EXA 402: Approaches for Quantifying Exposure
Instructor Notes

Course Description: Selecting the approach for quantifying exposure and dose, as well as determining the appropriate type and scope of the study are important first steps in planning an exposure assessment. This course is designed to explore the various approaches that may be used to measure or model exposure, including point of contact measurements, scenario evaluation methods, and dose reconstruction approaches. The purpose and utility of these approaches as well as their strengths and weaknesses will be covered. Participants will also be introduced to the types of quantitative methods (e.g., deterministic or probabilistic) and scope of assessments (e.g., single or multiple chemicals; national-scale, or specific location or industry). The use of exposure descriptors in the exposure assessment planning process will also be discussed.

Expected Course Duration: Approximately 1 hour

Terminal Learning Objective: Understand methods for quantifying exposure and dose

Enabling Learning Objectives:

- Understand characteristics of exposure situations, including: stressors, receptors, scope, scale, and methods for cumulative and aggregate assessment.
- Understand quantification methods for exposure assessment, including: tiered and screening-level assessments, deterministic and probabilistic methods.
- Understand exposure descriptors, including: central tendency, reasonable maximum exposure, and bounding estimate.
- Understand methods for quantifying exposure, including: point-of-contact, scenario evaluation, and dose reconstruction.

Course Materials

- Reading Packet

Course Overview/List of Slides

TITLE SLIDE

What You Can Expect to Learn from This Course (Slide 1)

- In the first part of the course, we'll discuss each of the types of approaches used in exposure assessment. Next, we'll cover issues related to defining the scope of the exposure assessment. After that, we'll move on to discuss some ways to describe different types of exposure and estimates of exposure.
- In the second part of the course, we'll talk more about the specific methods used to quantify exposure, focusing on three common exposure quantification approaches: point of contact assessment, scenario evaluation, and reconstruction of dose. We'll discuss each of the approaches, including examples, and discuss briefly the strengths and weaknesses of the approaches.
- The exposure assessment process begins with problem formulation. Let's talk about that first.

Preparing to Evaluate Exposure (Slide 2)

- The scope and parameters of an exposure assessment are dictated by the questions we want to answer regarding exposure. This makes problem formulation a critical first step in the process.
- We need to articulate our questions at the outset of an exposure assessment – during the problem formulation stage – because they help structure the design of the analysis and allow risk assessors, risk managers, and stakeholders to make sure they are all on the same page regarding the goals, depth, and focus of the exposure assessment. Articulating the exposure assessment questions helps us to develop a conceptual model for the assessment.
- Specifying the scope of the assessment helps us to further refine the conceptual model. In just a minute, we will talk more about defining the scope of the assessment.
- After formulating our exposure assessment questions and defining the scope of the assessment, we can decide on our preliminary approach for the assessment.
- As we go through the problem formulation and planning and scoping phase of our assessment, it is also important to consider cost, assessment constraints, sampling capabilities, and other details to further refine our scope and approaches, which are shown on the left side of the figure.
- We can combine the results of this phase into a conceptual model to help us visualize how the inputs, quantitative approaches, and our assumptions will help us answer our exposure assessment questions.
- Source: (U.S. EPA, 2007)

SCOPE OF THE EXPOSURE ASSESSMENT (SLIDE 3)

- In this section, we'll go over some concepts that are fundamental to defining the scope of our assessment and the quantitative methods we'll use to evaluate exposure.

What is the Scope of the Assessment? (Slide 4)

- Once we've begun to define the problem our exposure assessment seeks to answer, we need to define the elements that we will and will not include; in other words, the scope. We need to identify the stressors, sources, receptors of interest, pathways, and endpoints that we will evaluate (U.S. EPA, 2003).
- The scope of the assessment can be refined based on legal statutes and regulations that require certain assessments. For example, the Clean Air Act requires assessment of human health and exposure in setting the National Ambient Air Quality Standards.
    - There are a number of regulatory parties from state, to federal, to industry regulators that might want to have a role in shaping an exposure assessment. These parties might all contribute to defining the scope of a given exposure assessment.
- The scope of an assessment could also be limited by environmental factors, such as assessing a chemical in only one environmental medium like air, water, or soil. Scope can also vary by geographic scale, depending on the extent of the issue under evaluation.
- Demographic factors such as age, health status, occupational exposures, or dietary patterns can also affect the scope of an analysis. For each scenario, there might be one or more demographic factors that affect the scope of the analysis, especially if there is a specific population of interest.
- The chemical stressor of interest can also affect the scope of the assessment. Some stressors might have multiple metabolites or related compounds to consider that could expand the scope; others might have characteristics that make them unique, narrowing the scope.
- Finally, the level of analysis required for an assessment can also affect the scope. For example, a screening level approach may be used in some cases, but a more in-depth, higher tier approach may be more appropriate for complex situations.
- A tiered approach allows for an iterative evaluation of risk estimates from each tier, which helps inform risk management decisions.
- In the next slides, we will talk more about how we refine the scope of our assessment based on geography, demographics, and chemicals.

What is the Geographic Scale? (Slide 5)

- The geography for an exposure assessment is dictated not only by the questions to be answered, but also by the sources of the stressors and nearby populations. The geographic scale can range from a small-scale local assessment to a regional or even national or international one.
- The geographic scale is also influenced by the cost of the assessment, which receptor populations are selected, the industries and areas affected, the remediation options considered, and any legacy or lifetime exposures that might result. Ultimately, we have to review the overall purpose of the assessment and the questions to be answered to determine the proper scope.
    - A specific singular, location might be a hazardous-material spill on the freeway or a single leaking underground storage tank.
    - A specific, regional assessment might include multiple locations such as all underground storage tanks in a given area.
    - An example of a national-scale issue is the exposure assessment for phthalates in plastics.
    - PCBs in wildlife could be considered an international issue – they are very long-lived in the environment, so they have become distributed across the globe.

Demographics: Who Are the Receptors? (Slide 6)

- To refine the scope of our assessment based on demographics, we can specify which receptors are included in our assessment. A **receptor** is the individual or "group actually or potentially exposed" (U.S. EPA, 2003). We might define the population by location such as a watershed or a city or by other demographic characteristics such as cultural practices or age. We need to consider what makes some populations more susceptible to exposure than others.
- Susceptibility is defined as "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)."
- Some receptors may be more susceptible to specific stressors than others. For human health exposure assessment, these could include children, women of child-bearing age, the elderly, and people with compromised immune systems.
- Some individuals might be more highly exposed due to their dietary or activity patterns, such as individuals that eat fish or produce that is contaminated by the stressor.
- Other individuals might have "differential exposures;" that is, they have historical exposure to the chemical or the area they live in has higher background levels. Differential exposure might also result from on-the-job or occupational exposure, or other activities that result in higher exposures. Sometimes these populations are called "populations of concern" or "highly exposed populations."

Chemicals: What Are the Stressors? (Slide 7)

- We can also further refine the scope of our assessment by focusing on specific stressors. A **stressor**, as discussed in EXA 401, is any biological, chemical, or physical entity that can cause or induce an adverse response in a human or ecological receptor. This course will focus on chemical stressors, but we could also evaluate the effects or the added contributions of physical stressors, like noise, or socioeconomic stressors, access to health care, as well as other types of stressors.
- Traditional risk assessment has used a single-chemical or stressor approach. This approach has been used because we had neither the data required to add the risks from multiple stressors, nor the methodologies needed to consider the possible impacts from multiple exposures. Scientists now have methods and models that allow us to assess multiple stressors. For example, we can now evaluate cumulative and aggregate exposures, population-focused exposures, and risks from exposure to chemical mixtures [(U.S. EPA, 2003), pages 1-4].
- A key guidance document is EPA's (2003) Framework for Cumulative Risk Assessment.

Aggregate and Cumulative Exposures (Slide 8)

- Aggregate and cumulative exposures are two important concepts for exposure assessment.
  - Both exposure types consider multiple exposures, but they vary by the types of exposure and the number of chemicals that they consider.
- **Aggregate exposure** considers exposure to the same compound from many different sources.
  - This type of exposure assessment is used when there are multiple ways that a person can come into contact with a chemical.
- **Cumulative exposure** considers exposure to multiple compounds with similar mechanisms of action, through multiple exposure pathways.
- Aggregate and cumulative exposure assessments are the goal for exposure assessors, but in many instances there are not sufficient data to perform these types of assessments.

Assessing Aggregate Exposure (Slide 9)

- Aggregate exposure assessment considers combined exposures to a single chemical across multiple routes and multiple pathways.
- Aggregate exposure assessments often include a summation of all potential exposure pathways. This is a conservative, health-protective assumption, because it is unlikely that a single person will be exposed to the chemical through all possible exposure pathways (U.S. EPA, 2002).
- This approach is commonly used in the regulation of pesticides.
  - People can be exposed to pesticide residues in various ways. For example, residues of the same pesticide could be found on multiple foods, in water, and/or in products used in and around the home.
- EPA conducts risk assessments for active ingredients in pesticides by evaluating all of the potential pathways of exposure for pesticide residues to determine the potential risk from

aggregate exposure. The relevant pathways of exposure are dependent on the type of pesticide and its registered uses.

Assessing Cumulative Exposure (Slide 10)

- Cumulative exposure assessment is the evaluation of multiple stressors. In this process, the aim is to assess the cumulative, overall impact on human health of multiple chemicals that act by a common mechanism of toxicity. It is important to remember that the presence of multiple stressors does not necessarily mean that the stressor will cause or contribute to an adverse effect.
- Cumulative exposure assessment considers multiple chemicals and multiple pathways of exposure, and might consider groups of the population that are disproportionately at risk from exposure.
- Cumulative exposure assessment is not necessarily the simple sum of multiple, aggregate exposure assessments. Note that "aggregate exposures" and "cumulative exposures" are sometimes confused. Aggregate exposures consider individual chemicals and multiple routes and pathways of exposure, while cumulative exposures consider multiple chemicals and multiple routes and pathways of exposure.
- A good example of EPA's use of cumulative exposure assessment methods is the assessment of pesticide active ingredients with similar mechanisms of toxicity. In pesticide risk assessment, chemicals in the same family or group (or those with the same mechanism of action) are assessed together for cumulative risk.
    - As a specific example, EPA has conducted a cumulative exposure assessment for the pyrethroid pesticides, a family of chemicals with similar modes of action. For this assessment, EPA considered acute and chronic exposure to residues of pyrethroids in food, water, and any residential exposures.
- EPA also conducts a cumulative exposure assessment when it evaluates multiple chemicals with similar mechanisms of toxicity in their residual risk assessment of air toxics.

TIERED APPROACH TO EXPOSURE ASSESSMENT (SLIDE 11)

- After defining the scope our assessment, we need to decide on our analysis approach. In this section of the course, we'll discuss the use of a tiered framework and iterative approach to conducting exposure assessments.

What is the Tiered Approach to Exposure Assessment? (Slide 12)

- The tiered approach to exposure assessment is a step-by-step, iterative process. Using this approach, risk assessors progress from relatively simple to more complex analytical processes, as required by the given situation. Individual "tiers" correspond to iteratively more complex (and typically data-intensive) steps in the assessment (U.S. EPA, 2001).
- At each stage of a tiered exposure assessment, investigators evaluate whether the assessment results are sufficient to support useful risk management decisions (U.S. EPA, 2001).

- The goal of a tiered assessment approach is to strike a balance between the costs of adding detail and refinement to an assessment and the benefits associated with the additional refinement (U.S. EPA, 2001).
    - If the screening assessment results indicate that the risks are at or below acceptable levels using the most conservative assumptions, that will likely eliminate the need for more complex analyses.
- Shown on this slide is a depiction of a tiered approach developed by EPA for the evaluation of health risks. This approach divides the process into three tiers, each more refined and complex than the previous (U.S. EPA, 2001).

Screening-Level Exposure Assessment (Slide 13)

- A screening-level exposure assessment is often the first step in the tiered approach. The assessment produces a quantitative, conservative estimate of exposure using readily available data. The estimate can be used to make comparisons between multiple sites that are being evaluated or to prioritize sites for further analysis.
- The benefit of screening-level analysis is that it is simple to perform and may help indicate that there is not a significant problem. Screening-level assessments can prevent unnecessary resources from being devoted to an area that does not pose a substantial problem.
- For example, a children's toy might contain phthalates. The concern is that the phthalates could be present in the toys at levels that are hazardous to the children using them, especially because the children put the toys in their mouths.
    - Based on conservative assumptions and the expected use patterns, risk assessors would evaluate the expected exposure and determine whether it is above or below the Reference Dose (RfD). The results of this screening level assessment allow risk assessors to determine if more sophisticated modeling is needed (U.S. EPA, 2009b).

Refining an Exposure Assessment (Slide 14)

- If we decide that a site or scenario warrants a closer look following a screening-level assessment, we can refine our assessment with more specific measurement data, better inputs, or better models.
- For example, we might use site-specific measured data for environmental concentrations or parameters or for chemical release estimates. We could also use higher-precision sampling or analysis techniques.
- We can refine our assessment inputs by using site-specific data regarding exposure inputs, like ingestion rates or the distance between the receptors and the source.
- We can use more complex models if necessary. For example, rather than using a simple box model for fate and transport, we could use a model that explicitly estimates dispersion, deposition, and other movement of a chemical within the environmental compartments.

- We don't have to make all of these refinements at once. In many cases, we can conduct a sensitivity analysis of our screening assessment to determine which parameters affect our exposure estimate the most. Then we can begin by refining these parameters to determine if there is a problem or if we should continue to refine the assessment. In general, an iterative process for refining an exposure assessment is useful and efficient.

Deterministic Exposure (or Risk) Assessment (Slide 15)

- Directly related to the level of refinement incorporated into an assessment is whether the results of the assessment are a point estimate or a distribution of possible values.
- **Deterministic** exposure assessments use **point estimates** (or, single values) to quantify the amount of exposure that is likely to occur for all individuals.
- Using point estimates as inputs produces an exposure estimate that is also a point estimate. Carefully selected input values can provide assessors with meaningful estimates of central tendency or high end exposures within a defined population. We can assume that the results of a deterministic assessment fall somewhere in the distribution of possible exposure values.
- Deterministic approaches are used in screening-level assessments partly because of the economical and straightforward nature of the approach.
- Characterization of uncertainty and variability is limited when using deterministic approaches, but can be increased with multiple deterministic runs. In this way, we can usually identify those parameters or aspects of a deterministic evaluation that are uncertain or variable.
- This gives us an idea of uncertainty and/or variability by estimating several point estimates, using inputs from various points on the frequency distribution.

Probabilistic Exposure Assessment (Slide 16)

- **Probabilistic** exposure assessment approaches are another option for characterizing exposure. These approaches use distributions of data (either probability or frequency distributions) for various parameters to generate a distribution of possible exposure estimates as opposed to a single value.
- Probability distributions describe the range of values that certain variables may take, and estimate the relative likelihood (probability) that any of those values might occur in the given population (U.S. EPA, 2001). So the **probability distribution** helps to account for variability within the population.
- Guidance on developing and conducting probabilistic assessments is available in EPA's Risk Assessment Guidance for Superfund (RAGS) (1991) and also in EPA's Air Toxics Risk Assessment (ATRA) guidance (2004).
- Major issues with use of probabilistic approaches are the availability of confirmed distributions and properly accounting for interrelationships between variables.
- The most popular (but not the only) approach to estimating exposure with probability distributions is the **Monte Carlo simulation**.

- A Monte Carlo simulation, named after the casino in Monaco, is used in risk assessment to generate the probability distribution of exposure levels or risk values using specified variables.

What is a Monte Carlo Simulation? (Slide 17)

- In the case of exposure assessment, a Monte Carlo simulation could be used when data on the distribution of exposures in a population are not available, but data are available on the various parameters used to calculate the exposure or dose. These parameters might include daily intake of water or food, age distributions of the population, or other specified variables.
- Specifically, a Monte Carlo Simulation is:
  - "A technique for characterizing the uncertainty and variability in risk estimates by repeatedly sampling the probability distributions of the risk equation inputs and using these inputs to calculate a range of risk values" (U.S. EPA, 2001).
- Monte Carlo simulations and other probabilistic approaches can provide estimates of exposure, but doing a probabilistic assessment using Monte Carlo techniques may not be necessary in situations where risk or costs of remediation are low.

Monte Carlo and Probabilistic Methods (Slide 18)

- These methods might require more resources than using a deterministic approach since we have to find distributions for input parameters and possibly use more sophisticated modeling to sample from the distributions to estimate exposure, but Monte Carlo simulations and other probabilistic methods do allow us to estimate variability in exposure better.
- It's important to remember that probabilistic simulations are not always necessary. If we can answer our exposure question deterministically, spending time and money to do a probabilistic simulation might not make sense. And just like exposure assessment in general, a probabilistic simulation can be iterative. We can start by investigating a few parameters for which we already have distributions or those parameters that have a big impact on exposure. Then, depending on what we find, we might expand the simulation to other parameters.

"Garbage In, Garbage Out" (Slide 19)

- When using a Monte Carlo simulation or other probabilistic methods, it is important to remember that the model outputs can only be as accurate or representative as the data that were used to build the model. If low quality data are used to construct the Monte Carlo simulation, then the output of the model might be useless.
- Monte Carlo simulations are valuable tools that can produce complex and detailed distributions of results, but it is important to be aware that a complex probabilistic model simulation can be constructed from low quality data and assumptions and this will produce low quality results.
- A common pitfall is to confuse the seemingly robust, probabilistic Monte Carlo simulation with an accurate representation of the situation.

EXPOSURE DESCRIPTORS (SLIDE 20)

- Another consideration in selecting your approach to quantifying exposure is picking exposure descriptors.

Use of Exposure Descriptors (Slide 21)

- **Exposure descriptors** are estimates for a specific point on the exposure distribution.
- They are based on selected parameter values and can be defined for individual or population exposures. Exposure descriptors are useful when characterizing exposure, and can help exposure assessors communicate with risk managers.
- We'll talk about three exposure descriptors –bounding estimates, high-end estimates, and estimates of central tendency.

Bounding Estimates (Slide 22)

- A **bounding estimate** captures the highest possible exposure, or theoretical upper bound, for a given exposure pathway. We often use bounding estimates to complete screening-level assessments.
- To calculate an upper bound, we would use the highest intake rates, average body weight, and we might assume the highest possible exposure frequency and duration.
- Each of these values for the input parameters are individually higher than those that probably occur in the actual population and the combination of all of these assumptions is very unlikely to occur. However, if the value of an exposure pathway does not contribute significantly to total exposure when we calculate the bounding estimate, then we probably can eliminate that pathway.

High-End Estimates (Slide 23)

- High-end parameter inputs can be used to estimate exposure, dose, or risk for individuals at or above the 90th percentile of the population distribution. EPA defines high-end estimates as:
  - "An estimate of exposure, or dose level received [by] anyone in a defined population that is greater than the 90^{th} percentile of all individuals in that population, but less than the exposure at the highest percentile in that population."
- High-end estimates are expected to be more realistic, or more likely to occur, than the upper bound and are usually calculated using a combination of high and central inputs. Whatever inputs are chosen it is important to document the assumptions and the justification for those assumptions.
- Terminology for high-end estimates varies depending on the program using them. Two such definitions have been used by the Superfund program and in the Guidelines for Exposure Assessment, respectively.

- Superfund remedy decisions are often based on what is called the Reasonable Maximum Exposure (RME) level. The RME is the highest exposure reasonably likely to occur, generally assumed to be in the range of the 90th and 99.9th percentiles (U.S. EPA, 2001).
- The 1992 Guidelines for Exposure Assessment define the term "reasonable worst-case exposure" as the lower part of the high-end exposure range, which is above the 90th percentile, but below the 98th percentile. The range above the 98th percentile is termed the "maximum exposure" range (U.S. EPA, 1992).

- As the exposure estimate moves higher within the percentile range, the level of uncertainty increases.

Central Tendency Estimates (Slide 24)

- The **Central Tendency Estimate** represents the average or typical individual in a population, usually the mean or median of the population distribution. Central tendency estimates or CTEs, may under- or over- estimate exposure in some cases (U.S. EPA, 1992).
  - The **arithmetic mean** uses average values for all of the factors that comprise the exposure of interest. This value may not necessarily be representative of a single receptor or group, but falls within the actual distribution and is useful for characterizing the average population exposure. This value is sometimes called the "average estimate," but terminology varies from assessment to assessment.
  - The **median** is another useful descriptor of central tendency, especially when data on the receptor or exposure of interest are skewed as they are in a log normal distribution. This is often called the "**typical case**," but, the terminology can vary.
  - If both the **arithmetic mean** and **median** exposure estimates are available, but vary substantially from each other, it is useful to provide both values to risk assessors, to provide greater context about the exposure scenario [(U.S. EPA, 1992); pages 85-86].

THREE APPROACHES FOR QUANTIFYING EXPOSURE (SLIDE 25)

- We have finished discussing problem formulation and the planning and scoping step of an exposure assessment and we've also reviewed some useful exposure descriptors. Now let's discuss three approaches for quantifying exposure.

Approaches to Quantifying Exposure (Slide 26)

- The Exposure Assessment Guidelines (1992) describe three approaches for quantifying exposure during the analysis phase of an exposure assessment. They are shown in the center rectangle in this diagram:
  - Measurement of exposure at the **point of contact**
  - Estimation of exposure from **scenario evaluation**
  - Estimation of exposure by **reconstruction of internal dose**
- Each of these approaches can be used independently and each uses different sources of information to aid in quantifying exposure. However, the approaches can also complement each other, and each of them attempt to estimate exactly what the individuals were exposed to, for how long and, in some cases, the path the substances traveled through the body.

- You might also think about quantifying exposure in terms of **direct** or **indirect** measures.
  - **Direct measures** involve sampling or monitoring while **indirect measures** use methods like models and questionnaires to estimate exposure. The three methods of analysis or quantification that we are going to discuss describe how data are used to estimate exposure and dose [(U.S. EPA, 1992); page 19].

POINT OF CONTACT FOR EXPOSURE ASSESSMENT (SLIDE 27)

- Let's begin our discussion with point of contact approaches.

Point of Contact Exposure Measurement (Slide 28)

- For a **point of contact** exposure assessment, chemical concentrations are measured at the interface between the person and the environment, usually through the use of personal monitors.
- Point of contact exposure assessment was initially developed primarily for use in occupational monitoring.
  - More recently, monitors have been developed to measure chemical concentrations that the individuals are exposed to in the given media by sampling the individual's breathing zone, food, or water.
- A common example of a point of contact exposure assessment is the radiation dosimeter worn by people that work around radiation. Some examples of dosimeters are shown on this slide.
  - Workers in nuclear power plants or in hospital departments where radiation is used are usually required to wear dosimeters as part of a monitoring plan and to comply with OSHA requirements.

Where Does Point of Contact Fit? (Slide 29)

- In the continuum between source and effect, the point of contact approach measures exposure right at the nexus of the stressor and receptor domains.
- In other words, it's the point at which the chemical makes contact with the person or organism.
- Let's talk about some of the strengths and weaknesses of this approach.

Point of Contact Strengths and Weaknesses (Slide 30)

- Using point of contact results, we can measure exposures directly rather than inferring from measurements or model results.
- Point of contact methods, by their nature, are very representative of individual exposures, as compared to exposure models or population-level assumptions.
- If the measurement devices used to evaluate exposure are accurate, this approach obtains the most accurate estimate of exposure for an individual over a given time period.

- Unfortunately personal exposure monitors and the instruments used to evaluate them can be very expensive, to the point that they may be too costly for some studies.
  - This is not necessarily the case for radiation dosimeters, which are quite common in healthcare and other radiological exposure settings, and are relatively inexpensive.
- Also, point of contact methods are not always source-specific, although they are route-specific. That is, multiple sources could contribute to the exposure that a person records through their sampling device, so it is not usually possible to determine the source of the chemical.
- Devices are available for many substances, but not for all chemicals.
- The point of contact method relies on the accuracy of the mechanical device and the analytical methods used to evaluate the results and the participation of individuals in the study.
- Let's talk about the use of the point of contact approach in dermal exposure assessment.

Direct Measurements of Dermal Exposure (Slide 31)

- There are a number of methods that can be used to measure exposure to contaminants on the skin. They range from simple and inexpensive to complex, costly samplers.
- **Patches** were first used approximately 30 years ago to investigate exposure to organophosphate pesticides (Durham and Wolfe, 1962). These Band-Aid or sticker like patches are placed on the body to collect the contaminant of concern and have been used for a variety of substances, including PAHs, copper oxide, and dusts (Soutar, 2000).
- **Whole-body dosimeters** are intended to measure exposure to the whole body. They can range from badges worn on the clothing, to a coverall suit, to full-length cotton underwear (FIFRA SAP, 2007).
- **Removal methods** include rinsing, wiping, and tape stripping to collect the contaminants of concern from the skin to be analyzed.
- Fluorescent tracers are an example of **optical methods.** This involves treating the contaminant of concern with a nontoxic fluorescent tracer and then using video imaging to identify and quantify the points where the contaminant contacts the skin.
- For example, portable x-ray fluorescence analyzers have been used to detect bromine concentrations resulting from PBDE compounds emitted by consumer products from the homes of a cohort in the Great Lakes area (Imm et al., 2009). This method has been used as an improvement on existing methods and a way to more accurately characterize human exposure to PBDEs from household products.

Direct Measurements of Oral Exposure Concentrations (Slide 32)

- Duplicate diet studies are a way to measure concentrations of a chemical of concern in the diet. In these studies, individuals collect duplicate samples of all the foods they consume during a given period.
- The duplicate samples are evaluated by investigators to determine the concentration of chemicals of concern in the diet and the intake rates of those chemicals.

- Duplicate diet studies can provide direct measurements of chemical contaminants in food, as well as the intake rate of various foods, typically normalized to the body weight of each participant. These studies can also help characterize the total amount of the chemical of concern in different food types.

An EPA Point of Contact Assessment (Slide 33)

- The National Human Exposure Assessment Survey (NHEXAS) involved 550 people from several different states. The surveys were conducted between 1995 and 1997, and the results were published in 1999 (Clayton et al., 1999).
- The study was developed by EPA ORD to provide multipathway and multimedia exposure distributions for specific chemical classes. The study was piloted as a conceptual design for exposure assessment, with the goal of using similar methods on a larger scale in the future.
    - The aim of NHEXAS was to test the hypothesis that existing data and modeling estimates do not differ from the measurement-based exposure distributions found in the study.
- The NHEXAS study evaluated exposure to three groups of chemicals: VOCs (including TCE, benzene, PERC), metals (including lead, arsenic, and cadmium), and pesticides (including atrazine, chlorpyrifos, diazinon, malathion).

NHEXAS Results (Slide 34)

- In one of the many reports generated from the NHEXAS studies, Clayton and colleagues (1999) reported results of data collected in EPA Region 5, which includes states from the Great Lakes region.
    - The researchers found that solid food was a major source of arsenic detected in urine, while household lead levels from dust, air and beverages were all significantly associated with measured blood lead levels.
    - High correlations between tap water and biomonitors for lead and arsenic were observed. Moderate correlations were observed for VOCs and personal air sampling.

SCENARIO EVALUATION FOR EXPOSURE ASSESSMENT (SLIDE 35)

- Let's talk next about the scenario evaluation approach.

Scenario Evaluation for Exposure Assessment (Slide 36)

- The **scenario evaluation** approach estimates exposure indirectly by measuring, modeling, or using existing data on concentrations in the media, the time of contact, and information about the exposed populations. This information is combined to achieve an estimate of exposure.
- EPA defines an exposure scenario as, "A set of facts, assumptions, and inferences about how exposure takes place that aids the exposure assessor in evaluating, estimating, or quantifying exposure."
    - An exposure scenario is characterized by the elements that determine the exposures, including the setting, chemical characteristics and sources, the exposure pathways and

routes, the exposure media, intake and uptake rates, and characteristics of the exposed population.

- This approach is commonly used in exposure assessment at EPA, especially for characterizing situations that might not have taken place yet. We will discuss exposure scenarios in detail in EXA 403, so we will highlight only a few important points here.

Where Does Scenario Evaluation Fit? (Slide 37)

- The **scenario evaluation** approach encompasses the stressor domain of the source to effect continuum, from the source to the exposure nexus on the left side of this figure.
- The approach fills in the details in order to estimate exposure; you can think of it as a bottom-up approach.
- Data for stressor concentrations are collected from sampling or obtained from fate and transport models for stressor concentrations.
- Population characteristics are obtained from averages/assumptions or from interviews with people in the exposed population.
- Time of contact can be researched or estimated based on what is known about the exposure scenario.

Scenario Evaluation Strengths and Weaknesses (Slide 38)

- **Scenario evaluation** is typically the least expensive of the three exposure assessment methods, as it often relies on available data and involves limited equipment and time.
- Scenario evaluation is well-suited to evaluation of the risk consequences from proposed actions. It can also be performed with limited data on the actual exposure situation.
- However, the simplification of an exposure scenario using readily available data, that are sometimes limited in their scope, may lead to a less accurate assessment causing over- or under-estimation.
    - The limited data that are needed to conduct scenario evaluation can result in an estimate with a greater degree of uncertainty.

Implementing Scenario Evaluation (Slide 39)

- The data used in scenario evaluation are assumed to be representative of the exposed population. This may be true in varying degrees, depending on the data type and source, as well as the situation.
- It is also assumed that data on chemical fate and transport used in the assessment correspond with the actual fate and transport processes that are occurring.
    - For example, we could use a scenario evaluation approach to assess exposure to arsenic, mercury, and other metals from a battery recycling plant. Some things to think about: What assumptions need to be made? What are the exposures of concern? Who is the population at risk? How can we evaluate the exposure?
- Data that may be required include:

- Characterization of source strength (soil levels at the facility, emission rates from stacks, etc);
- Chemical concentrations in environmental media from sampling near the plant;
- Fate and transport data for the specific chemicals;
- Population statistics for the employees at the plant and the people who live nearby (including sensitive populations); and
- Time of contact and routes of exposure for each chemical and receptor.

Types of Models Used (Slide 40)

- If we don't have measured concentrations or other exposure data, we will need to use an alternate method to evaluate a scenario. In these cases, a model or a combination of models can be used to estimate the concentrations of a chemical in different environmental media as it moves from the source to the receptor.
- **Fate and transport models** like AERMOD and CMAQ estimate chemical concentrations in air.
  - EXAMS models chemical concentrations in surface water.
- **Exposure models** estimate exposures or doses based on chemical concentration inputs, exposure factors (such as ingestion rates), and, in some cases, time-activity patterns.
  - Time-activity patterns record the activities and locations of individuals through the course of a specific time period.
  - CHAD, EPA's Consolidated Human Activity Database, is perhaps the most familiar EPA resource for time-activity pattern data.
- Some models exist that **combine** fate and transport modeling with human exposure modeling to estimate the entire source to receptor continuum.
  - A couple of examples of combined models include the SHEDS and LifeLine™ models
- A helpful resource on exposure models is the paper by Williams et al. (2010), "An Overview of Exposure Assessment Models Used by the U.S. EPA."
  - This paper discusses many of the fate and transport models, exposure models, and integrated models currently in use. The following slides provide an overview of a few of the models discussed by Williams et al. (2010).

Fate and Transport Models (Slide 41)

- Fate and transport models simulate the movement of and changes affecting contaminants in the environment to predict concentrations of the pollutant in sediment, surface water bodies, ambient groundwater, or drinking water. Many types of models are used, and they differ in regard to the pollutants, receptors, and spatial and temporal scales they estimate.
- Let's talk about a couple of fate and transport models used by EPA.
  - **AERMOD** (AMS/EPA Regulatory Model) is an air dispersion model that simulates the fate of airborne pollutants based on local emission sources. This model may also be used to estimate airborne concentrations at different locations.
  - The **EXAMS** (Exposure Analysis Modeling System) model is a screening-level model that provides estimates of pesticide concentrations in water for use in drinking water or

other aquatic exposure assessments. The model accounts for chemical-specific characteristics, and can include site-specific information regarding pesticide application methods as well as the impact of daily weather patterns on treated fields over time.

Exposure Models (Slide 42)

- Now let's look at exposure models. Exposure models are used to predict exposures to individuals or populations through inhalation or multimedia exposure. The model results are based on environmental concentrations, population characteristics, exposure factors, and human activity patterns.
- As with fate and transport models, the inputs and outputs vary depending on the pollutants, receptors, and spatial and temporal scales used.
  - **APEX**, the **Air Pollutants Exposure Model**, estimates population-level exposures and doses to air pollutants for the general population and sensitive groups at local, urban, and metropolitan scales.
  - Another exposure model is **Dietary Exposure Evaluation Model**, or **DEEM™**. This model estimates individual or population-level dietary exposures and doses to pesticide residues in residential settings.

SHEDS: A Multimedia, Multipathway Exposure Model (Slide 43)

- Let's talk about a couple of integrated models used by EPA to estimate exposure for a scenario evaluation approach – the **SHEDS model** and **LifeLine™ model**.
- The **Stochastic Human Exposure and Dose Simulation** (**SHEDS**) Model was developed by U.S. EPA's Office of Research and Development (ORD), National Exposure Research Laboratory (NERL) in consultation with EPA's Office of Pesticide Programs (OPP).
- SHEDS is a state-of-the-art tool that provides a modeling framework for improving estimates of human exposure to environmental contaminants via multimedia and multipathway exposure.
- SHEDS is a physically-based, probabilistic model that simulates aggregate or cumulative exposures over time. SHEDS can then be used to estimate dietary and residential exposures based on different types of data and modeling.
- The model can help to describe or assess multiple exposure-related issues and questions. These include:
  - What is the population distribution of exposure, in light of variability and uncertainty?
  - What is the intensity, frequency, duration, and route of exposure?
  - How do modeled exposures compare with measured data?
  - How can we assess risk-based uncertainties?
  - Which factors, pathways or media can be targeted with the goal of reducing exposure?

SHEDS Model: What it Incorporates (Slide 44)

- The SHEDS model uses multiple inputs and data sources to estimate exposure.

- The inputs include: population characteristics, dietary exposure data, chemical fate and transport data, and data on chemical usage in the home.
- Population characteristics are estimated from U.S. Census and NHANES data.
- Sources for dietary exposure data include CHAD, NHANES, the Continuing Survey of Food Intake by Individuals, and others.
- Chemical fate and transport is estimated using a fugacity model and EPI suite.
- Home chemical usage comes from a database and ERDEM and other models are used to estimate exposure and dose.

The LifeLine™ Model (Slide 45)

- **LifeLine**™ is a probabilistic model for assessing aggregate and cumulative exposures and risks from pesticides and other chemicals. It was developed by a non-profit organization called the LifeLine Group. The model simulates longitudinal, aggregate exposure to pesticides for each member of a simulated population. LifeLine™ then uses the simulated individuals to create a model population for which exposures are simulated.
- The model simulates inter-individual differences in exposure-related behaviors within the model populations. This assigns all of the individual's characteristics in an internally consistent way and in such a way that it reflects the population of interest. LifeLine™ also simulates each individual's behavior over time.
- The LifeLine™ model can consider exposures to chemicals from many different sources, including: diet, home environments and products, drinking and tap water, consumer products, and pesticide use.
- The routes of exposure considered in the modeling software are inhalation, dermal, dietary, and oral exposures to children from mouthing behaviors. The model parameters can be adjusted to represent a wide range of dietary and behavior specifications.
  - The LifeLine™ model has been used to estimate exposures of interest for indigenous and other targeted populations.
- Source: (U.S. EPA, 2009a)

Combined Models (Slide 46)

- The SHEDS and LifeLine Models are just two of many combined models used for multimedia and multi-pathway exposure modeling.
- A number of popular models, including some of the most used combined models, are discussed by Williams et al. (2010). A selected few are E-FAST, TRIM, and 3MRA.
  - **E-FAST**, the Exposure and Fate Screening Tool, is supported by the EPA's Office of Pollution Prevention and Toxics. The E-FAST model provides screening-level estimates of the concentrations of chemicals released to air, surface water, landfills, and from consumer products. As of 2010, version 2.0 of EFAST was available from EPA.
  - **TRIM**, the Total Risk Integrated Methodology, is one of the models that Williams et al. (2010) posited as potentially representing the "next generation" (along with 3MRA) of highly-integrated, multimedia models. The TRIM framework was developed by the U.S. EPA Office of Air Quality Planning and Standards to support agency activities such as

the Integrated Air Toxics Strategy and the Residual Risk Program. TRIM can be used to estimate environmental media concentrations, fate and transport, and population-level exposures and doses for both ecological and human receptors.
    - **3MRA**, the Multimedia, Multipathway, and Multireceptor Risk Assessment, was developed by the U.S. EPA Office of Research and Development to support the Office of Solid Waste's Hazardous Waste Identification Rule efforts. The model is used to conduct screening-level risk-based assessment of potential human and ecological health risks resulting from long term exposure to specific stressors.
- Many of the existing exposure models are used primarily for research purposes. To date, there have been limited successful applications of the models for exposure assessment purposes.
- That said, one practical application of the SHEDS model was in the risk assessment of children's contact with chromated copper arsenate (CCA)-treated wood in playsets. The model results were found to compare well with the results from other CCA exposure assessments, and the results were implemented in the risk assessment of CCA conducted by the EPA's Office of Pesticide Programs.

DOSE RECONSTRUCTION FOR EXPOSURE ASSESSMENT (SLIDE 47)

- Finally, let's talk about the third approach for estimating exposures: dose reconstruction.

Dose Reconstruction for Exposure Assessment (Slide 48)

- Doses to a specific receptor population are usually not available, but dose can be reconstructed using internal indicators of exposure, called **biomarkers**.
    - A **body burden** concentration of a chemical is an example of a biomarker. The body burden simply represents the amount of chemical present in the body. Biomarkers are important indicators of exposure and provide useful information about linking exposure to potential health impacts.
- Body burden information can be used to calculate dose in a biological model called a **pharmacokinetic model**.
    - Pharmacokinetic models combine data from physiological and metabolic processes with the body burden data to estimate dose.
- This reconstruction of the exposure from internal indicator to dose occurs after the exposure has taken place.
- **NHANES** includes a nationwide biomonitoring study that yields biomarkers of exposure for many different stressors. Data are stratified by age, race, sex, and other factors.

Where Does Dose Reconstruction Fit? (Slide 49)

- Dose reconstruction allows us to estimate exposure based on information from an effect or outcome, or a target dose.

Biomarkers for Dose Reconstruction: Strengths and Weaknesses (Slide 50)

- Biomarkers can provide proof of exposure to a compound or its metabolites.
- In addition, biomarkers provide valuable information about past exposures and potential health impacts that may result from those exposures.
- With an appropriate model, dose reconstruction has the potential to give the most accurate estimate of total exposure of the three methods discussed.
- Dose reconstruction does not tell us about the exposure pathway involved; biomarkers are not source-specific.
- Biomarkers are not always directly related to source chemicals because multiple chemicals may have the same biomarkers.
    - Once again, biomarkers are a chemical found in the body that may indicate exposure to a specific compound. The body burden is simply the amount of one or more biomarkers that may have resulted from a given exposure.
- Models are not always available that link dose with exposure for the stressor of concern. When models are available, we have to accurately parameterize them based on measured or experimental data.
- Biomarkers may indicate exposure to metabolites rather than the parent compound.
- Sampling for biomarkers may not always be possible, and databases with biomonitoring data might have to be used. Finally, due to the costs of sampling and evaluation, this method may be expensive.

Dose Reconstruction Example (Slide 51)

- Here's an example of a successful dose reconstruction study. Data were available from NHANES on urinary concentrations of cadmium for males and females over 6 years of age. Researchers at ATSDR, the CDC, and the University of Georgia recoded the parameters of an existing PBPK model for cadmium to estimate the dietary intake rates corresponding to the urinary concentrations of cadmium in the NHANES data.
- The researchers used age-specific data on dietary cadmium intake to model urinary cadmium levels for individuals in five separate age groups. To verify their methods, the researchers compared observed urinary cadmium levels from NHANES to those estimated with the model and found that the model results agreed well with the NHANES data.
- Tables 2 and 3 in the slide show a generally close comparison between the model and NHANES data. However, the model over-predicted values for non-smoking females and under-predicted values for adults over 60 years of age. The researchers noted that reasons for differences from measured levels might include lifestyle factors, age-related changes in kidney function, and the levels of essential nutrient intakes (Ruiz et al., 2010).

CONCLUSION (SLIDE 52)

Conclusions (Slide 53)

- Methods for quantifying exposure allow assessors to evaluate exposures to environmental stressors and their potential impacts on receptor populations.
- The ability to quantify exposure for a given scenario depends on many factors, including the availability of data, resources for monitoring, the exposure scenario of concern, identified stressors, and the receptors of interest.
- Tiered approaches help to guide and refine exposure assessments and identify priority approaches, helping assessors choose the methods appropriate for the assessment.
    - Tiered and screening approaches help determine if a deterministic or probabilistic assessment is needed.
- Exposure quantification approaches all have their strengths and weaknesses, and one - or multiple - approaches might be best for a given scenario.

Exposure Quantification Approaches at a Glance (Slide 54)

- This slide provides a summary of the three approaches to quantifying exposure. There are advantages and disadvantages to each approach, and each approach provides different types of information. In addition, there are different applications for each of the approaches, which are presented in the third column.
- This slide is provided in your reading packet.

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