for specific chemical classes
  - Tested the hypothesis that existing data and modeling estimates do not differ from measurement-based exposure distributions
  - Evaluated exposure to VOCs, metals, and pesticides

NHEXAS Results

- Data from EPA Region 5, includes Great Lakes region
- Results
  - Solid food was the major source of urinary arsenic
  - Blood lead levels significantly associated with household lead levels from dust, air, and beverages
  - High correlation between tap water consumption and body burdens of lead and arsenic
  - Moderate correlation between personal air samples and VOCs

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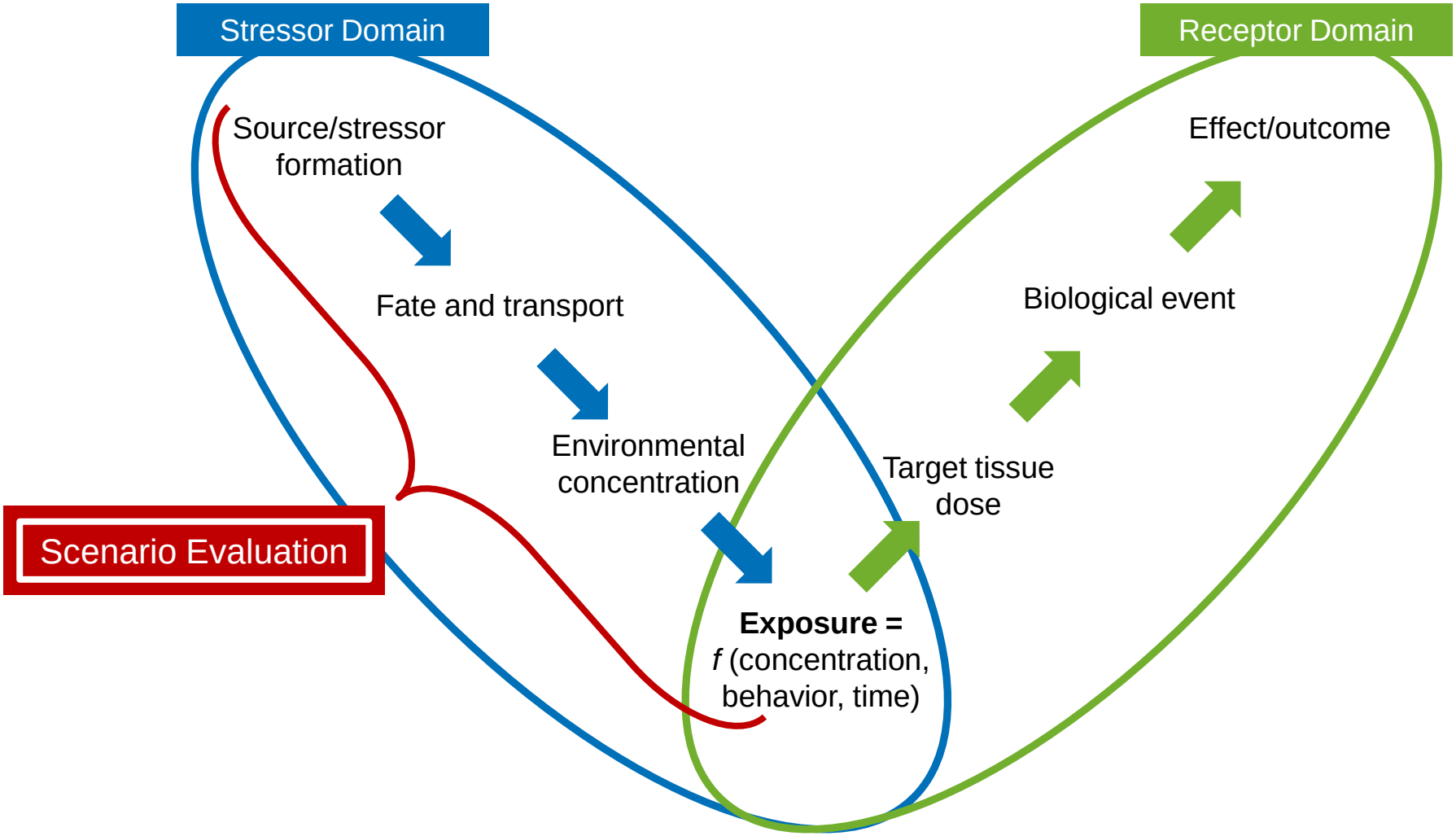
SCENARIO EVALUATION FOR EXPOSURE ASSESSMENT

Scenario Evaluation for Exposure Assessment

- **Scenario evaluation** estimates exposure by developing an exposure scenario to combine information on chemical concentration, time-of-contact information, and data on exposed persons
  - **Exposure scenario**: A set of facts, assumptions, and inferences about how exposure takes place that aids the exposure assessor in evaluating, estimating, or quantifying exposure
  - Characterized by:
    - Setting
    - Chemical characteristics and sources
    - Exposure pathways and routes
    - Environmental and exposure media
    - Intake and uptake rates
    - Characteristics of exposed population
- Will be discussed in detail in EXA 403

Where does Scenario Evaluation Fit?



Scenario Evaluation Strengths and Weaknesses

- **Strengths**
  - Can be economical, depending on the scale of the study
  - Well-suited to evaluating proposed actions
  - Can be done with limited data

- **Weaknesses**
  - Simplification of the exposure scenario leads to less accuracy
  - Limited data needed for approach means more uncertainty

Implementing Scenario Evaluation

- Assumptions
  - Data are representative of the exposed population
  - Data on chemical fate and transport correspond to actual exposure scenario

- Data requirements
  - Chemical concentrations from sampling, or fate and transport modeling results
  - Population statistics, including sensitive population groups
  - Time of contact and routes of exposure for each chemical and receptor

Types of Models Used

Models	Inputs	Output	Examples
Fate and Transport	• Emission rates • Fate and transport properties	• Pollutant concentrations (mg/m^3, mg/L, or mg/kg) in environmental media	• AERMOD • EXAMS
Exposure	• Concentrations in environments and microenvironments • Exposure factors • Time activity patterns	• Predicted exposures or doses (mg/m^3 or mg/kg-day)	• APEX • DEEM
Combined	• Population characteristics • Dietary exposure • Fate and Transport • Home Chemical Usage	• Population dist. of exposure • Model to measurement comparison	• SHEDS

Fate and Transport Models

- Simulate movement and changes in contaminants in the environment
- Predict concentrations in:
  - Sediment, surface water, groundwater, drinking water
- Vary regarding pollutants, receptors, spatial and temporal scales

AERMOD
(AMS/EPA Regulatory Model)

Air dispersion model that simulates fate of airborne pollutants and concentrations at different locations

EXAMS
(Exposure Analysis Modeling System)

Screening-level model that estimates pesticide concentrations in drinking water and surface water bodies

Exposure Models

- Predict exposures by inhalation or multimedia based on environmental concentrations, population characteristics, exposure factors, and activity patterns
- Vary with regard to pollutants, receptors, spatial and temporal scales

APEX
(Air Pollutants Exposure Model)

Estimates population-level exposures and doses to air pollutants for general population and sensitive groups at local, urban, and metropolitan levels

DEEM
(Dietary Exposure Evaluation Model)

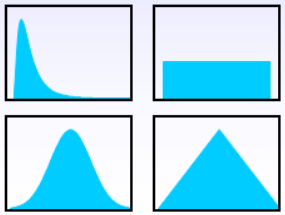
Estimates individual or population-level dietary exposures and doses to pesticides and pesticide residues in residential settings

SHEDS: A Multimedia, Multipathway Exposure Model

Input Databases

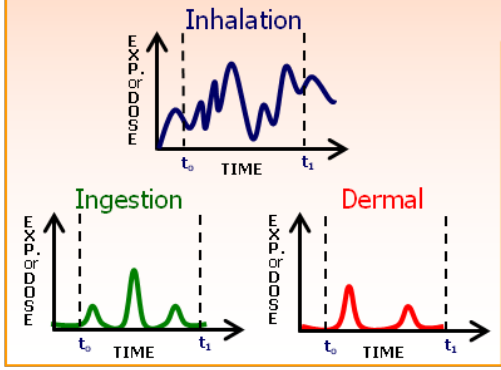
- Census
- Human Activity
- Residues
- Concentrations
- Recipe/Food Diary

Exposure Factor Distributions



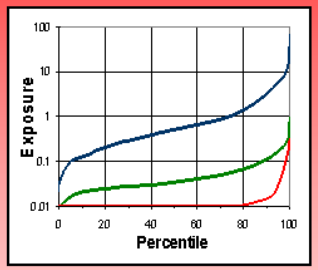
Algorithms

- Calculate Individual Exposure/Dose Profile

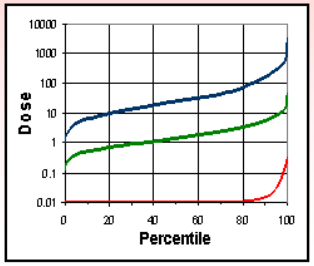


Output

- Population Exposure



- Population Dose



Source: SAP SHEDS Overview, 7/14/2010

SHEDS Model: What it Incorporates

SHEDS Inputs	Sources
Population Characteristics	• U.S. Census • NHANES – National Health and Nutrition Examination Survey
Dietary Exposure Data	• CHAD – Consolidated Human Activity Database • NHANES – National Health and Nutrition Examination Survey • CSFII – Continuing Survey of Food Intake by Individuals • RAW – Raw Agricultural Commodity • FCID – Food Commodity Intake Database • PDP – Pesticide Data Program • TDS – Total Dietary Survey
Chemical Fate and Transport	• Fugacity modeling • EPI Suite
Home Chemical Usage	• Home chemical usage database
Exposure and Dose Models	• ERDEM and other dose models

The LifeLine™ Model

- The **LifeLine™ Model** estimates aggregate and cumulative exposures and probabilistic risks from pesticides and other chemicals
  - Developed by the LifeLine Group, a non-profit organization
  - Models exposure for each individual within a population
  - Simulates inter-individual differences in exposure-related behaviors
- Exposures to chemicals from diet, home environments, drinking and tap water, consumer products, and pesticides use
- Routes of exposure include inhalation, dermal, dietary, and oral exposures for children
- Parameters can be adjusted to accommodate a wide range of dietary and behavior specifications

Combined Models

- SHEDS and LifeLine™ are only two of many combined models
- Discussion of models by Williams et al. (2010):
  - E-FAST (EPA OPPT): Screening-level estimates of chemicals released to air, water, landfills, from consumer products
  - TRIM (EPA OAQPS): “Next generation” model, estimates environmental concentrations, fate & transport, population-level exposures for ecological & human receptors
  - 3MRA (EPA ORD): Screening-level risk-based assessment of potential health risks from long-term exposure
- Many models are only used for research purposes
- Practical example: assessment of children’s exposure to CCA-treated wood in playsets by EPA OPP

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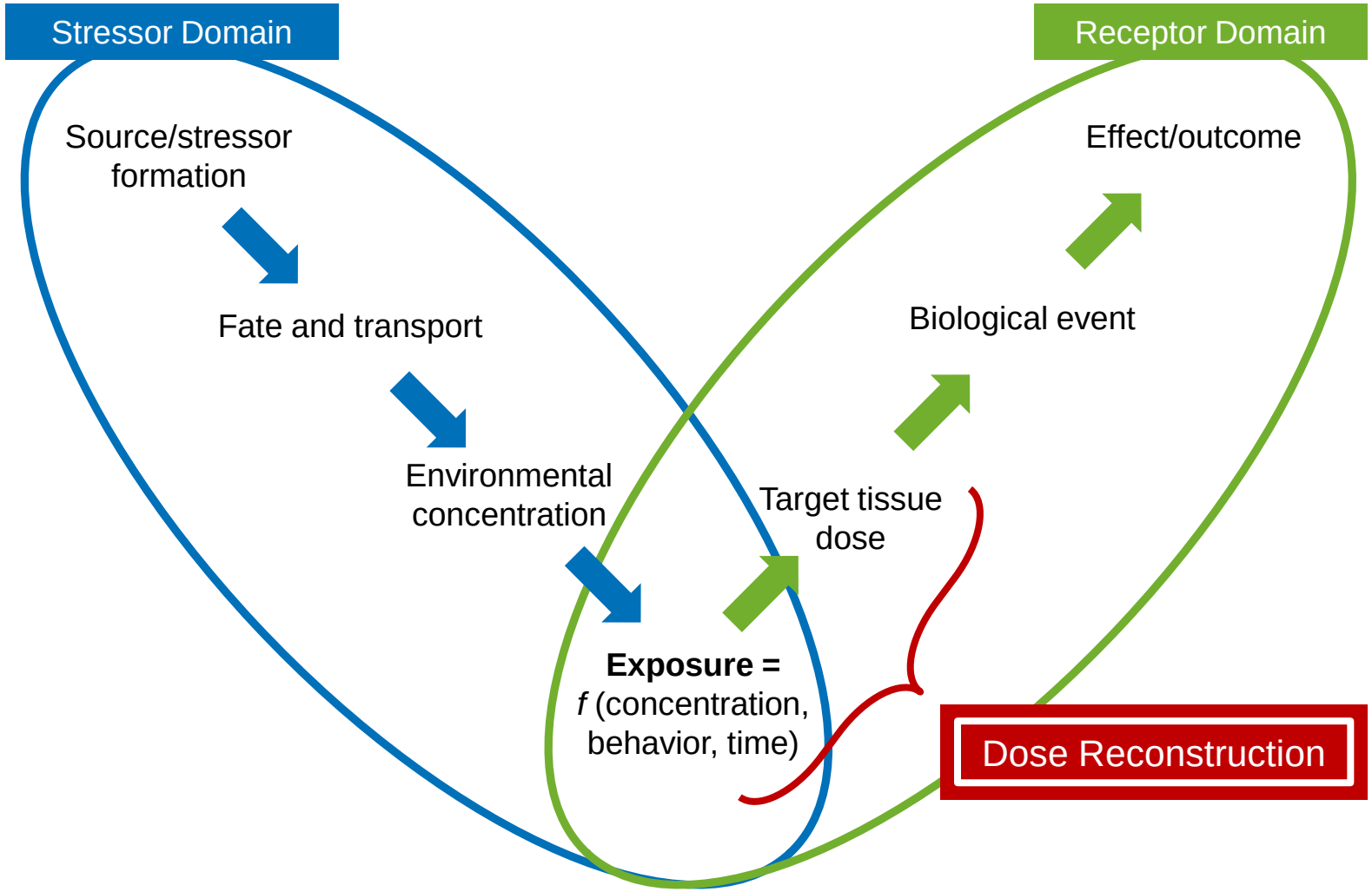
DOSE RECONSTRUCTION FOR EXPOSURE ASSESSMENT

Dose Reconstruction for Exposure Assessment

- **Dose reconstruction** uses pharmacokinetic (PK) models to estimate exposure from body burden data collected by biomonitoring

- NHANES data include national biomonitoring data collected by CDC
  - Stratified by age, race, and sex for numerous chemicals

Where does Dose Reconstruction Fit?



Biomarkers for Dose Reconstruction: Strengths and Weaknesses

- **Strengths**
  - Provide evidence of exposure
  - Biomarkers are an important dose metric with regard to potential health impacts
  - Most accurate estimate of total external dose, with appropriate model

- **Weaknesses**
  - Not linked to pathway or source
  - Requires pharmacokinetic (PK) model and parameters
  - Sampling and evaluation may be expensive

Dose Reconstruction Example

Table 2
Geometric mean urinary cadmium concentrations (μg Cd/g of creatinine) found in the nonsmoking U.S. population by age from the National Health and Nutrition Examination Survey 2003–2004 (NHANES).

Age (years)	Males (95% confidence interval)	Females (95% confidence interval)
6–11	0.088 (0.071–0.11)	0.088 (0.072–0.108)
12–19	0.074 (0.066–0.083)	0.103 (0.089–0.118)
20–39	0.125 (0.114–0.137)	0.179 (0.159–0.202)
40–59	0.208 (0.184–0.234)	0.342 (0.305–0.383)
60+	0.366 (0.324–0.414)	0.507 (0.46–0.558)

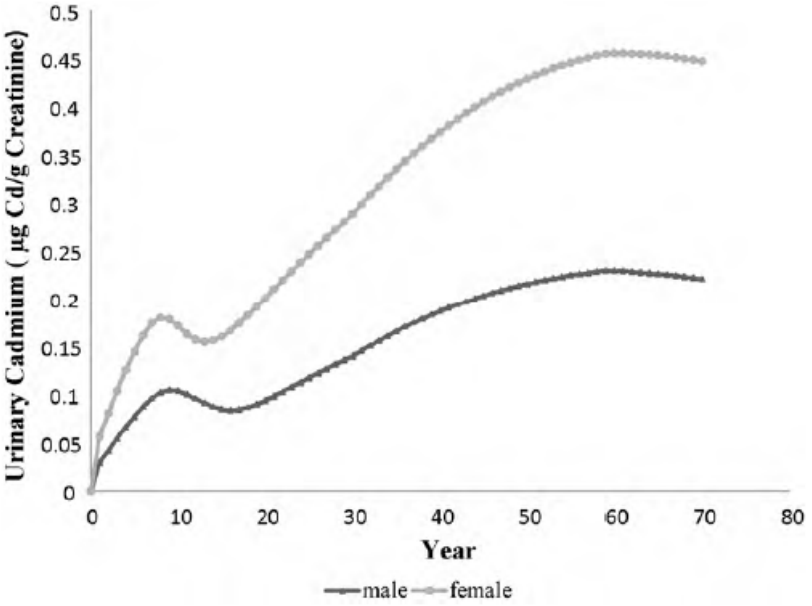


Fig. 1. Model predictions of urinary cadmium excretion in the U.S. population (males and females). The upper model simulation shows the female cadmium urinary excretion and the lower shows the male cadmium urinary excretion.

Table 3
Dietary cadmium intake and model predictions of urinary cadmium in the nonsmoking U.S. population (corrected for creatinine) (μg Cd/g creatinine).

Age (years)	Males		Females	
	Cd intake U.S. (GM)[a] (μg Cd/day)	Model predictions	Cd intake U.S. (GM)[a] (μg Cd/day)	Model predictions
6–11	15.0	0.101 (0.088–0.11)	13.5	0.172 (0.152–0.188)
12–19	19.7	0.087 (0.078–0.095)	15.1	0.163 (0.136–0.190)
20–39	22.4	0.137 (0.082–0.190)	16.2	0.285 (0.182–0.386)
40–59	22.1	0.214 (0.188–0.241)	16.5	0.427 (0.377–0.477)
60+	17.6	0.226 (0.221–0.232)	14.4	0.453 (0.447–0.459)

GM: geometric mean.
[a] From Choudhury et al. (2001).

Ruiz, et al. 2010. Interpreting NHANES biomonitoring data, cadmium. *Toxicology Letters* 198. 44-48.

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CONCLUSION

Conclusions

- Quantifying exposure allows assessors to evaluate exposures to stressors and impact on receptor populations
- Depends on data, resources, exposure of concern, stressors, and receptor populations
- Tiered approach helps to guide, refine, and select appropriate methods
  - Deterministic versus probabilistic
- Quantification approaches all have strengths and weaknesses, one or multiple might be best, depending on the scenario
  - Point of contact
  - Scenario evaluation
  - Dose reconstruction

Exposure Quantification Approaches at a Glance

Approach	Key Points	Examples
Point of Contact	• Quantifies exposure as it occurs, at the interface between the person and the environment. • Representative of individual exposure. • Most accurate method of quantifying exposure. • Can be expensive; not source-specific; relies on accuracy of the device used for sampling.	• Whole-body radiation dosimeters • Patch or tape stripping measurements • Duplicate diet studies
Scenario Evaluation	• Scenario that combines data on chemical concentration, time-of-contact, and population characteristics. • Elements that determine exposure: setting, chemical characteristics, sources, exposure pathways and routes, intake and uptake. • Can be economical; well-suited to evaluating proposed actions; can be done with limited data.	• Fate and transport models: AERMOD, CMAQ • Exposure models: APEX • Integrated models: 3MRA
Dose Reconstruction	• Estimate of exposure from dose, based on monitoring. Dose estimated using biomarkers of exposure. • Can provide unambiguous proof of exposure, may give most accurate estimate of external dose. • Does not provide exposure pathway, amount, or source. Data not always available, may be expensive.	• Biomarkers of exposure: NHANES