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# Guidelines for Human Exposure Assessment

Risk Assessment Forum

EPA/100/B-19/001
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**Risk Assessment Forum**
**U.S. Environmental Protection Agency**

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# TABLE OF CONTENTS

# LIST OF TABLES

# LIST OF FIGURES

# LIST OF BOXES

# ABBREVIATIONS AND ACRONYMS

| | |
|---|---|
| ADME | absorption, distribution, metabolism and elimination |
| CDC | Centers for Disease Control and Prevention |
| DQO | data quality objective |
| EPA | U.S. Environmental Protection Agency |
| EPC | exposure point concentration |
| FOIA | Freedom of Information Act |
| GIS | geographic information system |
| HSRRO | Human Subjects Research Review Official |
| IRB | Institutional Review Board |
| NHANES | National Health and Nutrition Examination Survey |
| NRC | National Research Council |
| OMB | Office of Management and Budget |
| OPP | Office of Pesticide Programs |
| OPPT | Office of Pollution Prevention and Toxics |
| PBPK | physiologically based pharmacokinetic |
| PK | pharmacokinetic |
| PM | particulate matter |
| QA | quality assurance |
| QC | quality control |
| SHEDS | Stochastic Human Exposure and Dose Simulation model |
| SHEDS-HT | Stochastic Human Exposure and Dose Simulation-High Throughput model |
| SOP | standard operating procedure |

# PREFACE

This document builds on and supersedes the U.S. Environmental Protection Agency's (hereafter "EPA" or "the Agency") 1992 *Guidelines for Exposure Assessment* (U.S. EPA 1992c) to incorporate advances in exposure assessment reflecting the best science currently conducted across the Agency in all offices, programs and regions (hereafter "programs"). EPA's Risk Assessment Forum obtained broad participation in its efforts to revise the 1992 document. The Risk Assessment Forum convened a colloquium of EPA exposure assessment scientists in 2005 to assess the state-of-the-science, discuss Agency practice and identify emerging issues. This colloquium was followed by meetings with scientists from EPA, state agencies and the broader scientific community (Bangs 2005a; Bangs 2005b; Dellarco and Bangs 2006), at which the intention to revise the *Guidelines for Exposure Assessment* was announced and developments in the field since 1992 were reviewed. In 2006, the Agency consulted with the Science Advisory Board, describing its approach to the revision and summarizing comments received from Agency scientists, the scientific community and the public. This revised document, *Guidelines for Human Exposure Assessment*, benefits from many additional years of experience with exposure assessments across the Agency, conversations with the broader scientific community and products from the Science Advisory Board and the National Research Council of the National Academy of Sciences.

This *Guidelines for Human Exposure Assessment* is designed to aid exposure scientists in preparing exposure assessments, analyzing status and trends, developing mitigation strategies, making regulatory decisions and conducting epidemiological studies. This revision focuses on human exposure to chemical agents and presents the general principles of exposure science (including assessment and monitoring). It is not a detailed instructional manual. In addition, the focus of the work is on exposure assessment as currently practiced by programs at EPA. This document does not include an exhaustive description of emerging topics such as high-throughput exposure assessment or the implications of *in vitr*o-based risk assessments on the field of exposure assessment. Aspects of these programs published in the peer-reviewed literature, however, are included. As emerging topics mature, EPA might update or supplement this document. This *Guidelines for Human Exposure Assessment* is intended principally for exposure and risk assessors in the Agency and consultants, contractors or others who perform this type of work under Agency contract or sponsorship. It also serves as a resource for others as to how EPA conducts exposure assessments. EPA risk managers/decision makers also need to be familiar with this document because it describes approaches, defines terminology and summarizes methods exposure and risk assessors use to support regulatory decisions.

Assessors need to consult with their programs for specific standard operating procedures or guidelines. The technical materials cited and hyperlinked throughout this document provide specific information for individual exposure assessment situations. At the time of publication, all cited materials and hyperlinks were correct and functional.

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# EXECUTIVE SUMMARY

The mission of the U.S. Environmental Protection Agency (hereafter "EPA" or "the Agency") is to protect human health and the environment. This mission is, in part, accomplished by understanding, characterizing and managing health risks associated with exposure to environmental contaminants and other agents. Exposure science characterizes, estimates and predicts exposures; it also provides information for preparing exposure assessments and for developing effective strategies to reduce exposure and manage risk.

This *Guidelines for Human Exposure Assessment* provides an updated resource on assessing human exposure for exposure and risk assessors in the Agency, and for consultants, contractors or others who perform this type of work under Agency contract or sponsorship. EPA risk managers/ decision makers need to be familiar with this document because it describes approaches, defines terminology and summarizes methods assessors use to support regulatory decisions. It also serves as a resource for others as to how EPA conducts exposure assessments. This document builds on and supersedes the 1992 *Guidelines for Exposure Assessment* (U.S. EPA 1992c), incorporates advances in the field since then, reflects current scientific practice across Agency programs and includes pertinent topics identified during public meetings and from a literature survey, including publications issued by the National Research Council of the National Academy of Sciences. It briefly describes the principles of exposure science and assessment, provides guidance on the various approaches for conducting an exposure assessment and presents references for more detailed information. It does not serve as a detailed instructional manual or supplant specific exposure guidance in use by Agency programs, nor does it endorse specific models or approaches that could have limited applicability or have become outdated. In addition, this Guidelines focuses on exposure assessment as currently practiced in EPA programs. This document does not include an exhaustive description of emerging topics, such as high-throughput exposure assessment or the implications of in vitro-based risk assessments on the field of exposure assessment. Aspects of these advances that have been published in the peer-reviewed literature, however, are included. Finally, this Guidelines provides links to exposure assessment tools and technical documents that address particular exposure assessment needs.

The focus of this *Guidelines for Human Exposure Assessment* is on human exposure to chemical agents in the non-occupational environment. The exposed populations (i.e., receptors) to which this document refers are adults and children or other vulnerable groups within the human population.

This document is organized in chapters, each of which explores a component of the exposure assessment process.

Chapter 1 introduces this *Guidelines for Human Exposure Assessment* and discusses the purpose and scope of the document.

Chapter 2 provides a general review of exposure science concepts and principles, including approaches and tools for consideration when planning and conducting exposure assessments. Topics include an overview of exposure science, the role of exposure assessment in the risk assessment process, concepts and types of exposure assessments, equations and input variables for estimating exposure, presentation of exposure assessment findings and a brief history of exposure science.

Exposure characterization is an important step in all exposure assessments, and the chapter presents guidance regarding the synthesis of exposure information.

Chapter 3 describes a process for the planning and scoping and problem formulation steps for an exposure assessment. The process builds on the Agency's *Guidance on Cumulative Risk Assessment: Part I. Planning and Scoping* (U.S. EPA 1997a), *Lessons Learned on Planning and Scoping for Environmental Risk Assessmen*t (U.S. EPA 2002g) and *Framework for Human Health Risk Assessment to Inform Decision Making* (U.S. EPA 2014f). It emphasizes the importance of establishing goals and objectives; building an interdisciplinary team; developing a conceptual model; identifying assessment options, available resources and data needs; producing an overall assessment plan; engaging and involving appropriate stakeholders; engaging and involving the community; establishing data quality objectives; and conducting peer review.

Chapter 4 discusses possible increased risk of adverse health effects from environmental contaminants for different lifestages, vulnerable groups and populations of concern because of disproportionate exposure or varied responses to exposure. Consistent with the Agency's guidance in *Framework for Cumulative Risk Assessment* (U.S. EPA 2003d), exposure assessors need to be aware of environmental justice issues, including unique population characteristics and sociodemographic factors that might increase exposure or predispose a lifestage, vulnerable group or population to greater risk. These factors can include age, sex, genetic susceptibility, cultural characteristics, behaviors, occupation, socioeconomic status, access to a healthy diet, race/ethnicity and geographic location. This chapter assembles other existing Agency guidance, along with examples of case studies, to discuss where techniques and considerations associated with lifestages, vulnerable groups and populations of concern can be applied in exposure assessments.

Chapter 5 discusses various aspects of data used for exposure assessments, including determining the data needed; whether data are currently available and their quality; and when data are not available, whether they need to be developed. Understanding data availability, applicability, characteristics, quality issues and limitations is critical to conducting a scientifically-sound exposure assessment. This chapter presents guidance on the assessment of data uncertainty and variability. It also emphasizes the importance of transparency and communication of findings to the risk manager/decision maker and stakeholders.

Chapter 6 highlights basic concepts in modeling, including the principles of the modeling process. It provides an overview of modeling for exposure assessment, outlines the criteria for choosing appropriate models based on the goals and data quality objectives and describes how to evaluate a model that might be useful for an exposure assessment. Chapter 6 includes information on modeling inventories and clearinghouses and describes resources that support the use of models of various levels of complexity, including probabilistic models.

Chapter 7 provides details on planning an observational human exposure measurement study. Various parts of the Agency use such studies to quantify people's exposures to chemicals in their everyday environments during their normal daily activities. The studies involve measurements of chemical, physical or biological agents in environmental media; collection of information about study participants and their homes, work environments and activities; and collection of personal

exposure and biological samples. This chapter discusses the aspects of planning an observational human exposure measurement study, including budget and logistical planning, establishing a study design, planning and executing a pilot study and a full field study and the importance of conducting peer review. It also addresses ethical considerations that exposure assessors need to consider when interacting with study participants and the community. *Scientific and Ethical Approaches for Observational Exposure Studies* (U.S. EPA 2008c) examines both the scientific and ethical issues associated with observational human exposure measurement studies in more detail and is an important resource in the design and implementation of this type of study.

Chapter 8 discusses the compounded effects of uncertainty and variability in exposure assessments, accounting for uncertainty and variability in planning and scoping and problem formulation (Chapter 3), and uncertainty and variability within the data used for exposure assessments (Chapter 5). Chapter 6 highlights how an assessor uses these concepts in the application of models in an exposure assessment.

Chapter 9 synthesizes the concepts presented in the previous eight chapters into a communication plan and supplements them with more specific information. Chapter 9 emphasizes the importance of identifying the intended audience, the types of communication products, communication plans that might be appropriate for different exposure assessments and related ethical considerations.

Chapter 10 provides references for all cited documents.

Assessors need to consult with their programs for specific standard operating procedures or guidelines. The technical materials cited and hyperlinked throughout this document provide specific information for individual exposure assessment situations. At the time of publication, all cited materials and hyperlinks were correct and functional. As appropriate, the Risk Assessment Forum will evaluate the need to update this document and make appropriate adjustments as the field of exposure science evolves.

# CHAPTER 1. INTRODUCTION

## 1.1. Overview

The mission of the U.S. Environmental Protection Agency (hereafter "EPA" or "the Agency") is to protect human health and the environment by understanding, characterizing and reducing health risks associated with exposure to environmental contaminants and other agents. Exposure science characterizes and predicts the intersection of an agent and receptor in space and time. It provides information to develop exposure assessments and the most effective strategies to reduce human health risk through mitigating exposure. The Agency needs to understand whether the agent could cause an adverse health effect, the level at which the effect might be observed, the likelihood of the effect's occurring and, if necessary, how exposure to the agent could be reduced. The increasing number and complexity of risk assessments the Agency conducts, and the attendant risk management decisions, present new challenges. Advances in exposure science require EPA to consider the best available science for conducting exposure assessments.

## 1.2. Purpose and Scope of the Guidelines

This document builds on and supersedes the *Guidelines for Exposure Assessment* (U.S. EPA 1992c). It incorporates EPA science policy, analytical methods, risk assessment guidance, methods and data developed since publication of the 1992 document, including:

- *New Policy on Evaluating Risk to Children* (1995b) and the 2013 reaffirmation of that policy (2013b)
- *Policy for Use of Probabilistic Analysis in Risk Assessment* (Hansen 1997a) and *Guiding Principles for Monte Carlo Analysis* (1997b)
- *Guidance on Cumulative Risk Assessment, Part 1. Planning and Scoping* (1997a)
- *General Principles for Performing Aggregate Exposure and Risk Assessments* (2001f)
- *Exploration of Perinatal Pharmacokinetic Issues* (2001e)
- *Example Exposure Scenarios* (2003c)
- *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (2005c)
- *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (2005h)
- *A Framework for Assessing Health Risk of Environmental Exposures to Children* (2006d)
- *Concepts, Methods and Data Sources for Cumulative Health Risk Assessment of Multiple Chemicals, Exposures, and Effects: A Resource Document* (2007c)
- *Scientific and Ethical Approaches for Observational Exposure Studies* (2008c)
- *Exposure Factors Handbook: 2011 Edition* (2011d) and *Highlights of the Exposure Factors Handbook* (2011e)
- *Recommended Use of Body Weight 3/4 as the Default Method in Derivation of the Oral Reference Dose* (2011h)
- *Benchmark Dose Technical Guidance* (2012b)
- *Microbial Risk Assessment Guideline: Pathogenic Microorganisms with Focus on Food and Water* (2012e)

- *Framework for Human Health Risk Assessment to Inform Decision Making* (2014f)
- *Peer Review Handbook, 4th Edition* (2015c)
- *Superfund Community Involvement Handbook* (2016e).

This Guidelines describes the principles of exposure science and exposure assessment, offers guidance to the reader on various approaches for use in conducting an exposure assessment and provides references for more detailed information, including exposure assessment tools and technical documents that address particular exposure assessment needs.

This *Guidelines for Human Exposure Assessment* does not serve as a detailed instructional guide or supplant specific exposure guidance in use by Agency programs, nor does it emphasize specific models or approaches that might have limited applicability or have become outdated. Its focus is on current practices in EPA programs. This document does not include an exhaustive description of emerging topics such as high-throughput exposure assessment or the implications of in vitro-based risk assessments on the field of exposure assessment. Aspects of these programs published in the peer-reviewed literature, however, are included. As emerging topics mature, EPA might consider updating this document. Agency exposure and risk assessors are encouraged to consult with their programs to obtain specific procedures and guidelines.

This *Guidelines for Human Exposure Assessment* focuses on human exposure to chemical agents under non-occupational scenarios.[1] Exposure assessments for physical and biological agents (e.g., noise, radiation, microbial hazards, nanomaterials) are beyond the scope of this document because of their unique characteristics. This document also does not address impacts of social stressors on the biological response to chemical agents.

This document focuses on the data and information used in exposure assessments conducted across the Agency. The type and purpose of an exposure assessment determine the data and information requirements. Screening-level exposure assessments require few resources and often use available data, whereas complex exposure assessments address the most demanding exposure questions and can include observational human exposure measurement studies.

Many other resources are available from the Agency and external sources for use with this *Guidelines for Human Exposure Assessment*. This document references sources with proven principles and approaches EPA uses.

## 1.3. Organization of Guidelines for Human Exposure Assessment

The order in which the contents of this document are presented is the same as the order of the steps that assessors commonly take in preparing exposure assessments:

- Chapter 2 – an overview of the basic concepts and principles of exposure science
- Chapter 3 – planning and scoping and problem formulation for exposure assessments

[1]We use the term "agent" throughout this document to indicate any entity that an exposure assessor might measure or analyze. An agent might or might not pose a risk at "environmental" levels. Chapter 2 uses the term "stressor" in place of "agent" for consistency with National Research Council documents.

- Chapter 4 – lifestages, vulnerable groups and populations of concern in exposure assessments
- Chapter 5 – collection and use of data for exposure assessment
- Chapter 6 – modeling for exposure assessment
- Chapter 7 – planning for an observational human exposure measurement study
- Chapter 8 – information on evaluating uncertainty and variability in exposure assessment
- Chapter 9 – the presentation and communication of results of exposure assessments
- Chapter 10 – full references for all cited documents.

Chapters 1 through 9 each conclude with a summary.

## 1.4. Summary

This *Guidelines for Human Exposure Assessment* incorporates EPA science policy, analytical methods, risk assessment guidance and methods and data developed since publication of the 1992 *Guidelines for Exposure Assessment*. Describing the fundamental principles of exposure science and exposure assessment, it presents information for taking various approaches to exposure assessment, supplemented by detailed information published in the literature.

# CHAPTER 2. PRINCIPLES OF EXPOSURE SCIENCE AND EXPOSURE ASSESSMENT

This chapter provides an overview of exposure science and exposure assessment principles and practices. It covers:

- Concepts and definitions for exposure science (Sections 2.1 and 2.2)
- Concepts for exposure assessment (Section 2.3)
- Equations and input variables for estimating exposure (Section 2.4)
- Development of exposure science and exposure assessments (Section 2.5)
- Emerging topics (Section 2.6).

Chapter 2 introduces key concepts discussed in detail in subsequent chapters. It is not intended as guidance for conducting exposure assessments but rather provides a review of the principles, approaches and tools that might be considered when planning and engaging in exposure studies and assessments. Supporting documents and resources are cited throughout the chapter.

Section 2.7 summarizes the chapter.

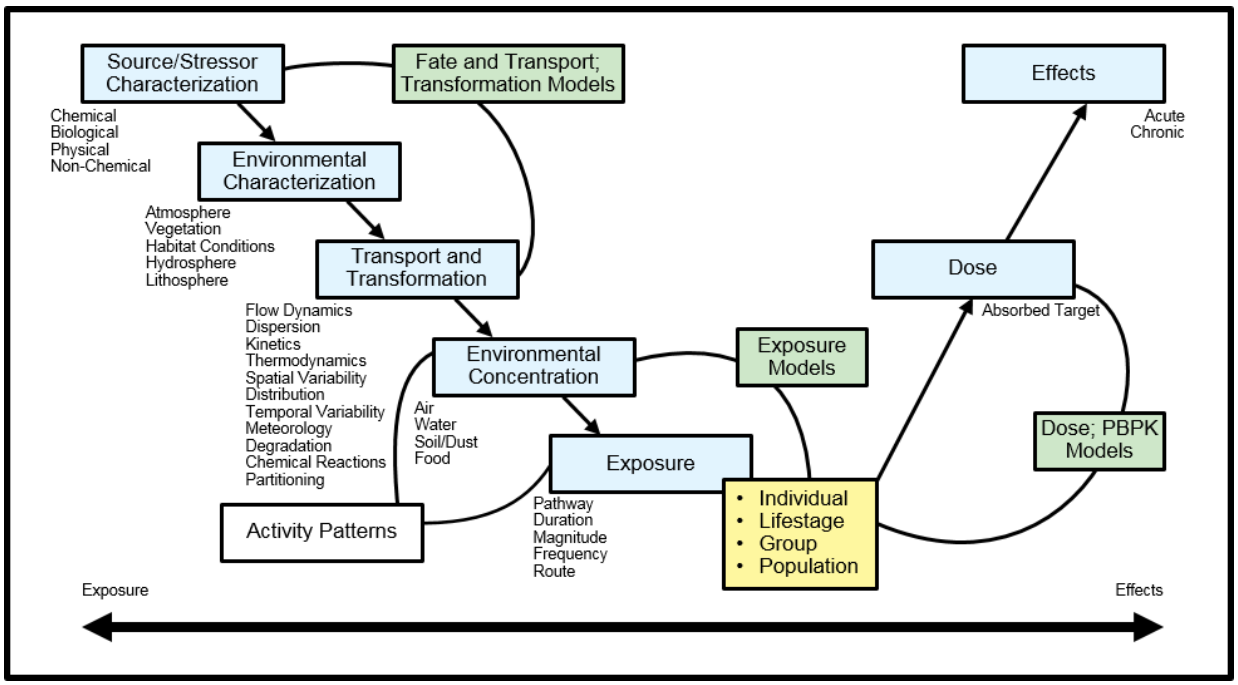
## 2.1. Exposure Science

Human exposure science is the study of human contact with chemical, physical or biological agents occurring in their environments. It is intended to advance the knowledge of the mechanisms and dynamics of events resulting in adverse health outcomes, either to understand their cause(s) or to prevent them (Barr et al. 2006). Exposure science describes the environment, the behavior of agents in the environment, the characteristics and activities of human receptors and the processes that lead to human contact and uptake of agents. Exposure science uses this information to describe conditions in the real world that could lead to human health risks. It provides the scientific knowledge, methods, data and tools for developing current, prospective and retrospective exposure assessments that link exposure to health outcomes and evaluate various options to manage exposures effectively (NRC 2012a; Sheldon and Cohen Hubal 2009; U.S. EPA 2009a).

In 2012, the National Research Council (NRC) published *Exposure Science in the 21st Century: A Vision and a Strategy*. That report defines exposure science as "the collection and analysis of quantitative and qualitative information needed to understand the nature of contact between receptors and physical, chemical, or biologic stressors" (NRC 2012a). Consistent with this definition, the NRC committee considered that exposure science extends beyond the exposure event itself (i.e., the point of contact) to study and describe the processes that affect the transport and transformation of agents from their source to a dose at a target internal organ, tissue or toxicity pathway associated with a disease process. The NRC committee chose to use the term "stressor" rather than "agent."

A source-to-outcome framework, as illustrated in Figure 2-1, helps visualize the processes and information important for exposure science. The text under each box in Figure 2-1 shows the information used to characterize the various processes and conditions represented in the boxes. The arrows between the boxes represent the models used to link the processes. The processes important for exposure science begin with a contaminant's entering the environment and end with dose characterization. Starting in the upper left-hand corner, a source releases agents into the environment. Chemical reactions and physical and biological degradation transform many contaminants. Contaminants or their transformation products move through the environment and can be found in many types of environmental media, including air, water, soil, dust, food and surfaces. The magnitude of exposure depends on the contaminant's concentration in the medium, activities that transfer a contaminant from an environmental medium to a receptor and duration of contact of the contaminant with the receptor. An exposure becomes a dose when the contaminant moves across the receptor's external exposure surface and is absorbed into the body; it then can disperse throughout the body in its native form, metabolized form or both. The endpoint for exposure science is the dose that the target internal tissue, organ or developing embryo/fetus receives: the location where the dose initiates the toxicity pathways that trigger the adverse effect. This endpoint serves as the starting point for toxicology (Pleil and Sheldon 2011).

**Figure 2-1. Source-to-Outcome Framework**

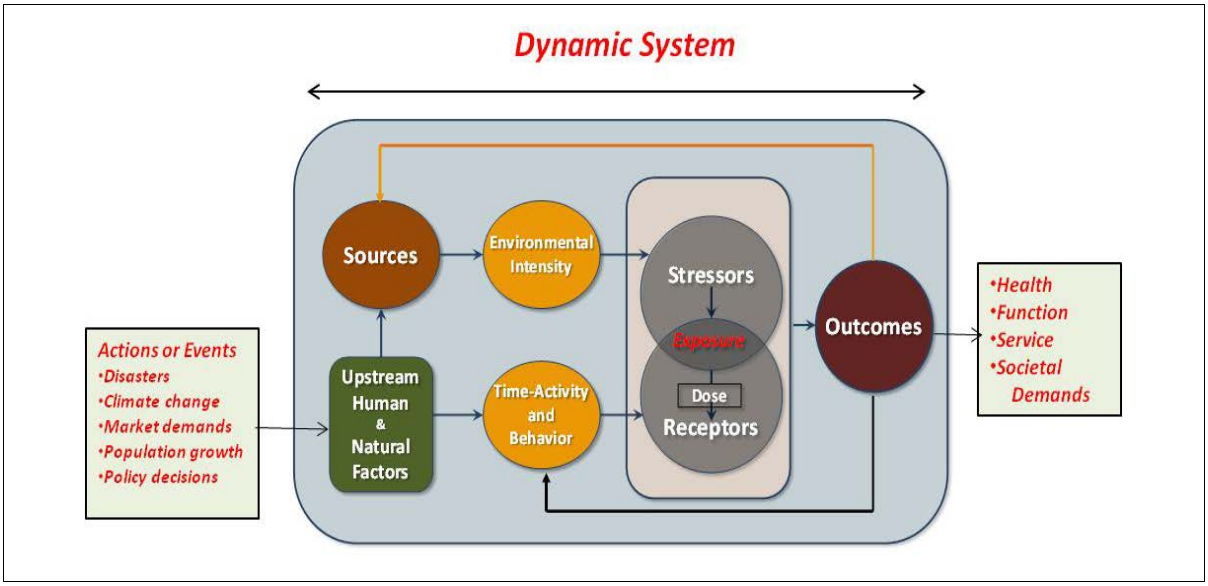



Note: PBPK = physiologically based pharmacokinetic
Adapted from NRC (1983); NRC (1997)

In 2012, the NRC committee built on the source-to-outcome framework to develop the conceptual systems framework for exposure science shown in Figure 2-2. In this figure, the basic components from stressor release to adverse outcome are the same. The committee, however, added several new concepts. On the left-hand side of Figure 2-2, actions or events might be sources for stressors that cause changes in human and natural factors or alter human behaviors or both. The outcomes on the right-hand side of the figure have feedback loops that, inherently, can

lead to stressors or to different actions or events. The arrow across the top suggests the dynamic nature of the system. The figure shows the instrumental role human activities play both in describing the exposure event and in developing or mitigating exposures or risk. The figure departs from a simple linear depiction of exposure by incorporating feedback loops resulting from exposures or actions to those exposures. Concepts depicted in this systems framework will become increasingly important as the Agency addresses issues of sustainability.

**Figure 2-2. Conceptual Framework for Exposure Science Developed by NRC**




Adapted from NRC (2012a)

The NRC committee also recognized exposure as a multiscale problem that needs to incorporate variations of exposure to multiple stressors across scales of time, space and biological organization; thus, exposure is considerably more complex than Figure 2-1 and Figure 2-2 depict. Multiple stressors can enter the environment at the same time from multiple sources. Stressors can remain unchanged or chemical, physical or biological processes can transform them. Stressors in their native forms or their transformation products can take many different pathways to reach human receptors. Exposure often is characterized for a single stressor, in a single medium or as a single pathway. Real-world scenarios involve multistressor, multimedia and multipathway exposures. Exposure scientists develop methods to characterize aggregate exposure, the sum of exposures to a single stressor from all sources, and cumulative exposure, which addresses exposures to multiple chemicals by multiple routes over multiple periods.

The focus for human exposure science often is the receptor and not the sources of the stressor, considering potential contact based on the human receptor's location and behavior. A receptor-based approach has two important advantages over a source-based approach. It simplifies the problem by narrowing the universe to stressors that are actually important for human exposure and health risk, and it enables us to develop a real-world description of risk by considering the multiple stressors by which exposure actually occurs. Exposure science, however, often is applied in the broader context of the source-to-outcome continuum where informing risk assessment and risk management decisions using exposure scenario or other approaches is essential and where understanding relationships between sources and exposures is critical.

Receptors can be individuals, groups at specific lifestages within a population or the entire population. Understanding the characteristics of human receptors, their behaviors and the relationship between these factors and exposure or dose is crucial for a receptor-based approach. Variability in exposure occurs because of location, occupation, activities within a location, socioeconomic status, consumer preferences, dietary habits and other lifestyle choices. Behaviors relative to lifestage can be particularly influential determinants for exposure, especially for infants and toddlers and for the embryo/fetus during pregnancy. Lifestage, health status, sex and genetic differences also can be important factors that determine dose. The drivers for human activities are complex and, unlike stressors, cannot be predicted using first-principle models based on physical/chemical properties. Instead, human activities are treated as stochastic properties (random variables) described by population distributions based on available (e.g., observational or modeled) data.

Vulnerability refers to characteristics of individuals or populations that place them at increased risk of an adverse health effect (U.S. EPA 2005c). It includes economic, demographic, social, cultural, psychological and physical states of the receptor or population that influence patterns of exposure to environmental contaminants and those states that alter the relationship between the exposure of the environmental agent and its health effect on the receptor (Gee and Payne-Sturges 2004). Vulnerability also can include external stressors of socioeconomic/sociopolitical origins (e.g., economic structural inequalities, psychosocial stressors) (NEJAC 2004; U.S. EPA 2003d). In addition, during certain lifestages (such as fetal development), specific and characteristic exposure routes can predominate, during which exposure might enhance adverse outcomes. Section 4.2 addresses vulnerability in detail.

Exposure science describes an open system—the environment, with sources, stressors and human receptors. As with all open systems, developing research and assessment strategies for which conditions are carefully controlled and systematically varied to develop a complete understanding of the important processes is not possible. Instead, we measure, observe and analyze conditions and variables to elucidate the relationships between multiple variables at one time. An important constraint associated with working in an open system is that we can confirm, but not prove, hypotheses about exposure. Observational methods provide important information for developing the science. Not all important parameters for describing human exposure can be identified and known in detail because of the nature of working in an open system. This limitation of an open system leads to increased uncertainty in exposure predictions. Exposure research iterates between methods, measurements and models to develop scientific understanding and principles. *Methods* research provides the tools that enable observational measurements and their interpretation. Methods for human exposure science pose many challenges, especially for personal exposure monitoring. Devices for personal monitoring need to be extremely sensitive, accurate, selective, lightweight, easy to wear and self-powered. *Observational human exposure measurement studies* (see Chapter 7) provide fundamental data to understand exposure processes and human activities. Measurement studies provide inputs for models and data for model evaluation. *Models* are the underpinnings for exposure science (see Chapter 6). Both statistical models and models based on physicochemical processes provide the ability to summarize and link our knowledge of exposure processes and to quantify and predict levels of stressors, exposure and dose. Research relies on models to develop exposure hypotheses, synthesize data on the state of the system, provide explanations of factors influencing exposure and identify gaps in our knowledge requiring additional data. Decision

making uses models to assess exposure/dose to stressors, weigh the contributions of different sources, project future conditions or trends, extrapolate to situations lacking observations and evaluate the impacts of different policies or future scenarios. Exposure scientists also use models to develop estimates of uncertainty and variability in predicted exposures.

## 2.2. Definitions

### 2.2.1. Exposure Definitions

Developing, applying and communicating exposure science requires a standardized vocabulary and consistent set of definitions for all concepts and technical terms. Exposure science overlaps with other disciplines, many of which use different terms for the same concepts. The definitions used in this document reflect the field of exposure science. Definitions of exposure, dose and related concepts are presented in (Zartarian et al. 2007). In addition, the International Programme on Chemical Safety developed and published a glossary intended to harmonize the terms used in chemical hazard and risk assessment, which the International Society of Exposure Science officially adopted (Zartarian et al. 2005). Table 2-1 summarizes general exposure-related terms directly cited from that glossary. We explain the concepts associated with these terms below.

Exposure is the contact of an agent with an external boundary of a receptor (exposure surface) for a specific duration (WHO 2004; Zartarian et al. 2005). For exposure to occur, the agent and receptor need to come together in both space and time. The time of continuous contact between the agent and receptor is the exposure period. Exposure can be described in terms of the magnitude (how much), frequency (how often) and duration (how long) of contact at an external boundary. External boundaries are characterized by external exposure surfaces, such as the surface of the skin or a conceptual surface over the nose and open mouth. For most contaminants, both magnitude and route of exposure are critical characteristics in determining adverse effects. In addition, the frequency, duration and timing (e.g., lifestage considerations, acute versus chronic exposure) of exposure/dose are influential in determining adverse effects. These factors depend on the source of the contaminant, its transport and fate, its persistence in the environment and the activities of individuals that lead to contact with the contaminant.

### 2.2.2. Dose Definitions

Dose refers to the amount of an agent that enters a receptor after crossing an external exposure surface. Dose profiles over time depend on the factors described for exposure and the kinetics of *absorption* into the body, *distribution* throughout the body, *metabolism* by various tissues within the body and *elimination* from the body (ADME); thus, the duration of the dose always is equal to or longer than the exposure duration.

Table 2-2 provides definitions for dose-related terms used in this document. When considering dose terms, understanding that different disciplines use different terms to define the same concepts is essential. As an example, within exposure science, the term “exposure” refers to the amount of agent in contact with an external exposure surface, whereas in toxicology, the terms “administered,” “external” or “potential” dose refer to this metric. The definitions of the terms in Table 2-2 derive from their use in exposure science. This document uses the exposure science definition of “dose”—the amount of an agent that enters a receptor after crossing an exposure surface.

## Table 2-1. General Exposure-Related Terms

| Term | Definition |
|---|---|
| Agent | A chemical, physical or biological entity that contacts a receptor. |
| Exposure | The contact between an agent and the external boundary (exposure surface) of a receptor for a specific duration.<br>Types of exposure include:<br>*Aggregate exposure:* combined exposure of a receptor to a specific agent from all sources across all routes and pathways.<br>*Cumulative exposure:* total exposure to multiple agents that causes a common toxic effect(s) on human health by the same, or similar, sequence of major biochemical events. |
| Exposure assessment | The process of estimating or measuring the magnitude, frequency and duration of exposure to an agent and the size and characteristics of the population exposed. |
| Exposure duration | The length of time of contact with an agent. For example, if a receptor is in contact with an agent for *x* minutes per day, for *y* days per year, the exposure duration is a year. |
| Exposure factors | Factors related to human behavior and characteristics that help determine a receptor's exposure to an agent. |
| Exposure frequency | The number of exposure events in an exposure duration. |
| Exposure pathway | The course an agent takes from the source to the receptor. |
| Exposure period | The time of continuous contact between the agent and receptor. For example, if a receptor is in contact with an agent for *x* minutes per day, for *y* days per year, the exposure period is x minutes per year. |
| Exposure point | The location at which the receptor contacts the agent. |
| Exposure point concentration | An estimate of exposure parameters in specific media (e.g., air, water, sediment). |
| Exposure route | The way an agent enters a receptor after contact (e.g., by ingestion, inhalation, dermal application). |
| Exposure scenario | A combination of facts, assumptions and inferences that define a discrete situation in which potential exposures might occur. |
| Exposure science | A discipline that characterizes and predicts the intersection of an agent and receptor in space and time. |
| Exposure surface (Contact boundary) | A surface on a receptor where an agent is present. For example:<br>Outer exposure surfaces (e.g., the exterior of an eyeball, the skin surface, a conceptual surface over the nose and open mouth).<br>Inner exposure surfaces (e.g., gastrointestinal tract, respiratory tract, urinary tract lining). |
| Medium | The material (e.g., air, water, soil, food, consumer products) surrounding or containing an agent. |
| Receptor | Any biological entity (e.g., a human, human population, lifestage within a human population) that receives an exposure or dose. |
| Source | The origin of an agent for the purposes of an exposure assessment. |
| Stressor | Any chemical, physical or biological entity that induces an adverse response. |

Source: Sobus et al. (2010); U.S. EPA (2009a; 2019c); WHO (2004; 2012); Zartarian et al. (2005; 2007)

**Table 2-2. Key Dose-Related Terms**

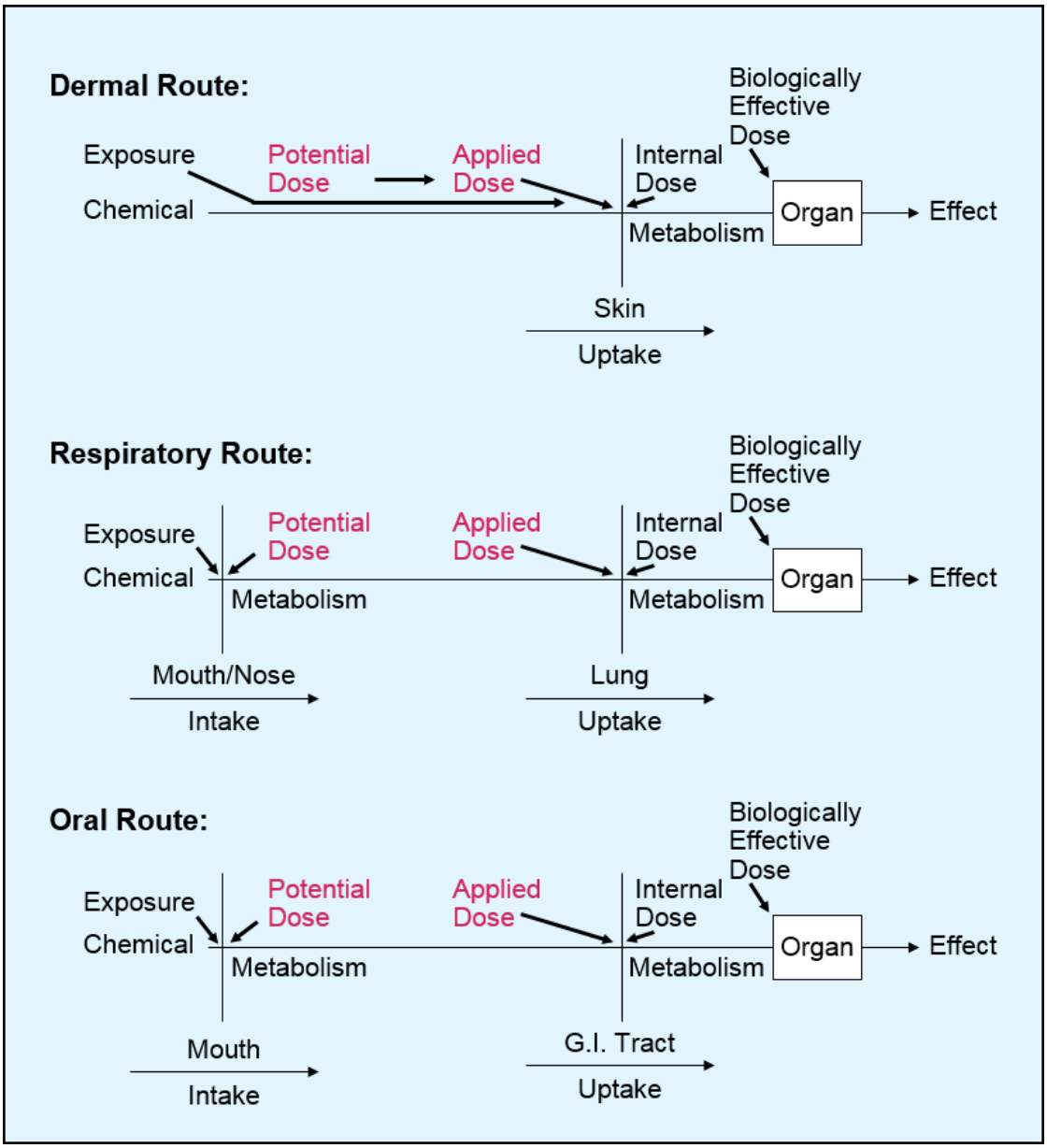
| Term | Definition |
|---|---|
| Absorption barrier | Any exposure surface that can retard the rate of penetration of an agent into a receptor. Examples of absorption barriers are the skin, respiratory tract lining and gastrointestinal tract wall (outer and inner exposure surfaces). |
| Bioavailability | The extent to which an agent can be absorbed by an organism and be available for metabolism or interaction with biologically significant receptors. Bioavailability involves both release from a medium (if present) and absorption by an organism. |
| Biomarker (Biological marker) | An indicator of changes or events in biological systems. Biomarkers of exposure refer to cellular, biochemical, analytical or molecular measures obtained from biological media such as tissues, cells or fluids that are indicative of exposure to an agent. Biomarkers of effect indicate cellular, biochemical or molecular changes occurring as a result of human exposure to the agent. |
| Dose | Types of doses include:<br>*Applied:* amount of agent at an absorption barrier.<br>*Biologically effective*: amount of agent that reaches the target internal organ, tissue or toxicity pathway where the adverse effect occurs.<br>*Delivered:* amount of agent transported to the location where the adverse effect occurs.<br>*Absorbed/Internal:* amount of agent that enters a receptor by crossing an exposure surface acting as an absorption barrier.<br>*Potential:* amount of agent that enters a receptor after crossing an exposure surface that is not an absorption barrier. |
| Dose rate | The dose per unit time. |
| Uptake (Absorption) | The process by which an agent crosses an absorption barrier. |

Source: WHO (2004; 2012); Zartarian et al. (2005; 2007)

Figure 2-3 expands the exposure-to-dose portion of the source-to-outcome framework. A chemical can cross the boundary of the body by two processes: (1) Intake is the process by which an agent crosses an outer exposure surface without passing an absorption barrier. Ingestion into the gut is an example of an intake process. (2) Uptake involves crossing an external exposure surface serving as a barrier and results in an internal dose. Absorption and transport through the stomach lining to the blood are examples of uptake processes.

The capacity for a chemical to be absorbed via uptake processes is the chemical's "bioavailability." Chemical properties, the physical state of the material to which an individual is exposed and the ability of the individual to physiologically absorb the chemical because of nutritional status or gut flora activity can all affect bioavailability. Bioavailability can vary by exposure pathway, chemical and medium. For example, the bioavailability of metals in soils depends on the physical and chemical characteristics of the soil and the interactions of the metals and the soil. Lifestage and other biological factors also can affect bioavailability. For example, the bioavailability of lead from the gut is higher for young children than for adults (U.S. EPA 2007j). The delivered dose, which internal processes such as transport, metabolism and excretion affect, is the amount of agent transported to the location where the adverse effect occurs. The biologically effective dose is the amount of agent reaching the target internal organ, tissue or toxicity pathway where the adverse effect occurs (Sobus et al. 2010).

**Figure 2-3. Schematic of Exposure/Dose Terms**




Note: Terms unique to toxicology are shown in red; G.I. = gastrointestinal

An exposure assessment can be used to develop any of the exposure or dose measures listed in Table 2-1 and Table 2-2. The specific measures selected depend on the objectives of the exposure assessment and the availability of toxicity data. The selected exposure measures need to match the dose measures used in the toxicity test to enable direct comparison between the exposure of human populations and health outcome data. As an example, if dose/response toxicity data are developed based on an inhalation dose, the exposure assessment needs to provide inhalation exposure data. Likewise, if the risk assessment relies on toxicity tests that use blood concentration as the dose measure, the exposure assessment needs to provide blood concentrations.

## 2.3. Concepts in Exposure Assessment

### 2.3.1. The Risk Assessment Process

Within EPA, the primary purpose of exposure assessment is to inform risk assessment. Effectively developing exposure assessments, therefore, requires understanding the risk assessment process. Briefly, risk assessment at EPA characterizes the potential health effects of human exposure to chemical, physical and biological agents. In 1983, the NRC's *Risk Assessment in the Federal Government: Managing the Process* (NRC 1983) introduced the concept of two distinct but interrelated steps in the risk assessment process: a determination of whether an agent constitutes a risk and what action is necessary to reduce that risk. Although the underlying science has evolved since that time, the NRC risk paradigm remains the cornerstone of EPA risk assessment practice (NRC 2009), and exposure assessment remains a fundamental component of both steps in the process.

As part of the first step, risk assessment synthesizes scientific information to evaluate the health effects associated with human exposure, generally viewed as a four-step process (NRC 1983).

- **Hazard identification:** identifies adverse effects (e.g., systemic effects, cancer) that might occur from exposure to a chemical or harmful agent.
- **Dose-response assessment:** estimates the toxicity or potency of an agent by evaluating the quantitative relationship between exposure/dose and response, generally derived from animal toxicity tests.[2]
- **Exposure assessment:** estimates exposure to the agent(s) of concern to the human receptor and describes the human receptor of concern. Because the exposure assessment is compared to the dose-response assessment, the two steps need to use similar measures for exposure and dose, where possible, or describe the uncertainty associated with using different measures.
- **Risk characterization:** estimates the potential for adverse effects resulting from a human exposure along with uncertainty in the findings.

The results of the risk assessment provide the basis for risk management decisions. *Science and Decisions: Advancing Risk Assessment* (NRC 2009) emphasized that risk management questions need to be an integral part of the planning process. Risk management entails determining whether and how risks are to be managed, reduced or eliminated, which is achieved most often by managing and reducing exposures. Managing risk relies directly on information about the sources, pathways and routes that lead to exposure developed by the exposure assessment.

### 2.3.2. Overview of Exposure Assessment

Exposure assessment is the process of estimating or measuring the magnitude, frequency and duration of exposure to an agent and the size and characteristics of the population exposed. Ideally, it describes the sources, routes, pathways and uncertainty in the assessment (WHO 2012; Zartarian et al. 2005; Zartarian et al. 2007); describes contact with agents as they occur in the real world at various lifestages; and provides data to understand and quantify health outcomes as they occur in various populations. Exposure assessments answer three key questions:

[2]A study of the potential for harmful effects of chemicals on particular plants or animals.

1. **What are the characteristics of exposure (e.g., magnitude, frequency, duration, route of entry)?** The primary purpose of the exposure assessment is to estimate exposure or dose, which then is combined with chemical-specific exposure-response or dose-response data (often from animal studies) to estimate risk.
2. **How can exposure be reduced?** Exposure assessment provides information on the individuals exposed and identifies the sources, routes and pathways for exposure. This information helps determine the most effective ways to reduce exposure and, thus, risk. Prospective exposure assessments can provide information on the overall impact of mitigation strategies, including both regulatory and nonregulatory actions.
3. **Has exposure changed over time?** Exposure assessments monitor status and trends in exposure over time. These assessments emphasize what the exposure is at a particular time and how it changes over time. This type of assessment evaluates the potential for emerging health risks and impact of risk mitigation actions.

## 2.3.3. Approaches for Exposure Assessment

The approach and methods used in an exposure assessment depend on the exposure assessment questions (see Section 2.3.2) of the risk assessment, the risk management objectives and, in some cases, the regulatory or statutory requirements, availability and cost of exposure mitigation technologies and political and societal considerations. For example, an exposure assessment can inform risk screening, priority setting, standard setting, permitting, enforcement, remediation decisions or program and policy evaluation.

Many choices are available when selecting the approach for conducting an exposure assessment. Table 2-3 summarizes the approaches and options for methods. Within an exposure assessment, the choices are not mutually exclusive, and an assessor may choose several approaches. Potential outputs of an exposure assessment include a population profile, a list of relevant chemicals, chemical groups for use in risk analysis and characterization and a conceptual model for risk.

**Table 2-3. Approaches for Exposure Assessments**

| Approach Considerations | Description | Options/Methods |
|---|---|---|
| Design | Determines the fundamental design of the exposure assessment | Direct<br>Indirect<br>Biomonitoring |
| Tiered approach | Considers the resources and the acceptable level of uncertainty | Ranges from screening-level assessments that are rapid and use few resources but are highly uncertain to very complex assessments that minimize uncertainty but are resource intensive |
| Population selections | Determines how the population is described | Scenario based<br>Population based |
| Estimation approach | Determines how the assessment is conducted | Deterministic<br>Probabilistic |
| Stressor evaluation | Determines how stressors are considered | Exposure to single stressor, single source, single pathway<br>Aggregate exposure<br>Cumulative exposure |

**Design—Direct versus Indirect versus Biomonitoring.** Quantitative approaches for estimating exposure use one of three approaches: direct measurements, indirect estimation or biomonitoring. *Direct (i.e., point-of-contact) methods* measure the contact of the person with the chemical concentration in the exposure medium over an identified period. Personal monitoring techniques such as the collection of personal air or duplicate diet samples measure an individual's exposure directly at a point in time. *Indirect estimation* uses available information on concentrations of chemicals in the exposure medium and information about when, where and how individuals might contact the exposure medium—activities that can lead to transfer of the agent from the exposure medium to the individual. Dose estimates rely on factors that lead to chemical uptake. The indirect approach develops specific exposure scenarios and then uses data (e.g., pollutant concentrations), a series of exposure factors (e.g., contact duration, contact frequency, breathing rate) and models to estimate exposure within the scenario. *Biomonitoring* measures the amount of a stressor in biological matrices. Models (Sobus et al. 2010; U.S. EPA 2012c) can be used with biomarker data (CDC 2012a) to estimate the amount of agent to which a person has been exposed, the corresponding dose or both. These modeling approaches use information collected following exposure and "downstream" of the point of exposure. Modeling tools can enhance estimates of exposure from biomonitoring data (see Section 6.2.3). An example is a pharmacokinetic model and the data necessary to run it such as physiological parameters, the biomarker measurement and information on the time between exposures and the time of measurement. Alternatively, biomarker data can be used directly in risk assessments if the toxicity data used in the assessment include biomarker data as part of the dose-response assessment (NRC 2006b). Biomonitoring data aggregate exposures from all routes and pathways, but not always equally or proportionally. Identifying sources for exposure when multiple sources or routes exist can be difficult.

**Complexity—Tiered Assessments.** Given the numbers of chemicals, other potential stressors or scenarios evaluated for environmental health risks, the need for efficiency, cost-effectiveness and focus in the risk assessment process is critical. Selection of the assessment tier depends on the purpose of the assessment and the quality and quantity of the available data, resources, level of acceptable uncertainty and statistical methodologies. Thus, assessments use a tiered approach, often starting with a screening-level assessment and increasing the level of complexity as required. Lower tier assessments can require few resources and can evaluate large numbers of agents. Complex risk assessments, in contrast, can address the most demanding problems in risk assessment. The goal is to design the exposure assessment to fit the needs of the risk managers/decision makers, balancing the complexity of the assessment against time and resource constraints. Exposure, hazard and risk management information need to inform each level.

- Screening-level exposure assessments determine whether further work is needed to aid the risk management decision. Readily available data, conservative assumptions and simple models are the primary bases for these assessments. For example, a screening-level assessment of a contaminated site might determine if additional data are needed or whether input parameters need refinement. Screening-level assessments often use point estimates (i.e., single exposure values). Depending on the needs of the assessment, an assessor can generate screening-level exposure estimates for multiple exposure scenarios.
- As the accuracy and precision needed to limit uncertainty increase, exposure assessments increase in complexity. Complex exposure assessments use sophisticated models or observational human exposure measurement studies, or both, to collect the data and

exposure factors, and they usually require more data. Complex exposure assessments often use probabilistic distributions for one, some or all of the parameters. Depending on the needs of the assessment, an assessor can generate complex exposure estimates for actual environmental conditions or prospective or retrospective scenarios.

**Population Selection—Scenario versus Population Based.** For this type of exposure assessment, either a scenario-based or a population-based approach describes populations. For the scenario-based approach, a distinguishable set of behaviors or locations that lead to exposure defines a specific receptor group of interest. Exposure scenarios then use sets of facts, assumptions and inferences about how exposure takes place under a specific set of conditions. The resulting exposure metric is usually a single point estimate (e.g., 95th percentile) for a specific population. Carefully selected exposure factors avoid making unrealistically conservative estimates. Population-based approaches provide information on the broader context of exposure for a selected population, including variability within that population or intrapersonal variability. One approach weights exposure input data in assessing the population of interest. Input data represent the population of interest, its variability and correlation among variables, and account for nonlinearity in exposure conditions. Interpersonal variability in influential exposure factors or use of a time-series approach could introduce additional complexity. Outputs from population-based assessments are population exposure and dose distributions.

**Estimation Approach—Deterministic versus Probabilistic.** Deterministic exposure assessments use point estimates (e.g., empirical data) as inputs to exposure equations or models. This approach most often is screening level. Conservative input variables result in a quick estimate of potential exposures and possible concerns. Depending on the purpose, exposure estimates can use exposure factors representing the high end (90th percentile or above), median (50th percentile) or low end (25th percentile or below) of the distribution.

Probabilistic exposure assessments use statistical (e.g., analytical) distributions for input variables, parameterizing these distributions and characterizing the conditions or probabilities associated with the use of particular distributions. Probabilistic approaches better account for the uncertainty and variability in influential input variables. The degree of complexity captured using a probabilistic approach can be far ranging, depending on the number of variables that use statistical distributions, whether correlation is maintained among multiple variables (e.g., body mass, fat-free body mass, overall fitness) and the degree to which the number and groups of receptors in the exposure assessment are expanded. The outcome of an exposure assessment using a probabilistic approach is a statistical distribution of the estimated exposures or doses for the receptors.

**Stressor Evaluation—Single Chemical versus Aggregate versus Cumulative.** Historically, exposure assessments largely have been oriented toward single-pathway and single-chemical evaluations that yield point estimates of exposure. Aggregate or cumulative assessments help describe real-world situations that consider multiple pathways and agents within a single assessment.

Aggregate exposure is the sum of exposures of an individual or a defined population to a specific agent from all sources and pathways. Aggregate exposure assessments provide qualitative or

quantitative estimates of the combined exposures of an individual (or a defined group or population) to a specific agent from all sources through all relevant exposure routes (i.e., inhalation, ingestion, dermal absorption); pathways (e.g., ingesting contaminated groundwater, inhaling volatilized chemicals while showering); and environmental sources (e.g., air, surface water, groundwater, soil, sediment, fish) (ILSI 1999; U.S. EPA 1991b). Often, physiologically based pharmacokinetic or other dose models combine estimated exposures from multiple sources, pathways and routes to provide a projected single dose or biologically effective dose metric. Alternatively, biomonitoring can aggregate chemical stressors.

The Food Quality Protection Act[3] mandates that EPA consider cumulative risk from exposure to all pesticides with common toxicity mechanisms (U.S. EPA 1996c; U.S. EPA 2002i). EPA's *Framework for Cumulative Risk Assessment* provides a more general definition that recognizes combined risks from aggregate exposures to multiple agents or stressors, which could be chemical, physical or biological agents or the absence of a necessity (e.g., food, shelter, clothing) (U.S. EPA 2003d). Cumulative risk assessment can be very complex and can involve several iterations to examine factors related to population vulnerabilities, public health information, toxicological and epidemiological data, completed exposure pathways, differential exposures and contact with environmental media and pollutant sources.

### 2.3.4. Uncertainty and Variability in Exposure Assessments

Exposure predictions that models generate provide a computational means of representing complex real-world exposures using available data and various assumptions. The model performance or predictions, however, vary in their reliability and accuracy, depending on many factors. The most critical factor that influences the exposure estimate is the ability to capture adequately the inherent variability in model inputs and parameters (e.g., those associated with time activity patterns, product use, emission rates, distribution of chemicals within the media of concern, exposure and ADME factors, physiological characteristics, dietary patterns, among others), both within and between individuals. For computational exposure modeling, incorporating the variability in the numerous information data streams as part of the integrative exposure model calculations can be challenging; probabilistic methods such as Monte Carlo or Bayesian modeling tools, however, can facilitate this procedure. More information on model uncertainty is available in Sections 6.3.4 and 8.3.

Uncertainty regarding exposure or dose predictions typically arises due to limitations of available information or input and parameter data, and limitations of the computational modeling techniques used to simulate complex and challenging physical, chemical and behavioral or stochastic processes. Unlike variability, which is due to inherent properties of the entire system, uncertainty is due to lack of knowledge in the vital parts of the computational exposure modeling process. Typically, three broad categories describe uncertainty: (1) scenario uncertainty (consisting of several parts), (2) parameter uncertainty and (3) model uncertainty. Accounting for and describing such uncertainties is critical for an exposure assessment. High-performance computing methods and software now provide the ability to evaluate propagation of uncertainties across each step of the source-to-exposure-to-dose continuum.

[3]Food Quality Protection Act of 1996, Pub. L. No. 104–170, 110 Stat. 1489 (U.S. EPA 1996c).

## 2.4. Calculating Exposure Estimates

By combining information and data describing exposure scenarios, concentrations, activity patterns and other exposure factors, an exposure assessor can develop a quantitative estimate of exposure for an individual or a population. As described previously, characterizing exposure requires definitions of mass and time.

This section presents route-specific equations and associated input variables used to estimate exposure via the inhalation, ingestion and dermal routes—the three most common exposure routes. General equations are presented here, and more detail is found in *Draft Protocol for Measuring Children's Non-Occupational Exposure to Pesticides by All Relevant Pathways* (U.S. EPA 2001b), including equations for estimating exposure via inhalation and dermal routes. Additional details on different forms of these exposure equations, including model default values used in various human exposure models, are found in Williams et al. (2010).

### 2.4.1. Inhalation Exposure

Exposure occurs via the inhalation route when an individual breathes a chemical. The chemical can directly affect the respiratory tract (point-of-entry effect) or enter the bloodstream through respiratory tract tissues, potentially affecting other systems of the body (target organ effect). A simplifying assumption is that inhalation exposure equals dose for gases, aerosols and fine ("respirable") particles less than 2.5 micrometers (μm). More refined estimates of dose require separate equations and models that account for ADME parameters of the stressor. Larger inhaled particles are less likely to reach the lowest parts of the lung (alveoli). Upper movement of cilia in the lungs can sometimes remove such particles, which an individual then swallows. Nanometer-sized particles might deposit in the upper airway and find their way to target organs (Oberdörster et al. 2007). Estimating the dose associated with intake from inhalation exposure is complicated because of the complex nature of the respiratory system as a portal of entry (U.S. EPA 1994b; U.S. EPA 2009f).

In its simplest term, inhalation exposure for a given exposure event is equal to the average chemical concentration in the air in the person's breathing zone multiplied by the inhalation rate, as shown in the equation below (U.S. EPA 2001b):

$$E_{inh} = (C_a)(IR)$$

where:

$E_{inh}$ = inhalation exposure (mass per time)

$C_a$ = airborne concentration of the chemical contacted by the exposed individual (mass of chemical per volume of air in breathing zone)

IR = inhalation rate (volume of air breathed per unit time)

Additional factors are considered for more refined estimates of exposure to specific chemicals. For example, for complex situations involving exposure to particulate matter, deposition in the lung and exhalation are also considered. Alternatively, exposure is estimated in terms of exposure concentration for a pertinent exposure period when deriving hazard quotients using EPA reference concentrations (U.S. EPA 2004a; U.S. EPA 2009f).

## 2.4.2. Ingestion (Dietary and Nondietary) Exposure

Ingestion exposures occur when an individual eats, drinks or inadvertently introduces a chemical into the gastrointestinal tract. Soil, dust or foreign objects can be ingested, and ingestion of both food and nonfood items can contribute to an individual's exposure. Depending on the properties of the chemical, absorption can occur throughout the entire gut. A chemical can directly target the tissue in the gut or be absorbed from various locations in the gut into the bloodstream.

Dietary (food, liquids) and nondietary (soil, dust, other materials) exposure can be estimated as shown in the equation below (U.S. EPA 2001b):

$$E_{ing} = (C_{ing})(IR)$$

where:

$E_{ing}$ = ingestion exposure (mass per time)

$C_{ing}$ = concentration of the chemical in food or other exposure media (mass of chemical per mass of medium or mass of chemical per volume of medium)

IR = ingestion rate (mass of medium ingested during the exposure per time)

When considering multiple media for ingestion exposure, exposure from each medium is calculated separately and then summed. Exposure events usually are expressed in terms of a frequency of ingestion event times the intake per event.

## 2.4.3. Dermal Exposure

Dermal exposure occurs when a chemical acts on or is absorbed through the skin to enter the bloodstream. Examples of how agents can contact the skin include through swimming, bathing, gardening, other hobby-related activities and use of personal care or cleaning products. Exposure to an aerosol, liquid, solid or contaminated surface is the most common cause of dermal exposure. Liquid or solid aerosols can result in measureable exposure, but gases generally produce very low dermal exposures (U.S. EPA 2007d). As with the other exposure routes, the chemical can affect the tissue directly or affect internal organs after it enters the bloodstream. Absorption through damaged skin or tissue (e.g., cuts, blisters) can be greater than absorption through healthy tissue. The chemical itself can act as the mechanism that damages the tissue and affects absorption. The medium carrying the contaminant to the skin is important for estimating absorption—for example, whether it is hydrophilic or lipophilic or causes skin damage.

Dermal exposure for a given exposure event can be estimated as the concentration or mass of chemical in the medium contacting the skin. A general equation for estimating dermal exposure is shown below (U.S. EPA 2001b):

$$E_{derm} = (MR_{medium})(C)(SA)$$

where:

$E_{derm}$ = dermal exposure (mass per time)

$MR_{medium}$ = mass of medium contacting the skin per time (mass of medium per skin surface area per time)

C = average concentration in medium (mass of chemical per mass of medium)

SA = skin surface area available for contact (area)

This dermal equation is represented in different ways and with additional variables by different exposure models, depending on the medium considered (soil, dust, water, chemical residue on a surface), available measurement methods and the data collected for the chemical or medium transferred from a surface to the skin. For example, the equation differs slightly if a dermal transfer coefficient (in units of area per time) versus dermal transfer efficiency (unitless) is used to estimate the mass of medium contacting the skin per time. Some models also include terms for fraction of skin clothed to estimate the skin surface area. The Agency uses different variations of this equation (U.S. EPA 1997c; U.S. EPA 2004d; U.S. EPA 2007h).

Various programs at EPA evaluate dermal exposures using approaches specific to the program needs. EPA compiled and summarized these approaches in a single document, *Dermal Exposure Assessment: A Summary of EPA Approaches* (U.S. EPA 2007d). Quantifying dermal dose depends on several variables influencing how a chemical can pass through skin. In general terms, dose is calculated by multiplying exposure (mass per time) by the fraction of the chemical that actually penetrates the surface barrier. Dose equations are outside the scope of this document, but numerous Agency resources are available, including *Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment)* (U.S. EPA 2004d) and *Dermal Exposure Assessment: A Summary of EPA Approaches* (U.S. EPA 2007d).

## 2.5. Development of Exposure Science and Exposure Assessments Related to EPA Risk Assessments

Exposure science, in various forms, dates at least to the early 20th century and has provided inputs to three fields with even earlier origins: epidemiology (Nieuwenhuijsen 2015; WHO 1983), industrial hygiene (Cook 1969; Paustenbach 1985) and health physics (Upton 1988). Understanding and measuring exposures grew increasingly important in the 1970s because of greater public, academic, industrial and government awareness of chemical pollution problems and their potential health implications. At the same time, newly developed analytical methods enabled scientists to measure low-level, general population exposures for many chemicals. Thus, new data sources became available for exposure assessment.

In 1983, NRC published *Risk Assessment in the Federal Government: Managing the Process* (NRC 1983), commonly referred to as the "Red Book." NRC described exposure assessment as one of the four steps of risk assessment, noting then that "[d]iscussion of specific components in risk assessment is complicated by the fact that current methods and approaches to exposure assessment appear to be medium- or route-specific" and that "exposure assessment has very few components that could be applicable to all media."

Shortly after publication of the Red Book, EPA began issuing a series of guidelines for conducting risk assessments (e.g., cancer, mutagenicity, chemical mixtures, developmental toxicology and exposure). In the 1990s, the Agency adopted its basic model for human health risk assessment and ecological risk assessment.

In 1992, EPA's Risk Assessment Forum issued *Guidelines for Exposure Assessment* (U.S. EPA 1992c), which described steps to construct exposure scenarios or to collect data in field studies to estimate exposure. These guidelines used scientific advances to characterize exposure more

accurately, rather than assuming worst-case or hypothetical maximum exposures. These advances included more sensitive techniques to measure concentrations of contaminants in the environment, the use of probabilistic models to characterize the full range of possible exposures by a population and greater awareness of uncertainty in exposure assessments (Keenan et al. 1994). Various Agency programs have implemented the *Guidelines for Exposure Assessment* via standard assessment procedures that are consistent with their statutory authority, as illustrated in Box 2-1.

**Box 2-1. Agency-Specific Actions to Implement the Guidelines**

- The Office of Pollution Prevention and Toxics has consumer product use scenarios and generic scenarios for worker exposure and environmental release, which are the basis for and are consistent with the Exposure and Fate Assessment Screening Tool (E-FAST) and the Chemical Screening Tool for Exposures and Environmental Releases (ChemSTEER) models (U.S. EPA 2004b; U.S. EPA 2014b).
- Human health evaluation documents comprising the *Risk Assessment Guidance for Superfund* (U.S. EPA 1989b; U.S. EPA 1991b; U.S. EPA 1991c; U.S. EPA 2001g; U.S. EPA 2001h; U.S. EPA 2004d; U.S. EPA 2009f) are principal examples of the interpretation and expansion of the *Guidelines for Exposure Assessment* to meet the needs of risk assessors evaluating current and future risks under the Superfund program.
- The Office of Research and Development's National Center for Environmental Assessment has developed a summary report for dermal exposure assessment (U.S. EPA 2000h), as has the Superfund division of the Office of Land and Emergency Management (formerly the Office of Solid Waste and Emergency Response) (U.S. EPA 2004b).
- The Office of Pesticide Programs (OPP) has updated the residential standard operating procedures that describe standardized scenarios for evaluating consumer product usage and other standardized behaviors for exposure analysis (U.S. EPA 2012f). OPP also has guidance on risk assessment methods for children of workers in agricultural fields and pesticides with no food uses (U.S. EPA 2009e).

When the *Guidelines for Exposure Assessment* was issued in 1992, exposure assessments were devoted principally to chemical exposures of adults from the ambient environment in a single medium (air, water, diet, dust, surface contact). Since 1992, the field of exposure science has expanded and changed in several significant ways:

- Many more sources of exposure concentration data and information are available, ranging from national surveys and registries to small studies of individual chemicals. Some data sources are proprietary, and others are publicly available. Environmental and personal monitoring study data are available from the peer-reviewed literature and are summarized in government compendia.
- The *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011d) provides information on principles of exposure assessment, exposure factors and activities and behaviors that might influence exposures. EPA updates this handbook as study data are published and become available in the peer-reviewed literature.
- The exposure science field has evolved to recognize the contribution of individual characteristics and activities to exposure, acknowledging that not all individuals are alike, behave the same way or are exposed to the same concentration of a chemical. This recognition was realized, in part, through studies such as one on air pollution and mortality in six U.S. cities (Dockery et al. 1993); the Total Exposure Assessment Methodology Study (TEAM; U.S. EPA 1987c); the National Human Exposure Assessment Survey (U.S. EPA 2003f); the Children's Total Exposure to Persistent

Pesticides and Other Persistent Organic Pollutants Study (CTEPP; U.S. EPA 2005f); and the Detroit Exposure and Aerosol Research Study (DEARS; U.S. EPA 2011a).

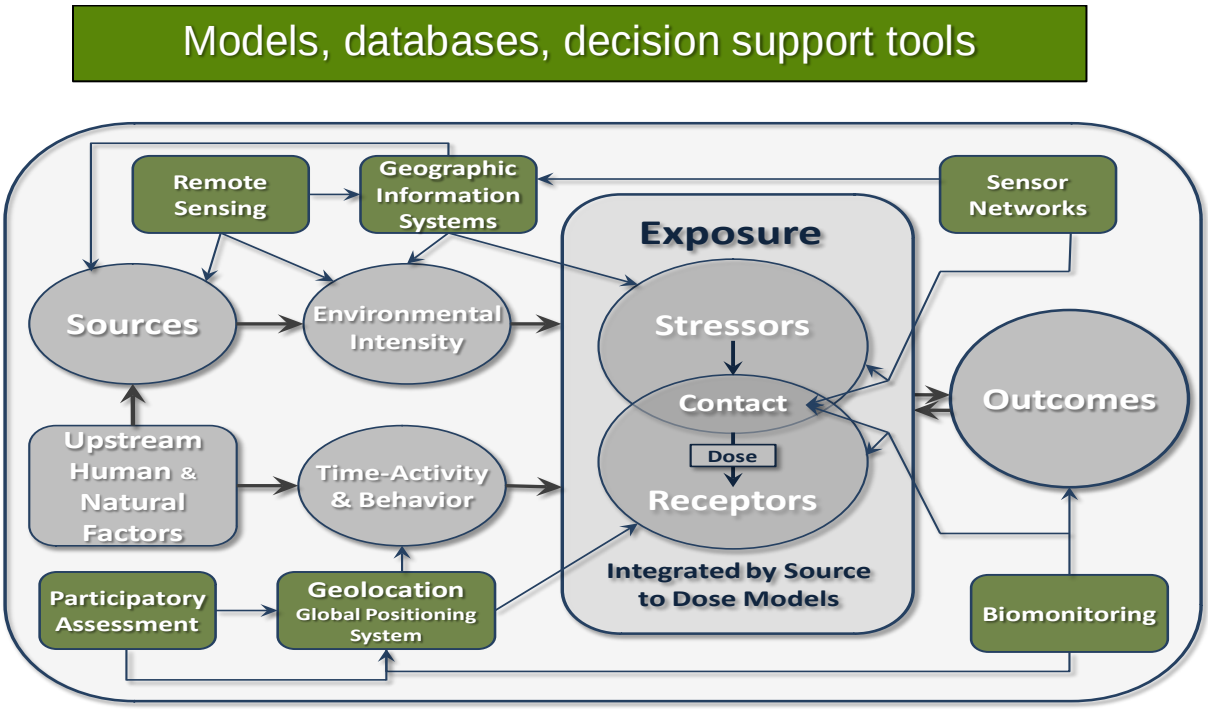
- Models that consider multipathway, multiroute exposures and apply probabilistic methods to simulate behavior patterns have advanced in recent years. Improvements in monitoring methodology and modeling now enable some exposure analyses and assessments to consider the influences of age, sex, culture, ethnicity, activity patterns and socioeconomic and demographic factors. Consequently, measurements and modeling of individuals' exposures to a variety of chemicals and other stressors as they perform their daily routines are now possible. This, in turn, provides a means to identify the sources and routes for stressors of interest and the amount of exposure incurred because of personal characteristics, location and behavior. As a result, for some stressors, exposure assessors can construct a more complete and often more complex picture of exposure to chemicals and other stressors in the environment.
- Advances in the field of analytical chemistry allow for biomonitoring programs that directly measure the concentrations of certain chemicals or their metabolites present in biological matrices, rather than in the environment (Paustenbach and Galbraith 2006). As part of its National Health and Nutrition Examination Survey, the Centers for Disease Control and Prevention continues to build a national database of biological levels to select chemicals (CDC 2012a). A framework and methods have been developed for the use and interpretation of biomonitoring data for assessing exposure and risk (Sobus et al. 2010).
- Improved exposure assessment models have been developed for use in the European regulations for REACH (Registration, Evaluation, Authorisation and Restriction on Chemicals) and other national authorities and international agencies such as Health Canada and the Organisation for Economic Co-operation and Development.

## 2.6. Emerging Topics

In 2010, EPA commissioned NRC to develop a report with the goal of advancing the science of exposure and its use. The NRC report, *Exposure Science in the 21st Century: A Vision and a Strategy* (2012a), has created an opportunity to develop a "new" exposure science. Figure 2-4 illustrates the types of new technologies that are becoming available and will provide the opportunity to:

- Extend data infrastructure for the collection, storage and retrieval of large quantities of traditional and nontraditional data for use in describing the multidimensional aspects of exposure more comprehensively
- Expand the data landscape by developing, evaluating and applying methods for efficient monitoring
- Advance modeling by strategically collecting data needed to build, evaluate and apply models
- Develop advanced analytical systems to convert data rapidly into information that captures the dynamic aspects of the environment, stressors and receptors
- Build complex systems models that can account for and predict positive and negative exposure influences on risks.

**Figure 2-4. New Technologies for Advancing Exposure Science**




Adapted from NRC (2012a)

Additional topics that will advance exposure science include:

- ExpoBox (EPA's EXPOsure toolBOX): created to help individuals assess exposure. ExpoBox is a compendium of exposure assessment tools that links guidance documents, databases, models, reference materials and other related resources.
- ExpoFIRST (Exposure Factors Interactive Resource for Scenarios Tool): brings EPA's *Exposure Factors Handbook: 2011 Edition* data to an interactive tool that maximizes flexibility and transparency for exposure assessors. ExpoFIRST allows exposure assessors to perform and document calculations for community and site-specific exposure assessment.
- ExpoCast and high-throughput screening: EPA develops and uses innovative methods to develop exposure estimates for thousands of chemicals to better protect human health and the environment.
- Systematic review principles: a structured process of identifying, evaluating and integrating evidence for exposure assessments developed as part of a risk assessment. Examples of approaches for systematic reviews include the Office of Pollution Prevention and Toxics *Application of Systematic Review in TSCA Risk Evaluations*; a National Academy of Sciences workshop on Strategies and Tools for Conducting Systematic Reviews of Mechanistic Data to Support Chemical Assessments; PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses); and a planned approach for the IRIS (Integrated Risk Information System) program to optimize the application of best practices for systematic reviews.

- Exposome research: EPA incorporates exposome research within its research framework to better understand the causal links between exposure and adverse effects on human health and the environment, in support of the Agency's mission.
- Microbiome research: EPA supports microbiome research within its research framework to better understand the role of the biome as a component of the body that influences the absorption and metabolism of ingested chemicals.
- Social determinants of health research: Within its research framework, EPA supports research on the interrelationships between chemical and non-chemical stressors and how non-chemical stressors might change the biological response to a chemical exposure, in support of the Agency's mission.

Looking to the future, an explosion of data is expected for characterizing the spatial and temporal dimensions of the fate and transport of multiple stressors in the environment and movement, activities and exposures to humans and ecosystems. New techniques for environmental measurements and biomonitoring will enable the detection and verification of exposures and their linkages to human and ecosystem outcomes. New models and informatics tools will allow better description of the current condition, prediction of future conditions and understanding the impacts of decision alternatives to reduce exposures. These new tools will enable EPA to address exposures to the most vulnerable and the most highly exposed individuals and communities. Communities and individuals will be able to understand their exposures and act to reduce them. EPA will incorporate these new data, techniques and models into the Agency's exposure assessments as they are evaluated and reviewed, as appropriate, for use in Agency decisions.

## 2.7. Summary

- Human **exposure science** is the study of the contact of humans with chemical, physical or biological agents in their environment.
  - Exposure science includes describing the processes influencing the transport and transformation of agents from their source to a dose at a target internal organ, tissue or toxicity pathway associated with a disease process.
  - Exposure is multiscale across time, space and biological organization; and exposure scenarios involve multiple stressors, multiple media and multiple pathways.
  - The focus for human exposure science is the receptor, which can be individuals, groups at specific lifestages within a population or the entire population.
  - Exposure predictions are uncertain, requiring iteration between methods, measurements and models to develop scientific understanding and principles.
- **Exposure** is the contact of an agent with an external boundary of a receptor for a specific duration.
- **Dose** is the amount of an agent that enters a receptor after crossing an external exposure surface.
- **Risk assessment** is a four-step process that synthesizes scientific information to evaluate the health effects associated with human exposure: (1) hazard identification, (2) dose-response assessment, (3) exposure assessment and (4) risk characterization.
- Exposure assessments answer three **questions**: (1) What are the characteristics of exposure? (2) How can exposure be reduced? (3) Has exposure changed over time?

- The exposure assessment questions, risk management objectives and any regulatory or statutory requirements, availability and cost of exposure mitigation technologies and political and societal considerations determine the **approach** for an exposure assessment.
  - Quantitative approaches for estimating exposure use direct measurements, indirect estimation or biomonitoring.
  - Approaches range from screening-level assessments to complex, resource-intensive assessments.
  - Populations are described using either a scenario-based or a population-based approach.
  - Deterministic exposure assessments use point estimates as inputs to exposure equations or models; probabilistic exposure assessments use statistical distributions for input variables, parameterize the distributions and characterize the conditions or probabilities associated with the use of particular distributions.
- **Uncertainty** is classified in three broad categories: (1) scenario uncertainty, (2) parameter uncertainty and (3) model uncertainty.
- **Variability** is due to inherent properties of the entire system.
- Inhalation, ingestion and dermal are the three **most common exposure routes**.
  - **Inhalation exposure** is the product of the chemical concentration in the air in the person's breathing zone and the inhalation rate.
  - **Ingestion exposure** is the product of the concentration of the chemical in food or other exposure media and the ingestion rate.
  - **Dermal exposure** is the product of the mass of medium contacting the skin per time, the chemical concentration in the medium and the skin surface area available for contact.
- **Exposure science has developed** to reflect the increased availability of sources of exposure concentration data and information.
- **Emerging topics** for future consideration include (1) an explosion of available data for characterizing fate and transport of multiple stressors in the environment, and movement, activities and exposures to humans and ecosystems; (2) new techniques for environmental measurements (e.g., sensors, citizen science) and biomonitoring; and (3) new models and informatics tools to describe current conditions, predict future conditions and understand the impacts of decision alternatives.

# CHAPTER 3. PLANNING AND SCOPING AND PROBLEM FORMULATION FOR EXPOSURE ASSESSMENTS

Three components comprise EPA risk assessments: hazard identification, dose-response and exposure assessment. Risk characterization integrates these three components. Planning and scoping and problem formulation are the first steps in the risk assessment process and in the exposure assessment component. Activities at this stage establish the purpose, scope, approach, participants, level of effort and resources (U.S. EPA 2002g; U.S. EPA 2014f). The decisions the assessment is intended to inform drive the planning. As with the risk assessment, multiple challenges and requirements can arise when conducting an exposure assessment. For example, an assessment completed as part of a regulatory action could involve various legal considerations: the statute under which it is being conducted (e.g., Clean Air Act,[4] Clean Water Act[5]) and the regulatory program of which it is part (e.g., Six-Year Review of Drinking Water Contaminants under the Safe Drinking Water Act,[6] Pesticide Registration Review, Risk and Technology Review program). Such legal considerations could influence specific aspects of the assessment.

As with EPA's *Framework for Human Health Risk Assessment to Inform Decision Making*, EPA has designed this *Guidelines for Human Exposure Assessment* to align Agency exposure assessments with the needs of Agency decision makers (U.S. EPA 2014f). The Human Health Risk Assessment Framework elaborates on the concepts of planning and scoping, including consideration of stakeholder involvement, peer review and problem formulation.

The level of complexity of the planning and scoping process is commensurate with the complexity of the assessment—from screening level to complex. EPA programs might implement specific requirements for planning and scoping and for problem formulation to meet the particular programmatic needs. We encourage risk assessors to consult with their programs and follow the programs' standard operating procedures (SOPs) during planning and scoping and problem formulation.

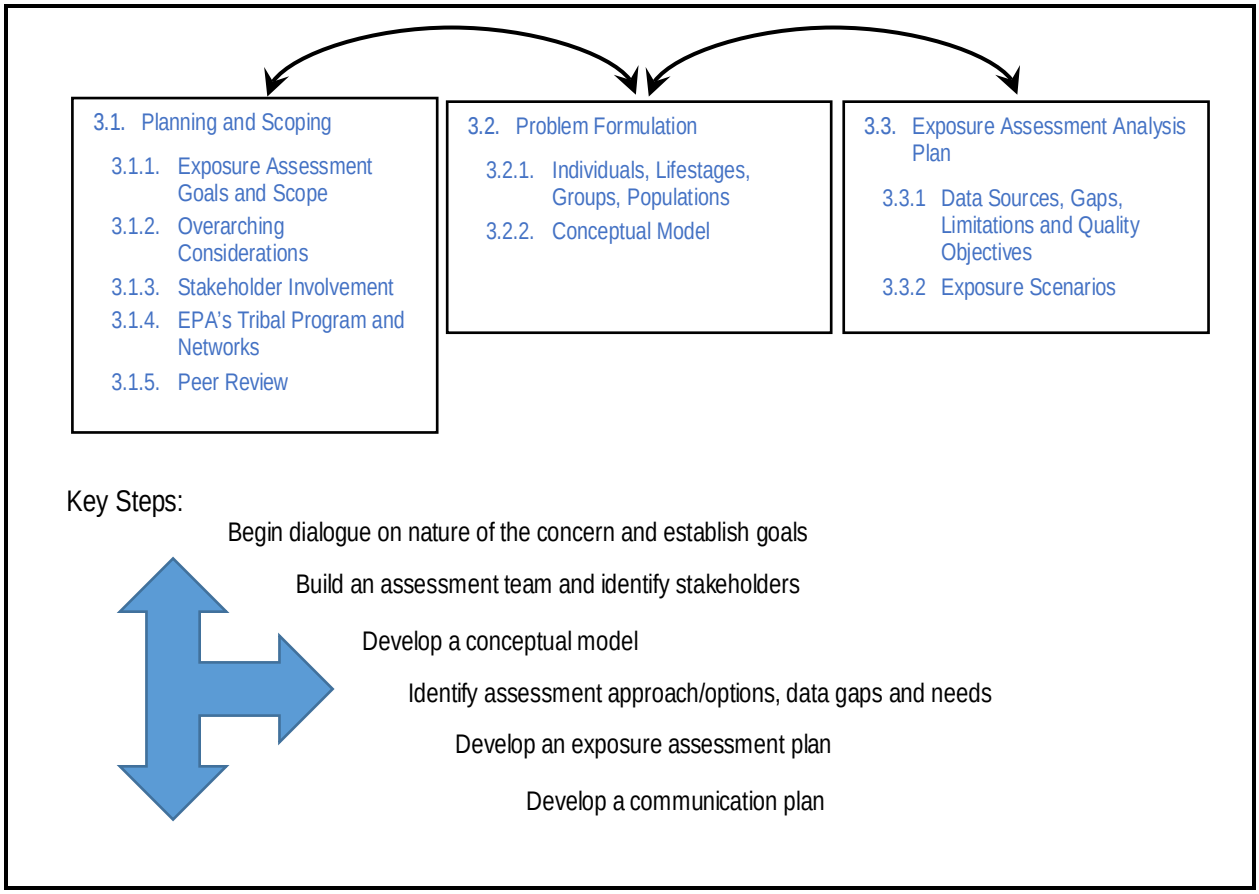
As in risk assessment, planning and scoping and problem formulation for exposure assessment involve a series of interrelated and iterative steps, including ensuring effective engagement of stakeholders. Figure 3-1 presents these steps, and this chapter presents guidance for each:

- Planning and scoping (Section 3.1)
- Problem formulation (Section 3.2)
- Exposure assessment plan development (Section 3.3).

Section 3.4 summarizes this chapter.

[4]Clean Air Act of 1963, 42 U.S.C. 7401 et seq.
[5]Clean Water Act of 1972, 33 U.S.C. 1251 et seq.
[6]Safe Drinking Water Act, 42 U.S.C. 300f et seq.

**Figure 3-1. Planning and Scoping and Problem Formulation for Exposure Assessment**




Adapted from U.S. EPA (2002g)

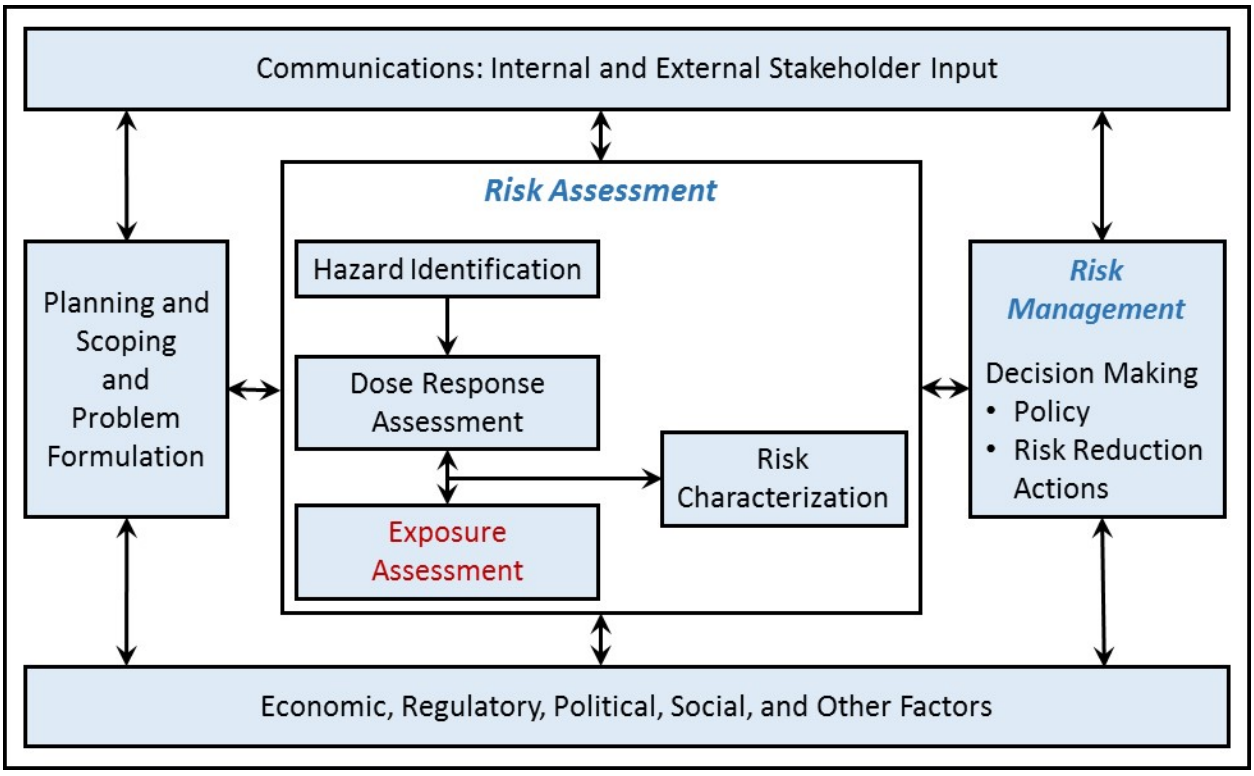
Factors specific to a given exposure assessment, such as resources, regulatory drivers and stakeholder considerations, will drive the nature and sequence of steps in the assessment. Regardless of the drivers, informed planning and scoping processes are key to the success of any exposure assessment. As exposure data are collected and analyzed during the development of an exposure assessment, the planning and scoping and problem formulation process might need to be revised or updated (Figure 3-2).

## 3.1. Planning and Scoping

Planning and scoping is an essential and integral part of exposure assessment. The planning component involves identifying the underlying question on which the assessment is focused and the constraints under which the assessment is conducted (timeframe, resources). Scoping entails a search and review of available information and approaches for conducting the assessment. A systematic and transparent planning and scoping process promotes:

- Assurance that exposures being assessed are relevant and important
- Efficient time and resource management
- Agreement among the exposure assessor, risk assessor and risk manager/decision maker on the exposure assessment's purpose

**Figure 3-2. The Overall Risk Assessment Process**




Adapted from NRC (2009)

- Communication within the risk assessment team and with stakeholders
- Trust, buy-in and realistic expectations of stakeholders and other interested parties
- Better-informed decisions that use high-quality data, derived using scientifically established methods, and are based on established objectives
- Participation from multiple disciplines to ensure the scope and degree of scientific complexity adequately inform the exposure assessment question(s)
- Documentation of all decisions and the rationale behind those decisions.

A team approach to planning exposure assessments can be beneficial (NRC 2009; U.S. EPA 2002g). For routine screening-level exposure assessments conducted in accordance with established SOPs, a project team might not be required; for more complex assessments, however, a project team often is essential. At a minimum, the project team includes individuals with the necessary scientific expertise, representative members of the exposure assessment team, human health assessors, the risk assessor and the risk manager/decision maker. The team composition reflects the specific expertise required during various parts of the exposure assessment, including the planning discussion. For example, the risk manager/decision maker might identify the regulatory needs of the risk assessment, timeframes and amount of resources available for the analysis. The project team might focus on evaluating the current and future concentrations of contaminants in various media. An exposure assessor could help the team consider the nature of the contaminants and understand potential sources, contaminant routes and pathways, environmental fate, extent of contamination and data availability at the national or local level.

### 3.1.1. Exposure Assessment Goals and Scope

The goals of the exposure assessment determine its scope. The planning and scoping process for an exposure assessment begins with a dialogue among the project team to define the question at hand or the hypothesis the assessment seeks to address. The intent of problem formulation is to develop the dimensions and elements of the exposure assessment and to define the objectives clearly. Some assessments might benefit from stakeholder input, such as a site-specific assessment for which the community has information unique to that site that is not readily evident to the assessment team. Information gathered during this goal-setting stage helps an exposure assessor answer questions such as the following: What questions should the exposure assessment address? Why is an exposure assessment necessary? How will the assessment results be used? What resources and expertise are needed? What is the timeframe? The more information gathered at this step, the more clearly defined will be the scope.

Exposure assessments are carried out for many reasons, including for use in risk assessment, status and trends measurements, mitigation, regulatory decisions, priority setting and epidemiological study support. Specific goals for an exposure assessment might include identifying exposed individuals, lifestages, groups or populations and disparities in that exposure; screening chemicals for potential exposure and identifying the source(s) of contamination; defining exposure pathways, fate and transport properties and routes of exposure; and assessing temporal considerations.

To ensure the final assessment product meets the needs of the decision makers, the assessment team needs a clear understanding of the exposure assessment's purpose. The particular purpose for which an exposure assessment will be used (e.g., location-specific versus regional or national decision) and the availability of data often have significant implications for the scope, level of detail and approach. In addition, the team needs to understand the regulatory basis for the risk assessment and the kind of information needed to satisfy such requirements.

The planning and scoping process defines the elements that will be included in an exposure assessment. It helps the project team determine such issues as the bounds of the exposure assessment and the approaches to consider. Understanding the boundaries of the problem helps define the scope. For example, does an exposure or risk occur in a local community or nationally (U.S. EPA 2014f)?

Reconciling the limitations of the scope with the assessment questions requires careful consideration. For example, if data limitations preclude addressing questions the risk manager/decision maker poses, the assessment team will have to consider alternatives. These alternatives might include limiting the scope of the assessment, willingness to accept a higher level of uncertainty in the analysis by relying on default assumptions rather than empirical data, delaying the assessment pending the completion of studies to provide the data or relying on modeling with the associated assumptions. Thus, defining the scope of an exposure assessment is a process that can include both analytical and deliberative aspects.

Reasons for limiting the technical scope of an exposure assessment need to be stated explicitly and can include details on resource limitations, data and assumptions, impact of risk elements on the risk estimate and available methods. If an exposure assessment study is considered necessary but the resource commitment is uncertain, assessors might find conducting "back-of-the-

envelope" sensitivity analyses helpful in determining how important the study parameters are to regulatory decision making or problem solving. When an element of risk is likely important but no valid data are available, an exposure assessor needs to highlight this deficiency or use judgment or default values to approximate the missing data. Both the exposure assessment and risk characterization present such judgments and approximations, along with their implications (see Chapter 8).

The purpose of the exposure assessment and the quality and quantity of the available data, resources, level of acceptable uncertainty and statistical methodologies determine the approach. Thus, assessments use a tiered approach, often starting at the screening level and increasing the complexity, as required. Lower tier assessments might require few resources and can be sufficient for evaluating large numbers of agents. In contrast, addressing the most challenging problems might require a complex assessment. A goal during planning and scoping is to balance the informational needs of the risk assessor and risk manager/decision maker with a judicious use of time, expertise and other resources.

The initial phase of an exposure assessment often uses screening-level exposure analyses. At this point, little location- or scenario-specific information typically is available, and an exposure assessor relies on default values selected to ensure the analyses examine exposures that would fall at or beyond the high end of the expected exposure distribution. The assumption is that, if—in a bounding estimate scenario—risks are not anticipated, assessors, risk managers/decision makers and stakeholders can be confident the exposure evaluated is not a concern (U.S. EPA 2004c). An exposure assessor also might use probabilistic exposure assessment approaches during the screening-level analysis to identify key exposure parameters for further evaluation (e.g., sensitivity analysis; see Section 8.3). These approaches, however, more often apply when refining an exposure assessment. EPA programs also can implement specific procedures that vary from this basic process. Exposure assessors need to consult with their programs and follow their SOPs to the extent applicable to the particular situation.

Regulatory considerations can determine the exposure assessment approach. Aggregate exposure assessments (see Section 2.3.3) are required under the Food Quality Protection Act,[7] Safe Drinking Water Act,[8] Clean Air Act[9] and other regulatory programs. Various statutes require assessment of cumulative exposure (described in Section 2.3.3) to assess cumulative risk. For example, the 1996 Food Quality Protection Act requires assessments based on multiple pesticides with a common mechanism of action (later interpreted as mode of action by the Office of Pesticide Programs), whereas the 1970 National Environmental Policy Act[10] requires more broadly based cumulative assessments that consider multiple chemical and nonchemical stressors.

More complex exposure assessments might focus on exposures that attempt to represent actual environmental conditions or "what-if" (hypothetical) scenarios. Such assessments might require more data, use sophisticated models or rely on observational human exposure measurement

[7]Food Quality Protection Act of 1996, Pub. L. No. 104–170, 110 Stat. 1489 (U.S. EPA 1996c).
[8]Safe Drinking Water Act, 42 U.S.C. 300f et seq.
[9]Clean Air Act of 1963, 42 U.S.C. 7401 et seq.
[10]National Environmental Policy Act, 42 U.S.C. 4321 et seq.

studies to collect data and determine exposure factors. Complex exposure assessments often use probabilistic distributions for one, some or all of the parameters.

A systematic and transparent planning and scoping process promotes efficient time and resource management. Questions to consider include the resources and time available for an exposure assessor and risk manager/decision maker to address the problem, regulatory deadlines and requirements. Available resources and the schedule for a decision determine the effort for obtaining and analyzing the data. When conducting an exposure assessment, particularly when constrained by time or resources, an exposure assessor needs to identify the essential questions; translate those questions into specific scenarios; evaluate existing literature (e.g., systematic review); and, using that information, design an exposure assessment that addresses the needs of the risk manager/decision maker. The need to meet external deadlines or to coordinate with the schedules of other organizations can become limiting factors in deciding what can be prepared. In summary, a well-documented and rigorous planning and scoping process involving the assessors and risk managers/decision makers needs to be systematic and transparent (U.S. EPA 2014f).

### 3.1.2. Overarching Considerations

Among the overarching themes that EPA's risk assessments might address are children's environmental health protection, cumulative risk assessment and environmental justice considerations. Although these considerations might not affect all analyses, early consideration and discussion of these issues can enhance the utility of the risk assessment. Additionally, they could receive particular attention in the risk management arena, depending on the decision context. Such attention can be independent of a risk assessment or might require additional data to address one or more of the overarching considerations. Exposure assessors need to be cognizant of these issues so they can consider them during the planning and scoping process. Chapter 4 considers lifestage, susceptibility and environmental justice more fully.

### 3.1.3. Stakeholder Involvement

For highly visible assessments (e.g., Superfund cleanup), communication is the foundation for stakeholder involvement. For this document, EPA defines "communication" as the exchange of information and viewpoints between the Agency and stakeholders to achieve a goal or objective such as fostering greater understanding of science and assessment methods or gaining greater insight into diverse public views and concerns about the scenarios affecting the potential for exposure of individuals or a community to a defined agent [adapted from NAS (2017)]. This definition is consistent with that provided in Superfund's Community Engagement Toolkit documents (U.S. EPA 2013c), which note that "risk communication is a dialogue—an interactive process of information exchange—among the Site Team and the community that discusses the nature of risk and other concerns. This dialogue should be a genuine and sincere conversation that aims to identify mutual solutions and respond to public concerns." "Internal communication" refers to the exchange of information among the exposure science, assessment and decision making team.

Technical experts and risk managers/decision makers need to work together, informed by stakeholder input where applicable, to develop the rationale and scope for the exposure assessment (Box 3-1). EPA's public involvement policy (U.S. EPA 2003g) and the framework for its implementation (U.S. EPA 2003e) provide guidance for ensuring the public is engaged

and informed. Involving risk managers/decision makers, stakeholders and exposure assessors up front is critical to evaluating the exposure assessment question(s) fully and ensuring the design of the exposure assessment supports the agreed-upon objectives. Communication and dialogue with community and tribal members need to be established during the initial phases of an exposure assessment. EPA's Superfund program developed the *Community Involvement Tools and Resources* website, which focuses on Superfund activities but has application to other offices whose programs involve community outreach. Chapter 9 provides additional information on communication throughout the exposure assessment process.

**Box 3-1. Definitions of "Public," "Stakeholder" and "Community"**

*Public Involvement* refers to the full range of activities that EPA uses to engage tribal and the American people in the Agency's decision making process (U.S. EPA 2014f).

*Stakeholders* are individuals or representatives from organizations or interest groups who have a strong interest in the Agency's work and policies (U.S. EPA 2014f).

- *Internal Stakeholders* include EPA programs (U.S. EPA 2007b)
- *External Stakeholders* include the public, affected industries, public health or environmental organizations and other government agencies (U.S. EPA 2007b)

*Community Involvement* is the process of engaging in dialogue and collaboration with community and tribal members (U.S. EPA 2014f).

At the outset of the process, the assessment team determines the purpose of the assessment, what its objectives are and how to proceed and if a communication plan is deemed essential. An effective communication process is a two-way interaction between EPA staff and stakeholders: EPA explains the purpose and scope of the assessment to stakeholders and addresses issues of risk perception and, as applicable, stakeholders provide information to EPA on unique considerations (demographics, cultural aspects, traditions, etc.) of the site or scenario. For this reason, consulting with the community on the conceptual model (see Figure 3-1) might be advisable. In addition, the EPA staff should consider which outreach vehicles are most effective for interacting with the community: news media, local listservs, social media, community meetings and others. As the project proceeds, an essential function of the assessment team is to maintain ongoing communication with the stakeholders.

This dialogue might include asking the community to define questions they want answered and the way in which they wish to receive the results of the exposure assessment. Payne-Sturges et al. (2004) noted that effective communication and translation of the exposure assessment approach enables the community to "credibly represent the study's implications to policy makers and other stakeholders, thereby closing the loop between science and the community." Stakeholder involvement helps ensure the exposure assessment process is transparent and risk-based decision making proceeds effectively, efficiently and credibly (IOM 2013; NRC 2009).

The development of exposure assessments for regulatory decisions might require adhering to administrative procedures that clearly define and describe the process for engaging stakeholders. Stakeholders might include federal agencies; state, local and tribal governments; the regulated community; community members affected by an environmental release; and members of the public. The Presidential/Congressional Commission on Risk Assessment and Risk Management (1997) suggests the following questions to identify potential stakeholders:

- Who might be affected by the exposure/risk assessment?
- Who has information and expertise that might be helpful?
- Who has been involved previously in similar exposure/risk situations?
- Who has previously expressed interest in being involved in similar decisions?

Deciding how and when to involve stakeholders depends on the goals of an exposure assessment (i.e., regulatory or non-regulatory). For routine or well-defined screening exposure assessments, input during planning and scoping might not be necessary, whereas for an exposure assessment considered divisive, stakeholder involvement is appropriate. For community-based or location-specific exposure assessments, seeking and encouraging community involvement is important. In some cases, continuing dialogue with the community throughout the process is encouraged. Each project plan should include a list of critical points for stakeholder input, such as discussions on purpose, scope and approach. The team might decide to assign stakeholders with relevant expertise to subgroups that have specific tasks within appropriate regulatory considerations (U.S. EPA 2003d).

EPA recognizes the community could be aware of unique activities or practices that might result in higher or lower exposure assumptions than the default assumptions used in an exposure assessment. Some members of the community might possess information that could influence exposure scenarios and health concerns. Types of information community members and local agencies might provide include:

- Local exposure conditions and exposure factors (e.g., population-specific survey(s) on food consumption)
- Community health concerns and observations (e.g., specific areas where children play)
- Critical information on potential or actual exposure scenarios (e.g., past actions at a landfill)
- Highly exposed or susceptible population groups (e.g., subsistence activities, proximity to a smelter).

Through community involvement practices and communication, a project team establishes a plan to work with the community to identify sources of exposure assessment-specific information and concerns and to communicate with them throughout the exposure assessment (U.S. EPA 2016e).

Community involvement activities are essential to meeting data quality guidelines (U.S. EPA 2002f) and help improve transparency of the exposure assumptions, ultimately building trust and credibility with the community. This is particularly important when dealing with scenarios that differ substantially from the general population such as tribal and indigenous populations (see Section 4.3.2). Information and suggestions regarding community involvement in the Superfund process (U.S. EPA 2016e) can be helpful for other Agency exposure assessments. Links to some relevant community involvement resources are provided in Box 3-2.

**Box 3-2. Community Involvement Planning Resources**

- U.S. EPA (1996a) *Community Advisory Groups: Partners in Decisions at Hazardous Waste Sites Case Studies*. EPA/540/R-96/043.
- U.S. EPA (2000f) *Presenter's Manual for "Superfund Risk Assessment and How You Can Help." A 40-Minute Videotape.* EPA/540/R-99/013.
- U.S. EPA (2001i) *Stakeholder Involvement & Public Participation at the U.S. EPA: Lessons Learned, Barriers, & Innovative Approaches.* EPA/100/R-00/040.
- U.S. EPA (2016e) *Superfund Community Involvement Handbook.* EPA/540/K-05/003.
- *Additional Resources for Citizen Involvement in Source Water Protection* website. U.S. EPA. Includes community resources on protecting drinking water and source water at the community level.
- *Community Involvement Tools and Resources* website. U.S. EPA. Includes community resources, community involvement policies and guidance and Superfund community involvement publications.
- *Plain English Guide to the Clean Air Act* website. U.S. EPA.
- *Public Participation Process for Registration Actions* website. U.S. EPA.

## 3.1.4. EPA's Tribal Program and Networks

EPA's Tribal Program has established working relationships with tribes. Assessors should engage with their Tribal Program Managers and with program-specific project managers and coordinate with other Agency risk assessors, where appropriate, to include tribal perspectives when conducting exposure assessments and to facilitate clear communication with tribal partners (Box 3-3).

**Box 3-3. Resources Relevant to Exposure Assessment for Tribal Populations**

- U.S. EPA (2003d) *Framework for Cumulative Risk Assessment*. EPA/630/P-02/001F.
- U.S. EPA (2006b) *Consulting with Indian Tribal Governments at Superfund Sites: A Beginner's Booklet.* Introduces EPA staff and managers to the basics of government-to-government consultation with Indian tribal governments within the context of the Superfund program.
- U.S. EPA (2007a) *Amendments to Superfund Hazard Ranking System Guidance Incorporating Native American Traditional Lifeways.* (OSWER-9200.0-66). Presents ways that EPA can consider traditional lifeways in the Hazard Ranking System to determine eligibility for a site on the National Priorities List under the Superfund program.
- U.S. EPA (2007c) *Concepts, Methods and Data Sources for Cumulative Risk Assessment of Multiple Chemicals, Exposures and Effects: A Resource Document*. EPA/600/R 06/013F.

The Agency's network of Tribal Partnership Groups facilitates the exchange of technical information and communication between tribes and EPA. The National EPA-Tribal Science Council works to integrate and increase tribal involvement in EPA's scientific activities, while the National Tribal Toxics Council provides tribal input on issues related to toxic chemicals and pollution prevention. Assessors should engage with these partnership groups, through EPA's Tribal Program, to better understand tribal lifeways and to discuss and collaborate on research needs.

## 3.1.5. Peer Review

EPA defines peer review as a documented process for enhancing an Agency product so that the decision the Agency takes based on that product has a sound, credible basis (U.S. EPA 2015c). Peer review is a critical appraisal of a specific Agency product conducted to evaluate the

technical and scientific quality of an Agency product. Peer review usually involves a one-time interaction or a limited number of interactions between the authors of the work product and the peer reviewers. EPA encourages peer review to take place during the early stages of the project or as part of the culmination of the work product, as appropriate (U.S. EPA 2015c). During the planning and scoping process, the risk manager/decision maker might need to determine whether any analyses or products of an exposure assessment merit a separate peer review. Evaluating potential peer-review requirements early will help ensure allocation of adequate resources. In addition, peer-review considerations are an integral part of setting exposure assessment milestones and schedules.

EPA's *Peer Review Handbook, 4th Edition* (U.S. EPA 2015c) provides detailed guidance for determining when peer review is required and how to plan and implement a peer review. The principle underlying the Agency's peer-review policy is that expert panels will peer review all influential scientific and technical work products used in decision making. The Office of Management and Budget considers specific types of exposure assessments to be examples of "highly influential scientific assessments" (U.S. EPA 2006e). A scientific or technical work product that has a major impact; involves precedential, novel or complex issues; or has a legal or statutory requirement to be peer reviewed needs to undergo peer review. For example, major assessments such as those involving arsenic, mercury or other agents with complex methodological or scoping issues require peer review. In general, conceptual models and exposure assessment plans can be candidates for peer review (U.S. EPA 2015c).

Exposure assessment products also could be the subject of public comment, as some specific regulatory programs require. Public commenters generally include a wide range of interested individuals not expected to provide the kind of independent, expert information and in-depth analyses obtained from the peer-review process (U.S. EPA 2015c). An exposure assessment also might benefit from other types of review such as peer input. EPA's *Peer Review Handbook, 4th Edition* defines peer input as "a form of peer involvement that generally connotes an interaction during the development of an evolving Agency work product, providing an open exchange of data, insights and ideas." The risk manager/decision maker needs to consider whether to include such reviews and factor them into the schedule and resources for the assessment.

## 3.2. Problem Formulation

Problem formulation builds on the information developed during the planning and scoping process. Problem formulation is the process by which the project team develops preliminary hypotheses about how exposure occurs and why adverse effects might occur or have occurred. Standard Agency practice integrates the problem formulation concept, as described in *Guidance on Cumulative Risk Assessment. Part 1. Planning and Scoping* (U.S. EPA 1997a), *Microbial Risk Assessment Guideline: Pathogenic Microorganisms with Focus on Food and Water* (U.S. EPA 2012e), *Framework for Cumulative Risk Assessment* (U.S. EPA 2003d) and *Framework for Human Health Risk Assessment to Inform Decision Making* (U.S. EPA 2014f). The National Research Council (NRC) emphasizes problem formulation as an integral component of any exposure assessment planning activity (NRC 2009). Problem formulation is a systematic planning step that identifies major factors for consideration in the exposure assessment, providing its foundation. It involves all relevant parties, including the exposure assessor, risk

assessor, risk manager/decision maker, communication specialist and, when appropriate, relevant stakeholders and other interested parties.

Three components comprise problem formulation: (1) identification of the individual, lifestage(s), group(s) or population(s) of concern that are the subject(s) of the assessment (e.g., general population, infants or nursing mothers, older adults); (2) a conceptual model that presents the anticipated pathway of the agent from source to the subject of concern; and (3) an analysis plan that lays out the approach for conducting the assessment.

### 3.2.1. Individuals, Lifestages, Groups, Populations

One important aspect of an exposure or risk analysis is the approach to representing the receptor (see Chapter 4). When data are limited, assessors sometimes use a scenario-based approach—based on a defined set of facts, assumptions and inferences about who is exposed and how—to estimate exposures based on intensity, duration and frequency of exposure. For such an approach, an exposure assessor defines a specific receptor of interest, usually because of a distinguishable characteristic or behavior that might predispose the individual, lifestage, group or population to a potentially greater exposure concentration.

Population-based approaches are common when assessors need exposure information within a broader context. The *Framework for Cumulative Risk Assessment* defines population-based approaches as those that look at one population for many stressors (U.S. EPA 2003d). The scenario-based approach is a hypothetical situation based on a combination of measured and, where data are unavailable, modeled estimates of a chemical in the environment or human tissue (NRC 2009) and can include screening for pathways and chemicals of concern (U.S. EPA 1989b). In contrast to scenario-based approaches, a population-based approach frequently incorporates probabilistic methods with an objective to better estimate interindividual variability in exposure.

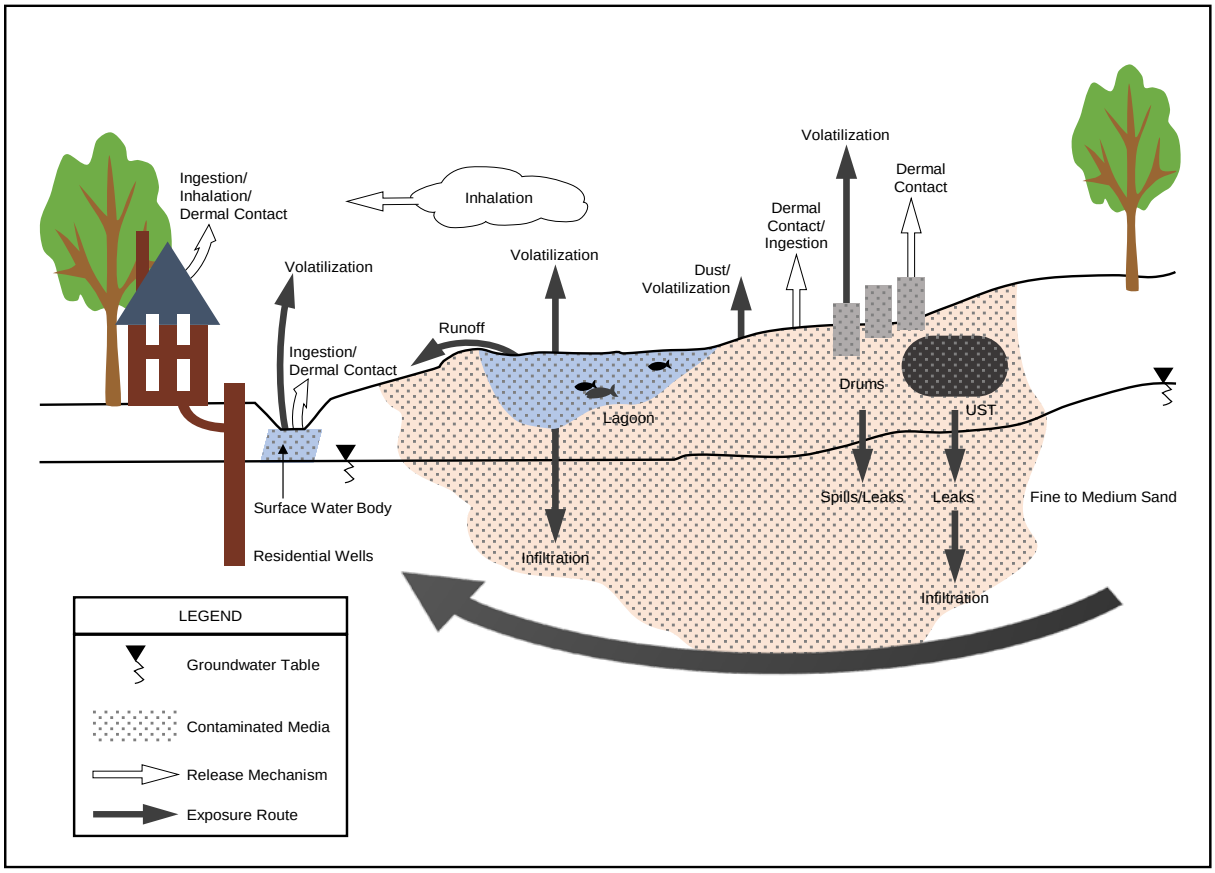
Exposed individuals or populations can be grouped by various characteristics (e.g., age, sex, culture, behavior, socioeconomic status, location relative to the release of a contaminant, occupation), lifestages or discrete populations for an exposure assessment. Exposure assessors need to identify and characterize the conditions that lead to the highest concentrations and resulting exposures and the situations that lead to exposure for the most susceptible individual, lifestage, group or population (U.S. EPA 2009a). An exposure assessor often needs to establish a dialogue with toxicologists/health scientists to consider whether a specific "window of susceptibility" during a given lifestage is important to a particular risk assessment.

An assessor frequently calculates individual risk for some or all of the individuals who represent the population. In reality, individuals within a population fall within a distribution of exposures based on personal characteristics and individual activities and behaviors. As a result of multiple broad-based exposure assessments (Dockery et al. 1993; U.S. EPA 1987c; U.S. EPA 2003f; U.S. EPA 2005f; U.S. EPA 2009f; U.S. EPA 2011a), the exposure science field has evolved to recognize the contribution of individual characteristics and activities to exposure, recognizing that not all individuals are alike, behave the same way or are exposed to the same concentration of a chemical.

## 3.2.2. Conceptual Model

The conceptual model is a planning tool used for various types of exposure assessments, including site-specific, local-scale and national-scale problems/assessments. The conceptual model identifies known or potential sources of contamination (soil, groundwater, surface water, air); release mechanisms and receptor routes; all potential exposure pathways (including secondary pathways); and the media and receptors associated with each (U.S. EPA 2001g). The conceptual model maps out a framework that demonstrates the theoretical links between the pollutant source or agent and exposure points. It provides a convenient format to present an overall understanding of the problem and organizes available information in a structure that facilitates identifying missing data or uncertainty. The conceptual model has features of both a scientific hypothesis and a work plan. Figure 3-3 shows an example conceptual model.

**Figure 3-3. Example of a Conceptual Site Model**




Adapted from U.S. EPA (1989a)

Developed at the start of a project, the conceptual model is refined and updated throughout the duration of the exposure assessment activities. The conceptual model serves as an important communication tool for the project team, stakeholders and other interested parties. Community members can provide input along the way to help refine exposure scenarios and health concerns.

When developing a conceptual model, a project team needs to consider the technical elements of the exposure assessment that are consistent with the six dimensions described in EPA's

*Guidance on Cumulative Risk Assessment: Part 1. Planning and Scoping* (U.S. EPA 1997a), and a seventh added to emphasize this important aspect of human health exposure assessment:

1. **Individual/lifestage/group/population at risk:** Who/what is at risk?
2. **Sources:** What are the relevant sources of agents?
3. **Stressors:** What are the agents of concern?
4. **Pathways, fate and transport and routes of exposure:** What are the relevant exposures?
5. **Health effect endpoints:** What are the health effect endpoints? Are there specific windows of susceptibility to address? How are the exposure outputs linked to the health endpoints?
6. **Timeframes of exposures:** What are the relevant frequency, duration, magnitude and overlap of exposure intervals for a chemical agent or mixture of agents?
7. **Exposure-to-dose considerations:** What is known about the toxicokinetics? How do lifestage, race, sex, genetics and other factors influence exposure-dose?

An early step in developing the conceptual model is identifying health effect endpoints and exposure-to-dose considerations, which are part of the hazard identification step of a risk assessment. EPA programs also might implement specific procedures that vary from this basic process. Exposure assessors need to consult with their programs and follow their SOPs regarding development of a conceptual model.

Another early step in developing a conceptual model is to identify possible sources of the agent(s). In some cases, the source is unknown. Whether the source is a point source (e.g., discharge from a pipeline) or nonpoint source (e.g., runoff from a field) is important. Identifying the principal source(s) can improve the ability to estimate the releases quantitatively and to predict the exposure better. The conceptual model describes the relevant exposure pathways and routes of exposure and the fate and transport of agents in the environment. Understanding the possible movement and transformation of chemicals from their source through the environment helps assessors evaluate the nature and form of the chemical that could reach the exposed population. Characteristics of the source and medium dictate the fate of the chemicals of interest. Physical (e.g., gas to aerosol or liquid) transformation of chemicals can occur over the exposure pathway. Chemical degradation also can change the form and amount of a chemical available for exposure (e.g., DDT [dichlorodiphenyltrichloroethane] degrades to DDE [dichlorodiphenyldichloroethylene] and DDD [dichlorodiphenyldichloroethane]). Processes that can alter the agent also can occur, including photolysis; reactions with other chemicals in air, water or soil; degradation by microbes; or adsorption onto the medium. Environmental media are sampled to characterize the concentration of chemicals in each medium and the fate and transport of chemicals from a source to receptors.

The conceptual model can take a variety of forms, such as a flow diagram or a pictorial depiction incorporating data, models and hypotheses (see Box 3-2). A detailed narrative explaining the rationale for the elements and their linkages, including the risk management options can accompany the graphical display. Examples of conceptual models are available from many sources including U.S. EPA (1991a); U.S. EPA (1996d); U.S. EPA (2001g); and Brady (2011).

In summary, a conceptual model involves identifying what chemical, physical and biological processes act on the agent and the product resulting from the process.

## 3.3. Exposure Assessment Analysis Plan

Assessors conduct exposure assessments at various levels of technical detail. Sometimes the estimation of exposure uses more than one approach. For example, the Total Exposure Assessment Methodology Study combined point-of-contact measurements, the microenvironment (scenario evaluation) approach and breath measurements for the reconstruction of dose approach (U.S. EPA 1987c). The intended use of an exposure assessment generally will favor one approach for quantifying exposure over others or suggest combining two or more approaches. The analysis plan for the exposure assessment specifies the technical details of how to conduct the exposure assessment. In developing the exposure assessment analysis plan, an exposure assessor considers the data sources, gaps, limitations, quality and needs; methods for developing exposure estimates; and exposure scenarios that reflect the conceptual model. Box 3-4 presents resources for technical study design for various types of data acquisition approaches.

**Box 3-4. Resources for Technical Study Design of Observational Human Exposure Measurement Studies**

*Data Acquisition*

- Database Design (U.S. EPA 2018c).
- Sample Size (Baguley 2004; Dell et al. 2002; Devane et al. 2004; Dupont and Plummer Jr. 1990; Dupont and Plummer Jr. 1998; Kieser et al. 2004; Marshall 1996; Rippin 2001; Salganik 2006; Vaeth and Skovlund 2004).
- Temporal Considerations (Buck et al. 1995).

*General Study Design*

- Observational Human Exposure Measurement Studies (Adgate et al. 2000; Buckley et al. 2000; Callahan et al. 1995; Daston et al. 2004; Fenske et al. 2005; Lebowitz et al. 1995; Morgenstern and Thomas 1993; Özkaynak et al. 2005; Pellizzari et al. 1995; Quackenboss et al. 2000; Rice et al. 2003; U.S. EPA 1998; U.S. EPA 2005d; Vojta et al. 2002).

For exposure assessments conducted as part of a risk assessment, the exposure assessment analysis plan describes how the data will be collected, analyzed and used in a risk assessment. Depending on the data needs, approach selected and complexity and interest in an exposure assessment, the analysis plan might need additional documentation. Such documentation includes descriptions of the sampling strategy (e.g., purpose, design, quality objectives/control measures), modeling approach (e.g., needs, goals, availability of input parameters, use of model outputs in the exposure assessment) and communication plan (e.g., personnel involved, types of communication planned and scheduled) (see Chapter 9). The exposure assessment analysis plan needs to be reevaluated throughout the life of the exposure assessment to ensure appropriate risk management decisions. Exposure assessors need to consult with their programs and follow any available SOPs.

### 3.3.1. Data Sources, Gaps, Limitations and Quality Objectives

The approach selected for an exposure assessment will determine data and information needs. As part of the exposure assessment analysis plan, a project team characterizes the type of data

needed to answer an exposure assessment question or hypothesis. The information and rationale described during the development of the conceptual model is instrumental in determining assessment-specific data needs. An exposure assessor might consider the nature of the contaminants, the location of the exposure, the extent of contamination and the availability and representativeness of data at national, regional or local scales.

The data necessary for meeting exposure assessment objectives could be available or additional data might need to be collected. Key steps in determining the availability of data include conducting a review of the literature, identifying existing datasets and evaluating possible critical data gaps and specific data needed to fulfill the assessment's data requirements.

The exposure assessment analysis plan also specifies data quality objectives and quality assurance measures for all data used in an exposure assessment. As specified in the *Guidance on Systematic Planning Using the Data Quality Objectives Process* (U.S. EPA 2006e), Data quality objectives are a set of performance and acceptance criteria that ensure the newly collected and existing data are of sufficient quality and quantity to address the project's goals (see Section 5.3).

A wide range of existing data can support an exposure assessment. When developing the exposure assessment analysis plan, the project team identifies datasets relevant to the conceptual model and associated assessment questions. Table 3-1 provides examples of the types of datasets linked to key exposure questions and conceptual model elements.

Chapter 5 addresses the topic of data availability and quality.

**Table 3-1. Examples of Datasets Useful for a Location-Specific Exposure Assessment**

| Populations at Risk | Sources | Environmental Data | Exposure Pathways | Exposure-to-Dose Considerations | Exposure Factors |
|---|---|---|---|---|---|
| • Demographic data<br>• Local survey data<br>• Site assessments | • Emission inventories<br>• Product information<br>• Land use (current, planned) | • Historical environmental sampling data (e.g., air, water, soil, biota)<br>• Personal monitoring data<br>• Climatic or meteorological data<br>• Hydrogeological data<br>• Stationary air sampling data | • Surveys of activity patterns used to establish exposure factors<br>• Human exposure factors data<br>• Land use (current, planned) | • Toxicological data<br>• Bioconcentration/bio-accumulation data<br>• Physiologically based pharmacokinetic models | • Activity patterns<br>• Physiological parameters |

## 3.3.2. Exposure Scenarios

Exposure scenarios describe the combination of facts, assumptions and inferences that define a discrete situation or activity in which potential exposures occur (Sheldon 2010; U.S. EPA 2003c). Exposure assessors create exposure scenarios to help estimate exposure of humans to chemicals in their environment. Exposure scenarios might include the source, exposed population (e.g., young children), timeframe of exposure, routes and pathways of exposure, microenvironment(s) and human activities. The term microenvironment refers to surroundings (e.g., home, office, automobile) treated as homogeneous or well characterized with regard to the concentrations of an agent. People are exposed to a variety of potentially harmful chemicals through the air they breathe, food they eat and products they use and by skin contact with treated or contaminated surfaces. Examples of sources are places, objects, activities or entities that

release chemicals (e.g., hazardous waste disposal facility, pesticide application, vehicular traffic, industrial or mining operations). Assessors might want to consider both current and future exposure scenarios because land use and associated activities can change over time.

## 3.4. Summary

- Systematic and transparent **planning and scoping** promotes efficient time and resource management; agreement on the assessment's purpose; communication within the team and with stakeholders; stakeholder buy-in and realistic expectations; better-informed decisions with high-quality data based on established objectives and using sound methods; participation from multiple disciplines; and documentation of decisions made and the rationales.
  - A thorough **understanding of the purpose** of the assessment ensures utility of the information evaluated in meeting the established **goals**. Understanding the boundaries of the problem helps define the **scope**.
  - Depending on the nature of the assessment, **involving stakeholders** is essential for meeting EPA's data quality guidelines, improving transparency of the exposure assumptions and building trust and credibility for the Agency.
  - The principle underlying EPA's **peer-review policy** is that all influential scientific and technical work products used in decision making need to be peer reviewed.
- **Problem formulation** has three key components: (1) identification of the individual, lifestage(s), group(s) or population(s) of concern; (2) a conceptual model presenting the anticipated pathway of the agent from the source to receptor of concern; and (3) an analysis plan that charts the approach for conducting the assessment.
  - Representing the receptor is critical to formulating the problem in exposure assessment. In many cases, especially when data are limited, assessors can rely on a **scenario-based approach.** Assessors might also use population-based approaches to better estimate interindividual variability in exposures.
  - Developed at the start of the exposure assessment and updated throughout the duration, the **conceptual model** identifies known or potential sources of contamination, postulates release mechanisms and receptor routes and suggests all potential exposure pathways and the media and receptors associated with each.
  - The **exposure assessment analysis plan** specifies the technical aspects of conducting the assessment, including the data sources, gaps, limitations, quality and needs; methods for developing exposure estimates; and exposure scenarios that reflect the conceptual model. For exposure assessments conducted as part of a risk assessment, an exposure assessment analysis plan describes how the data will be collected, analyzed and used in the risk assessment.

# CHAPTER 4. CONSIDERATION OF LIFESTAGES, VULNERABLE GROUPS AND POPULATIONS OF CONCERN IN EXPOSURE ASSESSMENTS

Differences in exposure and varied responses to exposure can occur across individuals, lifestages, specific groups and populations. Addressing one or more contributors of human vulnerability and susceptibility in exposure assessment presents a challenge. Where appropriate, exposure assessors consider unique characteristics and sociodemographic factors that might increase exposure or predispose an individual, lifestage, specific group or population to greater health risk. These factors include age, sex, genetic variation, cultural characteristics, behaviors, occupation, socioeconomic status, race/ethnicity and geographic location. Incorporating measures of population vulnerability (differential exposures), including racial, social and cultural aspects, in developing and implementing environmental regulations and policies is an important goal of EPA's environmental justice, children's environmental health protection and tribal programs.

The public expects EPA to make advancements in developing exposure assessments that better reflect reality, which is consistent with recommendations from the National Academy of Sciences and the EPA Science Advisory Board (NRC 2009; NRC 2012a; SAB 2000). Tools and methods are available and continue to be developed to incorporate vulnerability factors in exposure assessments. Programs might need to tailor their approaches to incorporate population-specific issues in exposure assessments to meet their regulatory, program or policy needs.

Assessments involving potentially vulnerable populations can consider economic, public health and other factors along with environmental conditions (see Section 3.2). As appropriate, exposure assessors identify and characterize those conditions that lead to the highest agent intensities and resulting exposures and those situations that lead to exposure for the most susceptible receptors (U.S. EPA 2009a). Considering vulnerability and susceptibility when making risk management decisions is essential for protecting not only the general population but also those populations at greatest risk (U.S. EPA 1995b; U.S. EPA 2010b).

This chapter describes available tools to identify and evaluate differential exposures of individuals, lifestages, vulnerable groups and populations of concern:

- The history of EPA's activities in addressing populations of concern in exposure assessment (Section 4.1)
- Vulnerability and susceptibility in exposure assessment (Section 4.2)
- Examples of exposure factors for populations of concern (Section 4.3).

Section 4.4 summarizes this chapter.

## 4.1. History of EPA Exposure Assessments for Lifestages, Vulnerable Groups and Populations of Concern

Numerous executive orders, policies and legislative mandates emphasize EPA's commitment to considering lifestages, vulnerable groups and populations of concern in exposure assessments (Box 4-1). Additional information on consultation and policies related to working with federally recognized tribes is found at EPA's website, *Environmental Protection in Indian Country*. Provisions in the Food Quality Protection Act of 1996, the Safe Drinking Water Act Amendments of 1996, the Frank R. Lautenberg Chemical Safety for the 21st Century Act (which amended TSCA) and other laws underscore these policy priorities by requiring a focus on the evaluation of unique population exposures, susceptibilities and vulnerabilities in the context of risk assessments and regulatory and policy decision making.

**Box 4-1. Provisions of Presidential Executive Orders**

- Executive Order No. 12898 (1994). *Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations*. Federal agencies, wherever practicable and appropriate, are required to:
  - Collect and analyze data assessing and comparing environmental and human health risks borne by ethnic minorities and low-income populations
  - Identify and address disproportionately high and adverse environmental or human health effects of its programs, policies and activities on minority and low-income populations.
- Executive Order No. 13045 (1997). *Protection of Children from Environmental Health Risks and Safety Risks*. For each regulatory action that meets the criteria of Executive Order 13045, federal agencies need to provide the following to the Office of Management and Budget's Office of Information and Regulatory Affairs for review:
  - An evaluation of the environmental health or safety effects of the planned regulation on children
  - An explanation of why the planned regulation is preferable to other potentially effective and reasonably feasible alternatives the Agency is considering.
- Executive Order No. 13175 (2000). *Consultation and Coordination with Indian Tribal Governments.* Federal agencies have an accountability process to ensure meaningful and timely input by tribal officials in the development of regulatory policies that have tribal implications.

A growing body of literature (e.g., Agency guidance documents, government reports, scientific articles, reports by environmental health and justice advocates) also highlights the importance of evaluating differences in exposures among sociodemographic groups and accounting for the social, cultural, economic and political context in which such exposures occur (Box 4-2).

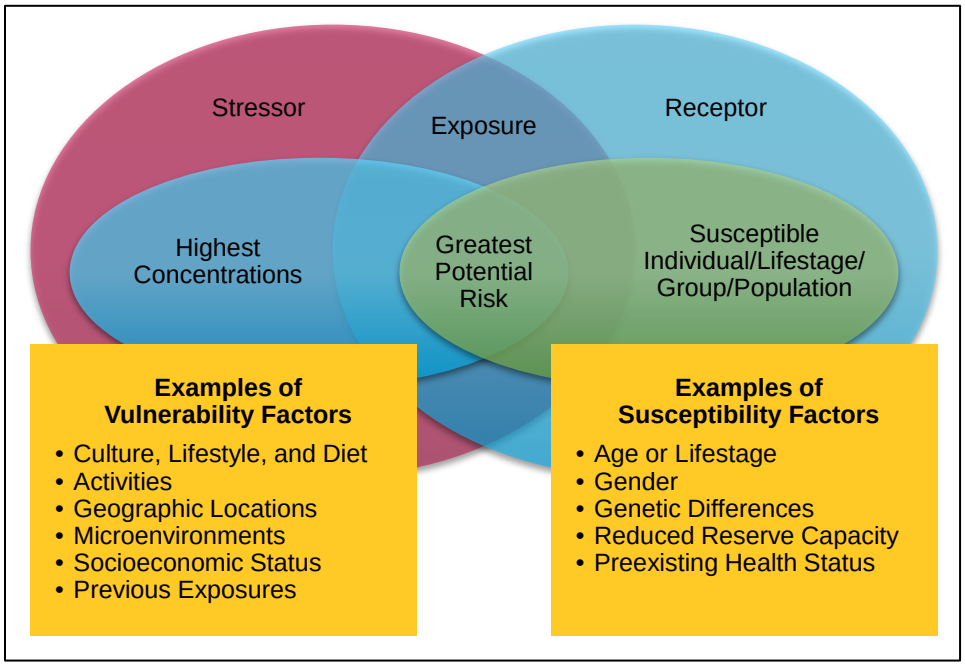
## 4.2. Vulnerability and Susceptibility in Exposure Assessment

Environmental exposures and health risks are distributed unequally across the landscape and, in some cases, are concentrated among certain population groups and in potentially vulnerable communities (Northridge 2011). The population characteristics related to vulnerability (e.g., lifestyle, culture, diet, daily activities) and susceptibility (e.g., genetics, lifestage, gender) are important because these factors, in conjunction with the toxicity of environmental contaminants, could translate into differential health risks. The planning and scoping phase of the exposure assessment is the optimal point for the exposure assessor to outline the approach for identifying and considering population vulnerability and for conceptualizing the linkages to health, exposure and risk. Figure 4-1 depicts vulnerability and susceptibility factors in exposure assessments.

## Box 4-2. Resources on Disparities in Exposure

- NRC (1993) *Pesticides in the Diets of Infants and Children.* Recommends changes in policy and risk assessment practices to better reflect children's health and exposure factors in evaluating exposure to pesticides in food and water.
- U.S. EPA (1999c) *Sociodemographic Data Used for Identifying Potentially Highly Exposed Populations*. EPA/600/R-99/060. A companion document to the U.S. EPA (2011d) *Exposure Factors Handbook: 2011 Edition*. EPA/600/R-09/052F.
- NEJAC (2004) *Ensuring Risk Reduction in Communities with Multiple Stressors: Environmental Justice and Cumulative Risks/Impacts*. Recommends incorporating measures of population vulnerability (differential exposures), especially social and cultural aspects, in risk assessments.
- U.S. GAO (2005) *Environmental Justice: EPA Should Devote More Attention to Environmental Justice When Developing Clean Air Rules.* Recommends more explicit analysis of disparities in exposures and risk because of air pollution.
- U.S. EPA (2006d) *A Framework for Assessing Health Risks of Environmental Exposures to Children.* EPA/600/R-05/093F. Assists in conducting exposure assessments for children.
- U.S. EPA (2006f) *Guide to Considering Children's Health When Developing EPA Actions: Implementing Executive Order 13045 and EPA's Policy on Evaluating Health Risks to Children*.
- U.S. EPA (2011d) *Exposure Factors Handbook: 2011 Edition.* EPA/600/R-09/052F.
- U.S. EPA (2011f) *Plan EJ 2014*. A roadmap for integrating environmental justice into the Agency's programs, policies and activities.
- *Frank R. Lautenberg Chemical Safety for the 21st Century Act* (2016) website. U.S. EPA. Defines potentially exposed susceptible subpopulations as a group of individuals within the general population that EPA identifies who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly.
- *Tribal Science Priorities* website. U.S. EPA. Presents environmental and health priorities the National EPA-Tribal Science Council identifies.
- *Environmental Justice* website. U.S. EPA. Presents information for environmental justice considerations for healthy environments and communities.
- EPA-ExpoBox, an online toolkit to help individuals in government, industry and academia and the public assess exposure.

**Figure 4-1. Vulnerability and Susceptibility Factors**




Adapted from U.S. EPA (2009a)

Vulnerability refers to characteristics of individuals or populations that place them at increased risk of an adverse health effect. Vulnerability includes economic, demographic, social, cultural, psychological and physical states of the receptor that influence patterns of exposure to environmental contaminants or alter the relationship between the exposure to environmental contaminants and the health effect of the exposed individual or population (ATSDR 1997; deFur et al. 2007; U.S. EPA 2003d). Susceptibility refers to the increased likelihood of an individual or population to be more affected by exposure to an agent as compared to the general population because of intrinsic biological factors such as lifestage, genetic polymorphisms, prior immune reactions, disease state or prior damage to cells or systems (U.S. EPA 2003d).

EPA's *Framework for Cumulative Risk Assessment* (U.S. EPA 2003d) describes four properties of vulnerability, the first two of which are most relevant for exposure assessment:

- **Differential susceptibility:** An increased likelihood of sustaining an adverse effect from exposure to an agent. For example, an individual, group or population might be more likely to show a response to an agent at a lower dose than the general population because of a preexisting health condition (e.g., asthma, cardiovascular disease, genetic variation, prior damage from exposure, concurrent exposures to other stressors or lifestage [e.g., children, older adults, pregnant women]).
- **Differential exposure:** Differences in exposure (e.g., magnitude, duration, frequency, pathway, route) from a variety of factors, including lifestage, socioeconomic status and cultural characteristics. For example:
  - Children might have a higher exposure and proportionally higher body burden of pesticides than adults because of their behavior patterns or food consumption (Moya et al. 2004; NRC 1993).
  - When neighborhoods are racially segregated, nonwhites might live in lower socioeconomic conditions where they experience higher exposures to air pollution (Lopez 2003).
  - Studies on fish consumption and subsistence fishing patterns have documented racial/ethnic differences (Burger 2000; Burger 2002a; Burger 2002b; Burger et al. 2001; Burger et al. 1999a; Burger et al. 1998; Burger et al. 1993; Burger et al. 1999b; Corburn 2002).
  - Native Americans can be exposed differentially to toxicants when dietary patterns involve consumption of locally caught fish or game for traditional or religious reasons (Fitzgerald et al. 1999; Fitzgerald et al. 1995; Fitzgerald et al. 1998; Fitzgerald et al. 2001; Harper et al. 2002; Schell et al. 2003).
- **Differential preparedness:** The coping systems and resources that an individual, community or population uses or can access to withstand the insult of agents.
- **Differential ability to recover:** Refers to resources and coping systems, such as income level, ability to move from an affected area or access to health care, which can affect recovery from the effects of an agent.

## 4.3. Examples of Lifestages, Vulnerable Groups and Populations of Concern in Exposure Assessment

Sections 4.3.1 through 4.3.3 discuss exposure concerns for lifestages (particularly for childhood), tribal populations (e.g., American Indian, Alaska Native, other indigenous populations), other racial and ethnic groups (e.g., African Americans, Hispanic or Latino Americans, Asian Americans, Pacific Islanders) and socioeconomically disadvantaged populations. Note that the concerns described under one section might overlap with another.

### 4.3.1. Lifestages

The term "lifestage" refers to a temporal stage of life with distinct anatomical, physiological, behavioral or functional characteristics that contribute to potential differences in vulnerability to environmental exposures (U.S. EPA 2006d). Unlike particular groups that form a relatively fixed portion of the population (e.g., groups based on ethnicity), lifestages or age groups encompass the entire population over time. Rather than considering children as a group, the Agency has moved toward viewing childhood as a sequence of lifestages from conception through fetal development, infancy and adolescence (U.S. EPA 2005c).

EPA's *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (U.S. EPA 2005c) follows the Agency's established policy of viewing childhood as a sequence of lifestages. Other lifestages to consider when assessing exposure and risk are pregnancy, nursing and older adults. For each lifestage, exposures typically differ. For example, during pregnancy, eating habits and nutritional needs change; in the third trimester, mobility can be affected, which in turn can alter exposure. During the nursing lifestage, fluid intake increases. As one ages, mobility, the level or intensity of exercise and caloric intake can decline, and aging can affect the body's ability to defend against toxic agents.

During the planning and scoping process (see Section 3.1), exposure assessors establish dialogue with toxicologists/health scientists to consider specific "windows of susceptibility" for an exposure assessment. For example, a window of susceptibility in development when an agent causes the greatest effect, a description of that period and an estimate of the exposure during that window are key in informing the exposure assessment. If data exist that support early life exposures leading to effects later in life, exposure assessors can discuss them during planning.

**Childhood**

In 1993, the National Research Council (NRC) issued *Pesticides in the Diets of Infants and Children*, which highlighted many important differences between children and adults regarding exposure to and risks posed by pesticides (NRC 1993). The NRC report provided the impetus for Executive Order 13045 (1997), which states that "each federal agency…shall ensure that its policies, programs, activities and standards address disproportionate risks to children that result from environmental health risks or safety risks." In response to these policies and statutes, EPA is improving methods for conducting exposure assessments for children.

In 1995, EPA released its *Policy on Evaluating Risk to Children*, which directs the Agency to take into account, explicitly and consistently, environmental health risks to infants and children in all risk characterizations and public health standards set for the United States (U.S. EPA

1995b). In 2013 and again in 2018, EPA reaffirmed its support of this important policy. Since fall 1996, the Agency has followed the *National Agenda to Protect Children's Health from Environmental Threats* (U.S. EPA 1996b). The Agency has developed guidance on selecting a consistent set of age groups to consider when assessing childhood exposure to environmental contaminants (U.S. EPA 2005c).

Childhood exposures to environmental contaminants often differ from those in later stages of life for several reasons, including differences in behavior and physiology (Cohen Hubal et al. 2000; Moya et al. 2004). Children consume more of certain foods (e.g., milk and fruit) and water and have higher inhalation rates per unit of body weight than adults. For example, consumption of apples by children between birth and 5 months of age is about 19 g/kg/day, whereas consumption by adults 20 years and older is approximately 2 g/kg/day, almost a 10-fold difference (U.S. EPA 2003b). Children also have higher excretion and metabolic rates per unit body weight than adults. Young children play close to the ground, contact soil outdoors, contact dust on surfaces and carpets indoors and display more hand-to-mouth and object-to-mouth activity than adults (Cohen Hubal et al. 2000; Moya et al. 2004; U.S. EPA 2011d).

Maternal exposures also can affect childhood exposures. Fetal exposures are uniquely tied to the pregnant mother through the placenta. Much research is reported in the peer-reviewed literature attempting to understand the relationships between maternal and fetal exposures (Ashley-Martin et al. 2014; Ashley-Martin et al. 2016; Ashley-Martin et al. 2015; Braun and Hauser 2011; Callan et al. 2016; Guan et al. 2010; Lin et al. 2011; Mattison 2010; Perera and Herbstman 2011; Perera et al. 2006; Ponsonby et al. 2016; Rothenberg et al. 2011; Whyatt et al. 2009). Similarly, nursing infants and young children are exposed to concentrations of chemicals in breast milk (Cooke 2014; Hines et al. 2015; LaKind et al. 2009; Lehmann et al. 2014). Information relating maternal exposure to chemical concentrations in breast milk, however, is sparse. EPA is developing models and other tools that can help exposure assessors evaluate this situation. For example, Appendix C of the *Human Health Risk Assessment Protocol for Hazardous Waste Combustion Facilities* (U.S. EPA 2005e) provides guidance for estimating concentrations of dioxins and dioxin-like PCBs (polychlorinated biphenyls) in breast milk. Development of additional validated exposure models will strengthen the understanding of the relationship between fetal and maternal exposures. Chapter 6 describes exposure and dose modeling.

Because childhood is a time of rapid behavioral and physiological changes, considering the differences between childhood age groups is important when preparing exposure assessments and calculating lifetime exposures that are integrated across all lifestages (Firestone et al. 2007). EPA developed *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (U.S. EPA 2005c) and *A Framework for Assessing Health Risks of Environmental Exposures to Children* (U.S. EPA 2006d) to assist in exposure assessments for children. Table 4-1 presents EPA's recommended set of childhood age groups (U.S. EPA 2005c), and Box 4-3 lists key sources of childhood exposure information. Figure 4-2 illustrates children's activities that influence exposure as a function of developmental age (color in the graph represents the gradual increase from "Initiating the Activity" to "Activity Most Likely Occurring"). Information on how lifestages affect susceptibility is found in *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (U.S. EPA 2005h).

**Table 4-1. Recommended Childhood Age Groups for Monitoring and Assessing Childhood Exposures**

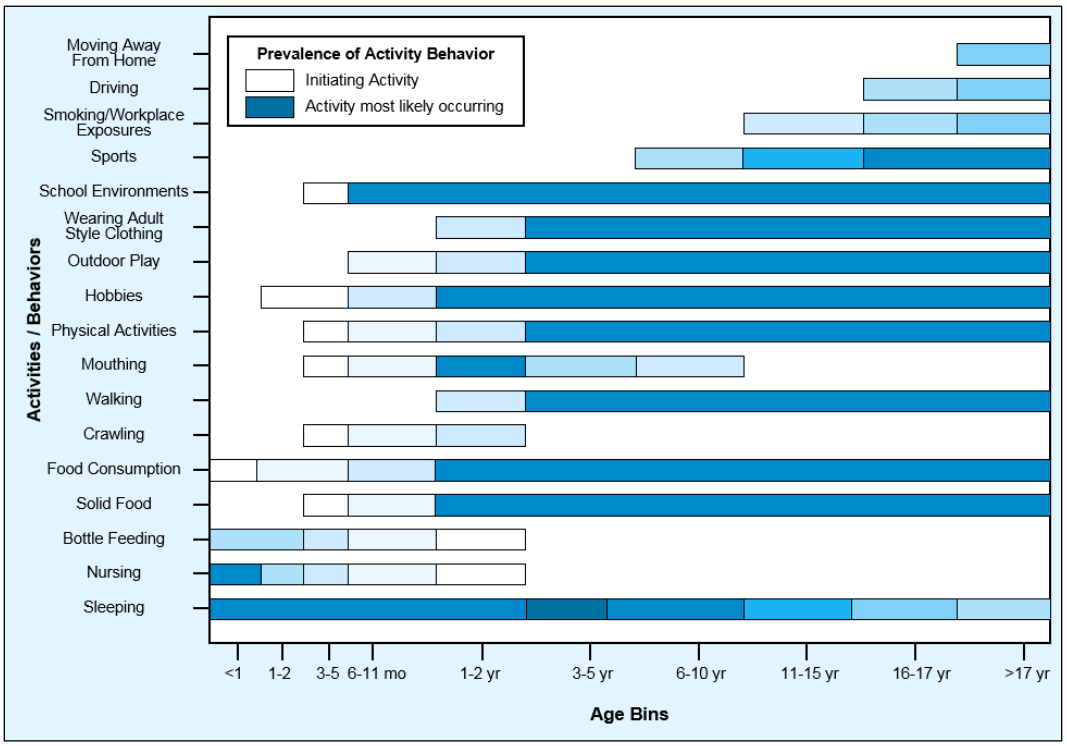
| Age Groups <1 Year | | Age Groups ≥1 Year | | |
|---|---|---|---|---|
| Birth to <1 month | 3 to <6 months | 1 to <2 years | 3 to <6 years | 11 to <16 years |
| 1 to <3 months | 6 to <12 months | 2 to <3 years | 6 to <11 years | 16 to <21 years |

Source: U.S. EPA (2005c)

## Box 4-3. Key Sources of Childhood Exposure Concentration and Exposure Factor Information

- U.S. EPA (2005c) *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (Final). EPA/630/P-03/003F.
- U.S. EPA (2006d) *A Framework for Assessing Health Risk of Environmental Exposures to Children.* EPA/600/R-05/093f. Extensively reviews sources of exposure data relevant to early lifestages. The lifestages considered need to match the periods of greatest susceptibility.
- U.S. EPA (2011d) *Exposure Factors Handbook: 2011 Edition.* EPA/600/R-09/052F. Provides exposure factor data for EPA-recommended childhood age groups in the following areas:
  - Breast milk ingestion rates
  - Food ingestion rates, including homegrown foods and other dietary-related data
  - Drinking-water ingestion rates
  - Soil ingestion rates
  - Hand-to-mouth and object-to-mouth activity associated with elevated ingestion rates
  - Dermal exposure factors such as surface areas and soil adherence
  - Inhalation rates
  - Activity duration and frequency in different locations and various microenvironments
  - Duration and frequency of consumer product use
  - Body weight data
  - Duration of lifetime.

**Figure 4-2. Children's Activities That Impact Exposure as a Function of Developmental Age**




Adapted from WHO (2006)

**Older Adults**

Examples of available resources and ongoing research associated with older adults include:

- In 2007, EPA convened an expert panel to consider the utility of an *Exposure Factors Handbook for the Aging*. The resulting report (U.S. EPA 2007i) summarizes the discussions held during the workshop, highlights several sources of existing data and provides recommendations for additional research. This panel agreed that older adults could have very different exposures than younger adults and recommended steps for addressing these unique exposures. The panel noted that exposures in the aging population were not wholly dependent on age but also were dependent on abilities (e.g., fully functioning, compromised functioning, low functioning).
- In 2010, EPA completed a report compiling information sources and data available for modeling environmental exposures in older adults in the United States. The report, *Data Sources for Modeling Environmental Exposures in the Older Adult Population* (U.S. EPA 2010a), contains exposure factors, physical activity data and general health information for people aged 60 years or older, with an emphasis on ages greater than 65 years.

**Integrating Age-Specific Values in Exposure Assessment**

When assessing long-term exposures to environmental chemicals, integrating age-specific values for both exposure and toxicity/potency is advisable when such data are available (U.S. EPA 2005h). Historically, when assessing cancer risks, the assumption has been that risk is proportional to the lifetime average daily dose for a "typical" adult. A lifestage-integrative approach is a departure from this historical approach because it assesses total lifetime cancer risk resulting from lifetime exposure or less-than-lifetime exposure during a specific portion of a lifetime. For example, when assessing risks to carcinogens with a mutagenic mode of action, different toxic potency adjustments are made for exposure of children less than 2 years of age and between 2 and less than 16 years of age. Ideally, except in the case of higher end screening assessments, average estimates of lifestage-integrative exposure are calculated by summing the time-weighted exposures across all relevant age groups, including children, adults and older adults, and averaging across the total exposure period (U.S. EPA 2005d; U.S. EPA 2005h).

Table 4-2 presents the exposure duration and potency adjustments for the recommended set of childhood age groups (from Table 4-1) (U.S. EPA 2005c). This information can be used to integrate age-specific values for exposure and toxic potency to assess cancer risks for those toxicants that cause cancer via a mutagenic mode of action.

**Table 4-2. Integrating Childhood Age Groups Used for Assessing Exposure and Potency for Selected Toxicants That Cause Cancer via a Mutagenic Mode of Action**

| Potency-Based Age Groups (U.S. EPA 2005h) | Exposure Age Groups (U.S. EPA 2005c) | Exposure Duration (Years) | Age-Dependent Adjustment Factors (U.S. EPA 2005h) |
|---|---|---|---|
| Birth to <2 years | Birth to <1 month | 0.083 | 10× |
| | 1 to <3 months | 0.167 | 10× |
| | 3 to <6 months | 0.25 | 10× |
| | 6 to <12 months | 0.5 | 10× |
| | 1 to <2 years | 1 | 10× |
| 2 to <16 years | 2 to <3 years | 1 | 3× |
| | 3 to <6 years | 3 | 3× |
| | 6 to <11 years | 5 | 3× |
| | 11 to <16 years | 5 | 3× |
| 16 years and above | 16 to <21 years | 5 | 1× |
| | 21 to <70 years | 49 | 1× |

## 4.3.2. Tribal and Indigenous Populations

EPA's relationship with federally recognized tribes differs from its relationship with other agency stakeholders. EPA engages with federally recognized tribes on a government-to-government basis (U.S. EPA 1984). Furthermore, EPA's interactions with tribes and other indigenous peoples is significantly influenced by their traditions and customs, referred to as lifeways. This section provides assessors with guidance on working with federally recognized tribes and indigenous populations focusing on planning, analysis and communicating results.

### Planning, Scoping and Problem Formulation for Assessing Tribal Lifeways

#### *Executive Order and Policies Establishing Tribal Lifeways in Exposure Assessments*

Inclusion of unique tribal lifeways into EPA human exposure assessments is established in one federal executive order and multiple policies (Box 4-4). These documents identify the need to consider tribal interests when the Agency takes action, conduct consultations on a government-to-government basis with federally recognized tribal governments and consider the impacts of actions on indigenous peoples.

**Box 4-4. Federal Executive Order and Policies Establishing Inclusion of Tribal Exposure Lifeways in Human Exposure Assessments**

- Executive Order No. 12898 (1994). *Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations*. Directs each federal agency to identify and address instances where disproportionately high levels of adverse human health or environmental impacts affect tribal populations by improving research and data collection to identify differential patterns of consumption of natural resources among minority populations.
- U.S. EPA (1984) *EPA Policy for the Administration of Environmental Programs on Indian Reservations*. Requires EPA to consider tribal interests when the Agency takes an action.
- U.S. EPA (2011b) *EPA Policy on Consultation and Coordination with Indian Tribes.* Directs EPA to consult on a government-to-government basis with federally recognized tribal governments when EPA actions and decisions might affect tribal interest.
- U.S. EPA (2014d) *EPA Policy on Environmental Justice for Working with Federally Recognized Tribes and Indigenous Peoples*. Requires EPA to consider impacts on indigenous peoples in agency actions.

#### *Definitions*

Box 4-5 lists the definitions for "Federally Recognized Tribe" and "Indigenous Peoples" as used in this document.

**Box 4-5. Definitions of "Federally Recognized Tribe" and "Indigenous Peoples"**

*Federally Recognized Tribe* – an Indian or Alaska Native tribe, band, nation, pueblo, village, or community that the Secretary of the Interior acknowledges to exist as an Indian tribe pursuant to the Federally Recognized Indian Tribe List Act of 1944, 25 U.S.C.479a. The elected officials for the federally recognized tribe and the government structure they administer are referred to as the federally recognized tribal government. When used in this document, "tribes" refers to federally recognized tribes unless otherwise specified.

*Indigenous Peoples* – state-recognized tribes; indigenous and tribal community-based organizations; individual members of federally recognized tribes, including those living on a different reservation or living outside Indian country; individual members of state-recognized tribes; Native Hawaiians; Native Pacific Islanders; and individual Native Americans.

**Exposure Assessment Methodologies for Assessing Exposures**

This section provides background information, important deliberations, examples and references for an assessor to consider when planning and conducting an exposure assessment involving tribes or indigenous populations.

***Subsistence Lifeways***

Tribes and indigenous populations are inextricably linked to their environments: They rely on natural resources to maintain traditional diets, customs and languages. Natural resources provide essential elements of tribal lifeways including economic, cultural, ceremonial, sacred, recreational and subsistence practices. Examples of tribal lifeways include subsistence hunting, gathering and fishing. Tribal and indigenous populations are interconnected with the ecosystem that provides a variety of food, medicine and products for various uses and trades. Each tribal and indigenous population has unique practices and cultural bonds to their environment. A subsistence lifeway is the basis of cultural existence and survival. It is a communal activity rather than an individual pursuit. Among many tribes, maintaining a subsistence lifestyle is a symbol of their survival in the face of mounting political and economic pressures. It defines who they are as a people (NPS 1999).

Tribal and indigenous people live across North America. EPA's ecoregion approach provides a framework to identify vegetation, land uses, wildlife and other relevant ecological characteristics that can assist assessors in understanding the type, quality and quantity of environmental and cultural resources. An ecoregion approach enables researchers to combine quantitative and qualitative descriptions of the environment when collaborating with tribal and indigenous populations.

***Unique Exposure Scenarios***

Exposure scenarios for tribal and indigenous populations differ from general population exposure scenarios, in that subsistence lifeways and diets are relevant, outdoor activities are prevalent and traditional and cultural activities are frequent. Unique tribal practices might expose tribal and indigenous populations to higher concentrations of contaminants through natural resources that could differ substantially from exposures the general population experiences. In addition, some tribal and indigenous populations live in areas with limited infrastructure that might result in higher exposures (U.S. EPA 2015a). Examples of EPA resources relevant to tribal exposure scenarios are presented in Box 4-6.

Limited data and information specific to tribes and indigenous populations are provided within EPA's *Exposure Factors Handbook: 2011 Edition*. For example, several exposure assessments have examined the exposure of Native Americans to contaminants in fish. Fish ingestion rates for recreational marine anglers (adults) from the northern Pacific region were reported as 6.8 g/day (95th percentile) and 2.0 g/day (average). By comparison, fish ingestion rates for Native Americans (adults) from the four Columbia River Nations of Oregon were 170 g/day (95th percentile) and 59 g/day (average) (U.S. EPA 2011d). The *Exposure Factors Handbook: 2011 Edition* also discusses exposure to chemicals via fish consumption and recommendations for adult tribal soil ingestion. Exposure assessors evaluating tribal exposures need to consult the *Exposure Factors Handbook: 2011 Edition* for information.

**Box 4-6. Tools and Reports for Evaluating Tribal Exposures**

- EPA Guidance for Conducting Fish Consumption Survey
  - Characterizes tribal subsistence fish consumption practices and rates, including estimates of heritage or historical fish consumption for the development of ambient water quality criteria
- EPA's Expo Box: Tools by Lifestages and Populations – Highly Exposed or Other Susceptible Population Groups
  - Includes tools for tribal and other populations that might experience greater exposure to environmental contaminants
- A Decade of Tribal Environmental Health Research: Results and Impacts from EPA's Extramural Grants and Fellowship Programs
  - Summarizes information collected through EPA's STAR (Science to Achieve Results) grant program that informs or improves health outcomes
- Wabanaki Traditional Cultural Lifeways Exposure Scenario
  - Informs Agency assessors on cultural lifeways and their application to risk assessments
- Traditional Tribal Subsistence Exposure Scenario and Risk Assessment Guidance Manual (Harper et al. 2007)
  - Provides a framework the grantee develops for evaluating risk in Indian country

An important consideration is that exposure scenarios developed for tribal and indigenous populations are drawn from historical (pre-European settlement) time frames and account for the many irreversible changes that have occurred in the United States that have fundamentally altered the practice of traditional tribal lifeways. More importantly, tribal exposures should be representative of current or plausible future conditions. *EPA's Guidance on Systematic Planning Using the Data Quality Objectives Process* (U.S. EPA 2006e) can help determine how information on tribal exposures is collected and used. This guidance ensures that Agency decisions are supported by data of known and documented quality.

***Traditional Ecological Knowledge***

Traditional Ecological Knowledge (TEK) is a body of knowledge, practice and beliefs, evolving by adaptive processes and handed down through generations by cultural transmission, about the relationship of living beings (human and nonhuman) with one another and with the environment. This knowledge, which can be specific to a location, includes the relationships among plants, animals, natural phenomena, landscapes and timing of events that are used for lifeways, including hunting, fishing, trapping, agriculture, forestry and sacred ceremonies. TEK encompasses the world view of indigenous peoples, which includes ecology, spirituality and human and animal relationships. Risk assessors should be aware that tribes have their own guidelines for sharing TEK with federal agencies.

EPA policy (U.S. EPA 2014d) directs management and staff, as appropriate and to the extent practicable and permitted by law, to integrate TEK into Agency environmental science policy and decision making processes to understand and address environmental justice concerns and facilitate program implementation.

***Community-Based Participatory Research***

Tribal and indigenous populations might have experienced historical trauma as a result of past unethical research imposed on them. Using community-based participatory approaches in tribal research involves partnering with the community when planning, implementing and conducting

needed research and exposure assessments to establish mutual trust and better understand tribal lifeways.

Accordingly, assessors need to work with their Tribal Program Managers and program-specific project managers to conduct outreach and coordination with tribes to learn about exposure scenarios. The tribal consultation process can afford EPA an opportunity to obtain meaningful input from tribes on exposures that directly impact them (U.S. EPA 2011b). A benefit of these processes is that assessors can better understand how tribes interact with their environment and can learn more about direct and indirect exposure pathways, estimated doses, risks and more (should a tribe be willing to share this information).

***EPA's Tribal Program and Networks***

EPA's Tribal Program has established working relationships with tribes. Assessors should engage with their Tribal Program Managers and program-specific project managers and coordinate with other Agency risk assessors to include tribal perspectives when conducting exposure assessments and to facilitate clear communication with tribal partners.

The Agency's network of Tribal Partnership Groups facilitates the exchange of technical information and communication between tribes and EPA. For example, the National EPA-Tribal Science Council works to integrate and increase tribal involvement in EPA's scientific activities, and the National Tribal Toxics Council provides tribal input on issues related to toxic chemicals and pollution prevention. Assessors should engage with these partnership groups, through EPA's Tribal Program, to better understand tribal lifeways and to discuss and collaborate on research needs.

### 4.3.3. Other Racial and Ethnic Populations

"Race" refers to the socially constructed groups the Office of Management and Budget specifies.[11] "Ethnicity" refers to cultural groups, such as Hispanic or Latino. As Directive 15[12] and numerous scholarly organizations note, racial and ethnic groups are social categories, not biological taxa (i.e., no biological basis exists for assigning people to a given racial class). Racial, ethnic and class differences and inequities in environmental exposures are related to underlying social structural dynamics in our society—for example, economic and political (Brulle and Pellow 2006).

Researchers have documented patterns of racial/ethnic differences in exposure to environmental contaminants by proximity to hazardous land uses (Bullard 1990; Chakraborty et al. 2011; U.S. GAO 1983; UCC 1987), ambient measures (Bullard 1990; CDC 2005; EJHU 2003; IOM 1999; Lopez 2002; Morello-Frosch and Lopez 2006; Morello-Frosch et al. 2002; Wernette and Nieves 1992; Woodruff et al. 2003), biomonitoring (Hightower et al. 2006; IOM 1999; McKelvey et al. 2007) and exposure modeling (Adamkiewicz et al. 2011; Houston et al. 2014; Morello-Frosch and Jesdale 2006; Morello-Frosch and Lopez 2006; Morello-Frosch et al. 2002). Review articles of such racial and ethnic disparities include Brulle and Pellow (2006) and Brown (1995). Other

[11]Revisions to the Standards for the Classification of Federal Data on Race and Ethnicity; Notice of Decision, 62 *Fed. Reg.* 58782 (October 30, 1997).
[12]Race and Ethnic Standards for Federal Statistics and Administrative Reporting; Directive No. 15 (May 12, 1977), http://wonder.cdc.gov/wonder/help/populations/bridged-race/Directive15.html.

examples include racial, ethnic and income disparities in exposures to lead, mercury and other metals, PCBs (polychlorinated biphenyls) and pesticides, and proximity to hazardous land uses.

Cultural traditions and practices can influence exposures for many diverse populations found throughout the United States. Exposure assessors need to be aware of these traditions and practices when conducting exposure assessments. For example, a 2003 study examined seafood consumption in Asian-American and Pacific-Islander populations in King County, Washington (Sechena et al. 2003). The study reported average and median seafood consumption rates of 117.2 g/day and 89 g/day based on an average body weight of 62 kg. Of significance to exposure assessors, however, is the considerable variation in consumption rates among ethnic groups, such as Vietnamese, Japanese and Hmong (Sechena et al. 2003; U.S. EPA 2001a). The study also reported people ate fish fillets with the skin 55 percent of the time and the head, bones, eggs or other organs 20 percent of the time. Crabmeat, including the hepatopancreas (which accumulates organochlorine compounds), was consumed 43 percent of the time. These differences in fish ingestion rates and preparation practices could require special considerations in the exposure assessment (e.g., data collection and selection of ingestion rates). In another example, Weintraub and Birnbaum (2008) suggested that catfish consumption might be a significant PCB source for the one million non-Hispanic black anglers who fish for catfish because they consume the entire fish.

### 4.3.4. Traditional Methods

Traditional methods include documenting the locations of locally unwanted land uses, such as hazardous waste sites, pollution emitters or highways. Possible data sources include the Toxics Release Inventory) and similar state databases of contaminants, pollution discharge permits and air monitoring data. Assessors then characterize the population surrounding these locations by race, income and other factors, usually from U.S. census data. The target area for these sites varies; it could be a census block group, census tract, ZIP code, county or selected buffer zone (often described using geographic information system methods). Assessors compare the populations in these target areas to the overall state or U.S. population or to other areas having no locally unwanted land uses. Researchers have noted methodological issues with these studies: Those using a ZIP code or larger area of analysis tend to find that income is a greater risk factor than race/ethnicity for exposure to environmental burdens, whereas studies using block groups or census tracts tend to find that race/ethnicity is a greater risk factor than income for exposure.

### 4.3.5. Case Studies

A case study describes a particular neighborhood or group's experience with an exposure or environmentally related condition over time. For the most part, case studies use descriptive statistics, document searches, ethnographic research or individual or group interviews as the basis for building the study. Although case studies might lack statistical power, they can be valuable for describing past exposures or understanding how and why certain exposures happened.

### 4.3.6. Neighborhood Methods

Neighborhood methods begin with the identification of particular areas that have high proportions of disadvantaged people or other populations of concern. The areas include census blocks, census tracts, ZIP codes, counties or specially or traditionally defined neighborhoods.

Researchers usually obtain data on neighborhood demographic composition from U.S. census data or other government surveys. Next, researchers measure or estimate the overall or specific level of contaminants or pollution sources using resources such as those described in Section 5.4. The neighborhood pollutant or pollution source levels then are compared to national or regional means. Neighborhood studies are useful for understanding cumulative risks or identifying areas already bearing high levels of environmental burdens.

## 4.3.7. Population-Based Methods

In a population-based method, analysts compare the overall or person-specific mean, percentile or distribution of exposure for a given population(s) of concern to that of a control population or to the mean, percentile or distribution level of exposure of the entire population. This comparison requires data on each person in a population and an assessment of whether that individual is a member of a particular population. In many cases, data on individual exposures are scarce. Analysts instead assign exposure values to individuals based on area data or surrogate exposure measures. Generally, the geographic area of interest is larger than a neighborhood—municipal, countywide, statewide, regional or national in scope. Population-based methods are useful in understanding population group-specific differences in health or in identifying priorities for health and environmental interventions.

## 4.3.8. Social Process Methods

Analysts use social process methods to assess the association between a social-level variable(s) and chemical exposures. The variables include measures of racial residential segregation, income inequality and poverty rates. The general method is to use regression analysis, treating these measures as independent variables and the exposure metrics as dependent variables. The regression models also often use other demographic, social or environmental measures as the independent variables. A subset of these methods uses hierarchical linear modeling (also called mixed or multilevel modeling). In this subset, at least two levels of effect are assessed, typically including the individual level (including race/ethnicity, sex, age, income) and the neighborhood or other higher level variables (including owner-occupied housing percentages, racial/ethnic percentages in a population or other social-level variables). These methods can be valuable in screening for potential associations between multiple risk factors and differences in health between racial and other groups. Assessing causation, however, requires additional evidence.

## 4.3.9. National-Level versus Local/Community-Specific Assessments

Differences in exposure to environmental contaminants by race, ethnicity, class, geography and other factors can be assessed within localities, between localities and across populations at the national level. The exposure assessor, in consultation with the risk manager/decision maker, will determine the most relevant geographic scope.

**National-Level Assessment**

At the national level, screening for differential exposure can use the large, comprehensive databases on pollutant concentrations in environmental media (e.g., air, water) and the locations of pollution sources that national organizations such as EPA, the U.S. Bureau of the Census and the Centers for Disease Control and Prevention develop. For example, the screening study might combine data on segregation and income inequality, metropolitan air quality indices, modeled air toxics concentrations and data from the Toxics Release Inventory.

One example of a national-level assessment is EPA's National-Scale Air Toxics Assessment (NATA), an ongoing comprehensive evaluation of air toxics in the United States. EPA developed the NATA program in 1996. These assessments estimate the risk of cancer and non-cancer health effects from inhaling air toxics, including estimates of exposures at the census-tract level. Assessments include estimates of health effects based on chronic exposure from outdoor sources. Assessments provide a snapshot of the outdoor air quality and the risks to human health that would result if emission levels of these pollutants remained unchanged. NATA is updated with new inventory and exposure data on a 3-year cycle.

**Local-Level (Community) Assessment**
Local-level exposure assessments are useful for responding to specific community concerns and planning for hazardous waste or brownfield site cleanups. In addition, local-level exposure assessments can help unmask unique or high exposure levels of specific community or population groups that would be "averaged out" in a national-level assessment. This situation is particularly germane for groups having traditional practices, including Native Americans and other ethnic and religious groups. Community-based risk assessment is an active area of research for EPA, in particular for EPA's National Center for Environmental Research. Several reports, including workshops, case studies and modeling tools (e.g., C-FERST [Community-Focused Exposure and Risk Screening Tool], T-FERST [Tribal-Focused Environmental Risk and Sustainability Tool], ReVA [Regional Vulnerability Assessment], community-based air toxics models, the Regional Air Impact Modeling Initiative, the Toxics Release Inventory Explorer, the Internet Geographic Exposure Modeling System) are available as resources (Barzyk et al. 2010).

## 4.4. Summary

- **Unique characteristics and sociodemographic factors** can increase exposure or predispose an individual, lifestage, specific group or population to greater health risk.
- Numerous executive orders, policies and legislative mandates emphasize EPA's **history of commitment** to considering lifestages, vulnerable groups and populations of concern in exposure assessments.
- Environmental exposures and health risks can be concentrated among certain population groups and in potentially vulnerable communities. **Vulnerability** refers to characteristics of individuals or populations that place them at increased risk of adverse health effects. **Susceptibility** refers to the increased likelihood that a stressor will affect an individual or population more than it will affect the general population because of intrinsic biological factors. The planning and scoping phase of the exposure assessment is the optimal point for outlining the approach to identify and consider population vulnerability.
- Certain lifestages, tribal populations, racial and ethnic groups and socioeconomically disadvantaged population groups can be particularly vulnerable to exposure and are of heightened concern to the exposure assessor.
    - "**Lifestage**" refers to a temporal stage of life with distinct anatomical, physiological, behavioral or functional characteristics that contribute to potential differences in vulnerability to environmental exposures.
    - EPA views **childhood** as a sequence of lifestages from conception through fetal development, infancy and adolescence for the purposes of exposure assessment.

- EPA provides guidance for use in assessing exposure in **older adults**, including *Data Sources for Modeling Environmental Exposures in the Older Adult Population*.
- Incorporating long-term exposures to environmental chemicals and **integrating age-specific values** for both exposure and toxicity/potency is advisable when appropriate.
- Assessors need to be aware of exposure issues and scenarios unique to **tribal populations** and be cognizant of special cultural and technical challenges when conducting exposure assessments.

- Many methods are available to exposure assessors for identifying lifestages, vulnerable groups and populations of concern.
  - **Traditional methods** include documenting the locations of locally unwanted land uses, such as hazardous waste sites, pollution emitters or highways.
  - **Case studies** describe a particular neighborhood or group's experience with exposure or environmentally related conditions over time; this method can be valuable for describing and understanding past exposures.
  - **Neighborhood methods** identify areas having high proportions of populations of concern and measure or estimate overall or specific levels of contaminants or pollution sources. The neighborhood pollutant or pollution source levels then are compared to national or regional means.
  - **Population-based methods** compare the overall or person-specific mean, percentile or distribution of exposure for a given population(s) of concern to that of a control population or to the mean, percentile or distribution level of exposure of the entire population.
  - **Social process methods** are used to assess the association between a social-level variable(s) and chemical exposures.
  - **National level and local/community-specific assessments.** At the national level, screenings for differential exposure use large, comprehensive databases on pollutant concentrations in environmental media and the locations of pollution sources.

# CHAPTER 5. DATA FOR EXPOSURE ASSESSMENTS

Data, defined in this *Guidelines for Human Exposure Assessment* as the sets of quantitative and descriptive information needed to answer exposure assessment questions, are the primary input to an exposure assessment. Possible data types include physical measurements of environmental and biological media, health survey and study outputs (e.g., the National Health and Nutrition Examination Survey [NHANES]) including data on various health outcomes, location-specific or population-based activity information and scientific research findings such as modeling data (see Chapter 6). The information an exposure assessor needs to consider has grown more complex due to advances in science and technology. Many new datasets and data collection methods have become available to support exposure assessments. As analytical techniques have improved and more sophisticated modeling and predictive tools have evolved, the ways to process data have become increasingly complex. For these reasons, understanding data availability, applicability, characteristics, quality issues and limitations is critical to conducting a scientifically sound exposure assessment. The process of identifying and addressing data needs is iterative, involving repeated reviews of data availability, quality and gaps. This chapter provides a framework for addressing data needs, including an overview of key data considerations and links to relevant data sources, resources and tools. Specifically, this chapter:

- Identifies the types of data used in an exposure assessment (Section 5.1)
- Discusses considerations in identifying data gaps and data needs (Section 5.2)
- Describes quality assurance/quality control (QA/QC) needs for an exposure assessment (Section 5.3)
- Discusses sources of existing data and methods for collecting additional data for exposure assessments (Section 5.4)
- Reviews data and decision uncertainty and variability (Section 5.5)
- Provides an overview of data management considerations (Section 5.6)
- Describes communication considerations specific to data (Section 5.7).

Section 5.8 summarizes this chapter.

## 5.1. Types of Data Used in an Exposure Assessment

Data used in an exposure assessment represent a wide variety of information, from chemical concentrations in various media to information about activities at the individual or population level. For each assessment, the exposure assessor needs to consider the relevance of various types of data: environmental data, biomonitoring data, exposure factors and activity patterns. Sections 5.1.1 through 5.1.5 discuss these data considerations and the role they serve in an exposure assessment.

Data support EPA's role of protecting public health and the environment. Laws and executive orders EPA uses to meet these mandates are discussed in published documents (U.S. EPA 2017d; U.S. EPA 2019b). Exposure assessment information used in protecting public health includes data on the source-to-outcome continuum (see Figure 2-1). Assessors need to consider coordinating with the appropriate program to ensure that data collected meet program-specific requirements for collection of new data and use of existing data.

### 5.1.1. Environmental Data

EPA defines environmental data as "any measurement or information that describe[s] environmental processes, location or conditions, ecological or health effects and consequences, or the performance of environmental technology" (U.S. EPA 2002h). Environmental data include information collected directly from measurements, produced from models and compiled from other sources, such as databases or the literature (U.S. EPA 2002e). Exposure assessments typically use environmental data to characterize:

- Sources of contaminants
- Fate and transport of contaminants in media
- Exposure pathways
- Likelihood exposure will occur
- Who is exposed
- Impact of variability and uncertainty in exposure estimates.

The use of environmental data occurs throughout the exposure assessment process. During planning and scoping, data can direct the development of a conceptual model by providing information about the chemical source, types of releases and potential transport mechanisms through the environment (see Section 3.2.2). Other data considerations include temporal variability in environmental and biological measures and representativeness of samples. For example, data on chemical concentrations in soil at a playground might highlight the importance of understanding incidental soil ingestion by children. Assessors also use environmental data when quantitatively estimating exposure. These data serve as fundamental inputs, either directly as exposure concentrations or indirectly in exposure models, which might include physicochemical models or databases. Data serve as input parameters for larger or higher level exposure models that estimate likely exposure concentrations. For example, the concentration of a solvent detected in an aquifer used as a drinking water source could directly represent an exposure concentration for the population that uses the source. The concentration of a solvent detected in groundwater upgradient of a drinking water well, on the other hand, could serve indirectly as an input value to a model used to predict potential contamination based on parameters such as groundwater flow, well pumping rates and groundwater velocity. Exposure assessors need to consider carefully the way in which the environmental data fit into the conceptual model (see Section 3.2.2) and the purpose of the assessment.

### 5.1.2. Biomonitoring Data

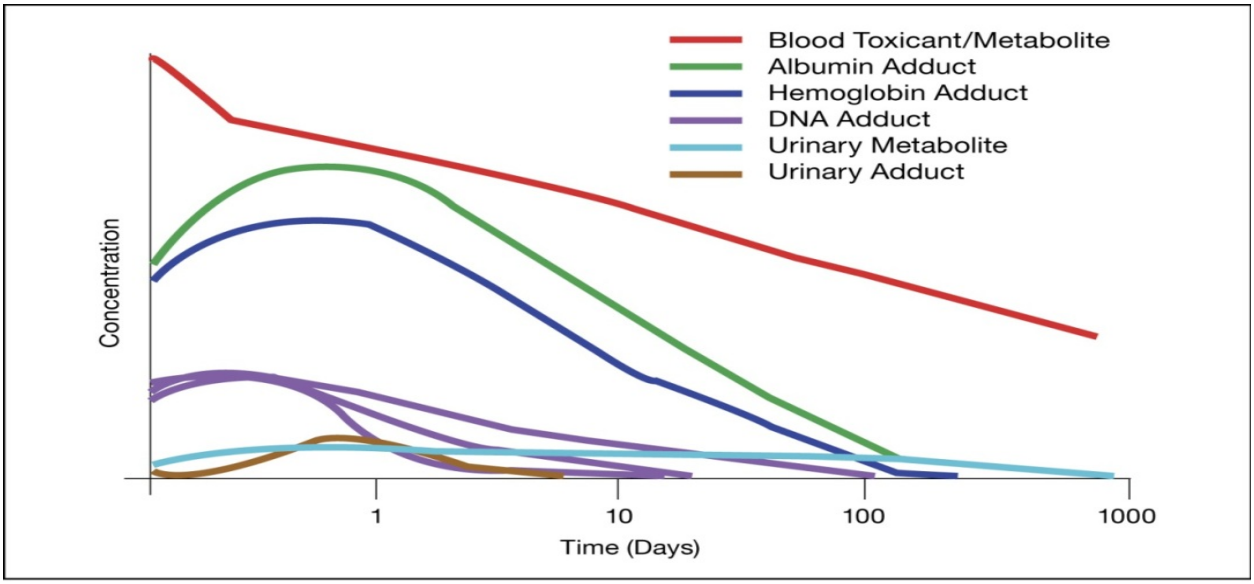
Biomonitoring is a useful method for assessing human exposure to chemicals by collecting human tissues or specimens, such as blood and urine (NRC 2006b), combined with information about environmental exposures from interviews and questionnaires. Measuring the chemicals or their metabolites in human tissues or specimens along with information about the use and timing of the chemical exposure (see Section 2.2.1) in relation to the collection of the specimen provides valuable data for understanding internal dose and total exposure of an individual. Biomonitoring data are useful in characterizing exposures when complete exposure data are not available for current, recent or historical exposures or when exposure to multiple chemicals might have occurred (Checkoway and Eisen 1998).

Biomarkers are cellular, biochemical, analytical or molecular measures, obtained from biological media such as tissues, cells or fluids, which indicate exposure to a chemical (WHO 2004). Biomarkers of exposure record the concentration of the chemical or its metabolites in biological media, whereas biomarkers of effect indicate cellular, biochemical or molecular changes occurring as a result of human exposure to the chemical (WHO 2004; WHO 2012; WHO 2015). Centers for Disease Control and Prevention's (CDC) NHANES regularly provides biomonitoring data from a nationally representative population sample for over 200 chemicals measured in blood or urine. Summary statistics are available from the *National Report on Human Exposure to Environmental Chemicals*, and individual observations are available in downloadable data files from the *NHANES* website (CDC 2009; CDC 2012a).

**What Are Biomonitoring Data?**

The ideal biomarker is sensitive, specific, biologically relevant, easy to collect, inexpensive to analyze, readily identified and persistent in the body for long periods (Metcalf and Orloff 2004; Needham and Sexton 2000). Figure 5-1 illustrates persistence of a hypothetical chemical or metabolite in human tissue after a single exposure, although residence times in the body can vary depending on the type of chemical (Needham and Sexton 2000; Sohn et al. 2004). Various adducts can form between blood components and toxicants that are both persistent or nonpersistent (Needham and Sexton 2000). Adduct-forming toxicants or their metabolites include DNA adducts having an electrophilic center that reacts with the neutrophilic center and protein adducts (e.g., hemoglobin and albumin) formed after exposure to xenobiotics (Needham and Sexton 2000). The *America's Children and the Environment* website discusses biomonitoring data for several chemicals including lead, phthalates and mercury. In addition, as described in Section 6.2.3, human dose models (forward and reverse dosimetry) can estimate a dose based on biomonitoring data. The CDC *Biomonitoring Summaries* website provides a brief general overview about the chemical or chemical group, including usage, environmental pathways, sources of exposure, toxicology, health effects and human biomonitoring information.

**Figure 5-1. Representative Profiles of Hypothetical Biomarkers Following a Single Exposure to a Persistent Chemical**




Adapted from Needham and Sexton (2000)

**What are Biomonitoring Equivalents?**
The "biomonitoring equivalent" (BE) approach estimates a single biomarker concentration (called the BE) that corresponds to a guidance value (e.g., Maximum Contaminant Level, Reference Dose), which then can be compared with measured biomarker data. The resulting "hazard quotient" estimates (HQ = biomarker concentration/BE) then can be used to prioritize chemicals for follow-up examinations (Phillips et al. 2014). Comparison of biomarker concentrations to corresponding BE values are useful in guiding the evaluation of multiple exposures in a population and to set priorities for research or reduction in exposures (Aylward et al. 2013; St-Amand et al. 2014).

EPA's Office of Pesticide Programs (OPP) used an approach comparable to the BE approach to evaluate triclosan and pentachlorophenol (U.S. EPA 2008a; U.S. EPA 2008b). OPP essentially used biomonitoring data (urine) from NHANES and reasonable assumptions to estimate the distribution of exposure (in μg chemical/kg body weight) to the U.S. population and subgroups.

**How Are Biomonitoring Data Used?**
Biomonitoring data provide a useful tool for assessors to identify chemicals in the environment and human tissues and to monitor changes in exposure over time (NRC 2006b). Assessors use biomonitoring studies to address data gaps associated with possible exposures, baseline conditions, trends in concentrations of specific chemicals within populations over time (e.g., NHANES data) and internal chemical or metabolite concentrations. Biomarkers of exposure provide information on chemical exposures in individuals, changes in levels over time and variability among different populations (U.S. EPA 2018b). Assessors can use biomonitoring data as a baseline or point of reference for comparing changes in concentrations over time. Baseline information provides the ability to analyze changes in chemical concentrations over time, including prevalence or magnitude of exposure, and to evaluate the impacts of removing chemicals from the environment by examining changes in blood or urine concentrations over time. Reference ranges describe general population exposures to chemicals for segments of the population (CDC 2009; CDC 2015a). Biomonitoring data complement environmental and modeling data in estimating exposure (e.g., temporal, scale, media, biodegradation).

**What Are the Quality Considerations in Using Biomonitoring Data?**
The CDC has developed specific guidance regarding assessing the quality of biomonitoring data. Information is available on the CDC *National Biomonitoring Program* website (Berman et al. 2001; CDC 2016).

**What Are the Limitations of Biomonitoring Data?**
The CDC's *Fourth National Report on Human Exposure to Environmental Chemicals, 2009* (CDC 2009) states the following caution in evaluating biomonitoring data:

> "The measurement of an environmental chemical in a person's blood or urine does not by itself mean that the chemical causes disease. Advances in analytical methods allow us to measure low levels of environmental chemicals in people, but separate studies of varying exposure levels and health effects are needed to determine whether such blood or urine levels result in disease. These studies must also consider other factors such as duration of exposure."

Biomonitoring data have several limitations. For example, analytical methods are unavailable for some chemicals, and interpreting results can be difficult due to background levels, confounding co-exposures, metabolic processes with uncertain transformation times and limited information correlating exposures to chemical measurements or metabolites. Assessors need to measure source data in the individual media or model them, as Section 6.2.5 discusses. Having data on sources of exposure and on internal biomonitoring information helps assessors understand how to reduce exposures. Also, having both biomonitoring data and modeling information helps identify the relative contribution from different sources of exposure. Another limitation includes the potential for intra-individual variability in the measurement of nonpersistent chemicals in urine. Permission or consent of individuals might apply to the collection and analyses of biological specimens and reporting of data. Biomonitoring data often are not available for young children because of difficulties in obtaining blood and urine samples. Human Studies Review Boards (see Section 7.2.10) should be consulted for additional guidance for obtaining consent on collecting and sharing biomonitoring data. Finally, the data on biologically equivalent doses that result in toxic effects are limited, making the comparisons necessary to assess health risks difficult. Before relying on biomonitoring data for an exposure assessment, the project team needs to be cognizant of limitations inherent in the biomarkers used.

**What Advances Are Expected in Biomonitoring Data?**

The science behind biomonitoring and biomarkers is advancing rapidly, and biomonitoring in human populations is becoming more common. Emerging research is expanding the Agency's knowledgebase of biomonitoring, biomarkers and links to environmental exposures. The CDC, for example, has been measuring chemicals in blood and urine from a subset of the U.S. population using advanced laboratory and innovative technologies for more than three decades as part of the NHANES program (CDC 2012a). NHANES is an ongoing program of surveys that collect data on the health and nutritional status of the noninstitutionalized population of the United States (CDC 2012a). The CDC reports detailed information and documentation on NHANES methods, datasets and data analyses. CDC periodically releases comprehensive reports, which are available on the *National Report on Human Exposure to Environmental Chemicals* website.

**What Special Considerations Are Needed to Use Biomonitoring Data?**

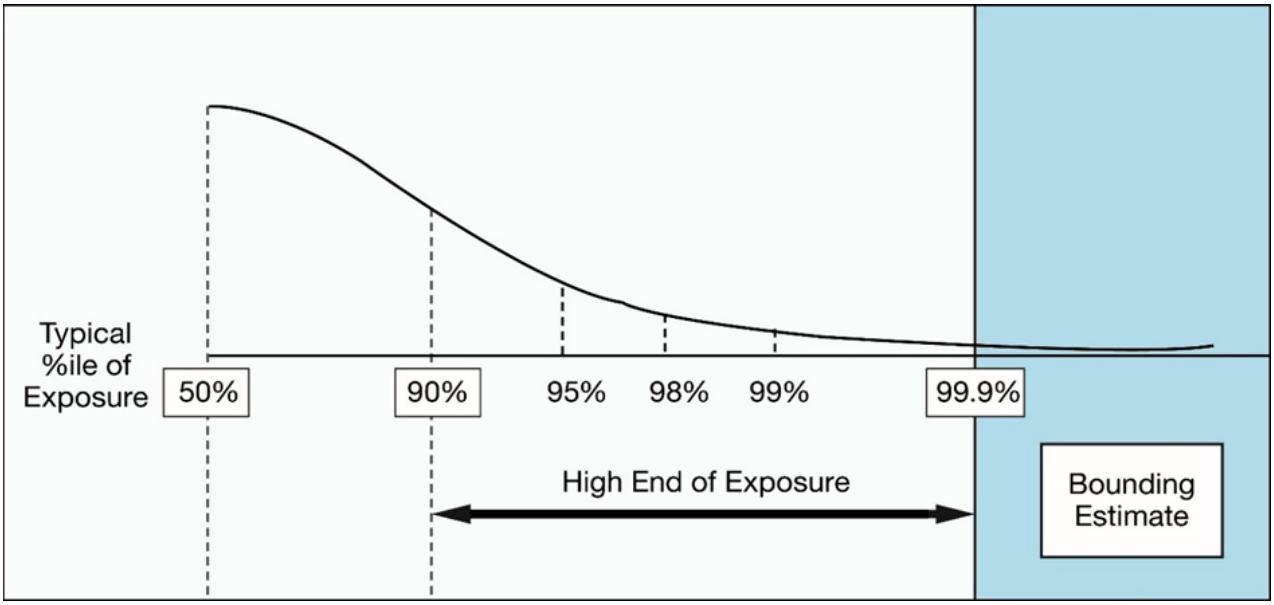
When using biomonitoring data in an exposure assessment, an assessor needs to be mindful of confidentiality and privacy considerations. Sections 5.4.2 and 5.4.4 discuss confidentiality concerns associated with using data from individuals. Section 5.4.4 further discusses the confidentiality and privacy issues associated with administering questionnaires and surveys and conducting observational human exposure measurement studies. Section 7.2.10 specifically discusses the confidentiality and privacy issues associated with conducting observational human exposure measurement studies.

## 5.1.3. Exposure Factors

As described in Section 3.2.1, individuals within a population fall within a distribution of exposures based on factors that include personal characteristics, individuals' activities and behaviors and frequency and duration of exposure to various media. Because uncertainty and variability are present in exposure assessments, EPA might incorporate a "high-end" exposure level to ensure protection of potentially exposed individuals or groups within lifestages or populations of concern (e.g., EPA's high-end levels are the 90th percentile and above, as

Figure 5-2 shows). When combining exposure factors, the assessor needs to consider both high-end and central-tendency exposure factors and ensure the combinations represent those that occur within comparable times and places to an individual and within the range of plausible exposures. Even with a high-end value, individuals could experience higher or lower exposures. EPA's programs estimate high-end and central-tendency values and often provide a range of exposures that encompass the actual exposure distribution for various individuals, lifestages, groups or populations (U.S. EPA 2004c).

**Figure 5-2. Schematic of the Distribution of Exposures for Individual Receptors within a Population**




Exposure descriptors characterize estimates for a specific point on the exposure distribution (e.g., mean, median, 95th percentile, maximum) for individual or population exposures. Exposures vary due to differences among individuals, populations, spatial and temporal scales and other factors. According to EPA's *Example Exposure Scenarios*, this "variability can be addressed by estimating exposure for the various descriptors of exposure (i.e., central tendency, high-end or bounding) to estimate points on the distribution of exposure" (U.S. EPA 2003c). Exposure descriptors are useful when characterizing exposure and aid communication between exposure assessors and risk managers/decision makers. Box 5-1 summarizes common exposure descriptor terms used to describe exposure distributions for various individuals. The terms include definitions based on the distributions, types of exposures and exposed individuals.

Assessors use exposure factors to estimate contact rates for different media (e.g., the amount of air inhaled in a breath, breathing rates). Other exposure factors include data on people's physical characteristics (e.g., body weight, skin surface area).

**Box 5-1. Terms Describing Exposure Distributions**

*Parts of the Exposure Distribution*

- High end of the distribution: occurs above the 90th percentile of the population distribution, but not higher than the percentile for the individual in the population who has the highest exposure.
- Maximum exposure range: above the 99th percentile in exposure.

*Types of Exposure*

- Bounding estimate: an estimate of exposure that is higher than the highest anticipated exposure to an individual, lifestage, group or population. Bounding estimates show that true exposures are not greater than estimated exposures. Assessors often use bounding estimates during screening-level assessments to eliminate exposure pathways of minor importance from further consideration or to determine whether they need more data and information to evaluate other pathways.
- Central tendency exposure: an estimate of exposure of individuals in the middle of the distribution (i.e., those near the median or 50th percentile).
- High-end exposure estimate: used in this guidance document as a plausible estimate of individual exposure for those individuals at the upper end of an exposure distribution. The intent of this designation is to convey an estimate of exposure in the upper range of the distribution while avoiding estimates that are beyond the true distribution.
- Reasonable maximum exposure: defined as the highest exposure reasonably expected to occur at a Superfund site, and intended to estimate a conservative exposure case (i.e., well above the average case) that is still within the range of possible exposures.
- Worst-case exposure: historically, used for the maximum possible exposure occurring when all events that can plausibly occur to maximize exposure occur. This worst-case exposure might fall on the uppermost point of the population distribution, but in most cases, will be somewhat higher than for the individual in the population having the highest exposure.

*Types of Exposed Individuals*

- Maximally exposed individual (MEI): describes the uppermost portion of the high-end exposure range, although actual usage has varied (e.g., section 112 of the Clean Air Act Amendments of 1990).
- Theoretical MEI: describes exposure under the worst case. It represents a hypothetical individual and an extreme set of conditions.
- Reasonably MEI: describes exposure under the reasonable worst case.

Assessors use exposure factors, with activity pattern information and other data inputs, in developing an exposure scenario and a conceptual model to estimate exposures. EPA's Exposure Factors Interactive Resource for Scenarios Tool Glossary, based on the *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011d), defines activity pattern (or time-use) data as "information on activities in which various individuals engage, length of time spent performing various activities, locations in which individuals spend time and length of time spent by individuals within those various environments." Activity information describes the types of activities in which individuals engage, the length of time people engage in that activity and where and when that activity occurs. Activity pattern information is collected by using time-activity diaries (e.g., paper diaries in which individuals record activities such as food consumed), electronic devices (e.g., geographic information system or other hand-held devices), questionnaires or surveys of activities.

EPA developed ExpoBox as a toolbox for exposure assessors and the Exposure Factors Interactive Resource for Scenarios Tool (ExpoFIRST) to help individuals access exposure data. ExpoBox is a compendium of exposure assessment tools that link to guidance documents, databases, models, reference materials and other related resources. Exposure assessment resources are organized into six tool sets, each containing a series of modules:

1. Approaches (e.g., direct measurement [point of contact], indirect estimation [scenario evaluation], exposure reconstruction [biomonitoring and reverse dosimetry])
2. Media (e.g., air, water and sediment, soil and dust, food, aquatic biota, consumer products)
3. Routes of Exposure (e.g., inhalation, ingestion, dermal)
4. Tiers and Types (e.g., screening level and refined, deterministic and probabilistic, aggregate and cumulative)
5. Lifestages and Populations (e.g., general population, residential consumers, lifestages, highly exposed)
6. Chemical Classes (e.g., pesticides, other organics, inorganics and fibers, nanomaterials).

ExpoFIRST enables users to draw on data found in EPA's *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011d) to develop user-defined scenarios based on route of exposure, medium, receptor(s), timeframe and dose metric for a contaminant.

Exposure factors might or might not be the same as those found in the *Exposure Factors Handbook: 2011 Edition*. Exposure assessors need to be aware of their program's specific exposure parameters for the assessment to help select appropriate exposure factors.

### 5.1.4. Observational Human Exposure Measurement Study Data

Observational human exposure measurement studies seek to quantify individuals' exposures to chemicals in their everyday environments during their normal daily activities. Described further in Chapter 7, these studies involve measurements of chemical, physical or biological agents in environmental media; collection of information about the study participants and their homes, work environments and activities; and collection of personal exposure and biomarker samples (Lioy et al. 2005; Sheldon 2010; U.S. EPA 2008c; U.S. EPA 2009a; Zartarian et al. 2005). Section 7.2.13 provides information on what the exposure assessor considers regarding the evaluation of data from observational human exposure measurement studies in line with the data quality objectives (DQOs).

### 5.1.5. Using Different Types of Data to Inform Decisions

Depending on the environmental question, individual data types can be used alone or in combination. For example, combining existing measurement studies with exposure modeling data is useful in evaluating contributions of individual routes of exposure or for model evaluation. Combining data with model estimates can help determine the need for data collection and inform study designs for observational human exposure measurement.

## 5.2. Identifying Data Gaps and Data Needs

The exposure assessment begins by evaluating existing data to determine whether the data address the needs identified during planning and scoping. When data are not available or are inadequate to represent potential exposures, the assessor needs to consider collecting data to meet the goals of the assessment. In addition, where appropriate, the assessor needs to consider obtaining measurements that characterize the nature and extent of chemical contamination and information needed to predict future contaminant concentrations.

Identification of data gaps and data needs begins with understanding the conceptual model, as presented in Section 3.2.2. Figure 3-3 in that section represents an example conceptual model that assessors can use in evaluating potential exposures due to the release of chemicals from drums that impact multiple media and receptors (U.S. EPA 1988a; U.S. EPA 1989a). Table 5-1 describes exposure routes and potential receptors for a hypothetical exposure scenario resulting from the release of chemicals from the spilled drums (U.S. EPA 2016b). Assessors need to consider both current and future exposure scenarios because land use and activities near the contamination source can change over time. The conceptual model helps identify the temporal and spatial extent of contamination, source proximity, wind or water flow direction and completed routes of exposures in the various media that might need sampling.

**Table 5-1. Hypothetical Exposure Scenario for Leaking Chemical Drums**

| Source of Contamination | Release or Transport Medium | Exposure Point | Exposure Route | Exposed Population |
|---|---|---|---|---|
| Drum spill<br>Contaminating soil | Ambient air volatile emissions<br>Dust | Ambient air<br>Dust | Inhalation | Residents (adult and child)<br>Workers<br>Site visitors |
| Soil gas/Groundwater | Indoor air/Vapor intrusion | Indoor air (Microenvironment of room or smaller area of a room)<br>Vapor intrusion | Inhalation | Residents (adult and child)<br>Workers<br>Site visitors |
| Volatilization of contaminants in soil and deposition | Soil | Residential yards | Ingestion<br>Inhalation<br>Dermal | Residents (adult and child) |
| | | On site | Ingestion<br>Inhalation<br>Dermal | Workers (adults)<br>Site visitors (adult and child) |
| Volatilization of contaminants in drums with deposition on soil | Windblown dust | Residential yards<br>Residential homes<br>Facility | Ingestion<br>Inhalation<br>Dermal | Residents (adult and child)<br>Workers (adults) |
| Leaching of contaminants from drums | Groundwater | Private wells | Ingestion<br>Inhalation<br>Dermal | Residents (adult and child)<br>Workers (adult) |
| | | Public water supply | Ingestion<br>Inhalation<br>Dermal | Residents (adult and child)<br>Workers (adults) |
| Uptake of contaminants from soil and groundwater impacted by leaking drums | Biota | Locally grown food<br>Naturally occurring food (e.g., berries, mushrooms)<br>Contaminated fish and game | Ingestion | Residents (adult and child)<br>Subsistence populations |

EPA provides resources for planning projects that use existing data (U.S. EPA 2018e). The recommendations emphasize the need to assess data against their intended use. Review of existing data needs to consider the data collection timeframe, relevance to the exposure assessment being developed and changes in analytical methods (e.g., detection limits) over time. Other resources include:

- Chapter 3 of the Guidance for Quality Assurance Project Plans (G-5) – identifies elements to consider when planning projects that use existing data

- Checklist for Quality Concerns About Using Data from Other Sources – provides step-by-step guidance to ensure that secondary data meet project quality objectives
- Quality Assurance Project Plan Requirements for Secondary Data Research Project – provides example guidance by the QA managers in EPA's National Risk Management Research Laboratory
- EPA's Science Policy Council Assessment Factors – presents general assessment factors for evaluating the quality of scientific and technical information
- Software – For links to free software for performing data quality assessment, see Quality-Related Resources – Software.

Program-specific guidance for evaluating existing data recommends that assessors consider the objective of the study or program that gathered the data, collection and analytical methods, QA/QC procedures used and key study and data uncertainties (EPA's *Resources for Planning Projects that Use Existing Data* website). EPA's *Guidance for Data Usability in Risk Assessment (Part A)* provides information on the minimum quality and quantity of environmental data required to support a Superfund risk assessment (U.S. EPA 1992b). The concepts outlined in these program-specific guidance documents could apply to exposure assessments serving functions beyond the specific program. The exposure assessment/characterization captures decisions to use existing data, including appropriate discussion of any data limitations and situations that preclude use of existing data. Coordination with appropriate programs is important in determining if an assessment can use existing data.

### 5.2.1. Identification of Data Gaps—Existing Data

The review of available data examines the nature/kind of data available and examines its quantity. The assessor uses this information to identify information gaps. The exposure assessor considers what gaps in knowledge the assumptions, estimates, models, default values or targeted data collection will fill. Planning discussions within the project team about filling data gaps strive to answer the following types of questions:

- Is the quantity of data sufficient to perform the exposure assessment, despite having particular data gaps?
- If data are pending, when will the results be available? The exposure assessor and project manager need to weigh the impact of delaying an assessment or decision while acquiring new data.
- Will the missing data make a substantive difference in the exposure assessment? In other words, what is the direct relevance of the data to the problem or exposure assessment objectives?
- How do the missing data relate to anticipated or known specified stakeholder concerns about exposures?

### 5.2.2. Developing a New Data Sampling Program

Before planning a sampling program, the project team needs to evaluate the needed resources (Whitmore et al. 2005). Sampling often is a resource-intensive endeavor requiring substantial time and money. The following questions, modified from the Office of Pollution Prevention and Toxics (OPPT) Considerations When Evaluating Exposure Assessments, are appropriate to

consider when assessing the implications of implementing a sampling program to provide data for an exposure assessment:

- Do the objectives, methods, scope and size of the proposed sampling program support the objectives of an exposure assessment?
- Are appropriate data collection and analytical methods available? Has the scientific community adopted or otherwise accepted these methods? Does EPA have standard operating procedures (SOPs) for these methods? Has EPA validated the methods?
- How many samples are needed to meet the objectives of the study?
- What QA/QC procedures are required?
- What will the sampling program cost?
- What is the timeframe for the decision and is this timeframe sufficient for collecting the data to support the decision?
- Will the uncertainty in the data (e.g., timeframe of data collected, number of samples, detection limits) substantially limit usability of the data for the exposure assessment?

Depending on the answers to these questions, an exposure assessor might decide that a sampling program cannot fill the data gaps (e.g., the appropriate sampling or analytical methods are unavailable; the uncertainty is too great to reduce the data gap). The assessor might decide that a sampling program sufficient to fill data gaps is more extensive than is possible within the resource, time and institutional constraints of an exposure assessment. Alternatively, the assessor might determine that a sampling program would provide valuable information to support an exposure assessment and would be feasible within the available framework. Although it can be an iterative process, an exposure assessment needs to address its purpose, the timeframe of the decision and the point at which enough data are available to support the decision.

## 5.3. Data Quality for New Data Collection

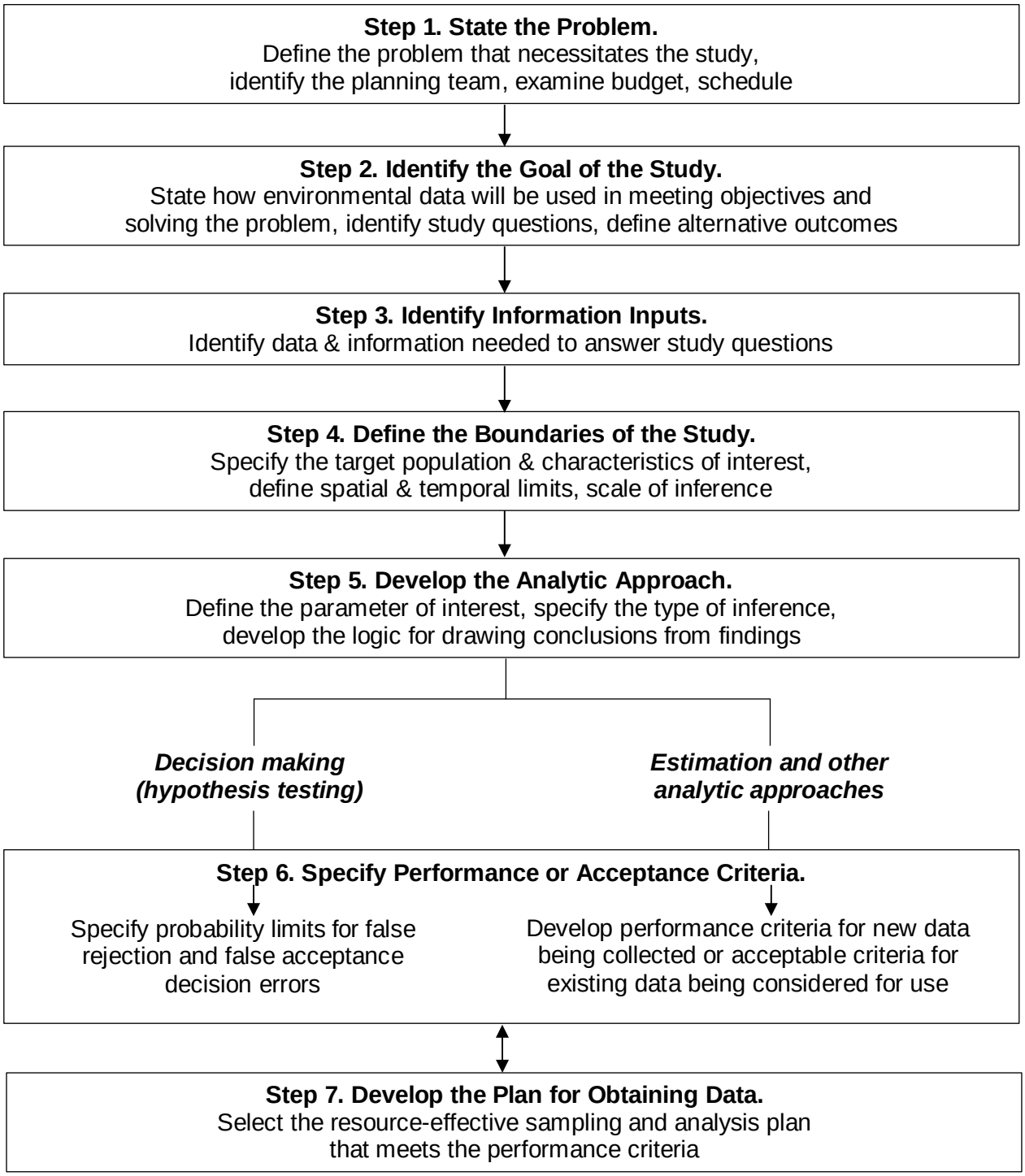
The quality of the exposure characterization, and ultimately the risk characterization, depends on the quality of data used to conduct the exposure assessment. EPA has published guidance and compiled resources on data quality for existing data and new data to meet this objective. Figure 5-3 outlines the process, and Box 5-2 lists selected guidance documents and resources most relevant to data used in exposure assessments.

EPA's *Assessment Factors: A Summary of General Assessment Factors for Evaluating the Quality of Scientific and Technical Information* (U.S. EPA 2003a) also describes quality considerations the Agency takes into account when evaluating scientific and technical information. These include five general assessment factors:

- **Soundness.** The extent to which the scientific and technical procedures, measures, methods or models employed to generate the information are reasonable for and consistent with the intended application.
- **Applicability and utility.** The extent to which the information is relevant for the intended use.
- **Clarity and completeness.** The degree of clarity and completeness in documenting the data, assumptions, methods, QA, sponsoring organizations and analyses employed to generate the information.

- **Uncertainty and variability.** The extent of evaluating and characterizing the uncertainty and variability (quantitative and qualitative) in the information or in the procedures, measures, methods or models.
- **Evaluation and review.** The extent of independent verification, validation and peer review of the information or of the procedures, measures, methods or models.

**Figure 5-3. The Seven Iterative Steps in the Data Quality Objectives Process**



### Box 5-2. EPA Quality Assurance/Quality Control (QA/QC) Websites and Resources

EPA's Quality System manages the quality of the Agency's environmental data collection, generation and use. The Quality System ensures that environmental data are of sufficient quantity and quality to support the data's intended use. Under the EPA Quality System, EPA organizations develop and implement supporting quality systems. Similar specifications may also apply to contractors, grantees and other recipients of financial support from EPA. The Quality System also covers the implementation of the EPA Information Quality Guidelines.

The website www.epa.gov/quality includes the following information categorized by the following titles:

- Quality, Regulations, Policies and Guidance. Includes information on EPA's system-related regulations and Assistance Agreements; Policies and Procedures about Quality Assurance for EPA Organizations including training; list of Agency-wide quality system documents; and quality specifications for non-EPA organizations to do business with EPA.
- Quality Assurance Tools. Includes management tools for projects; descriptions of tools for data quality assessment such as references to A Reviewers Guide (QA-G9R), Statistical Tools for Practitioners (QA-G9S), Checklist for Quality Concerns, and EPA Science Policy Council Assessment Factors; training courses on Quality Assurance and Control Activities; and examples and other on-line resources.
- Information Quality Guidelines. Includes guidelines for ensuring and maximizing the quality, objectivity, utility and integrity of information disseminated by the EPA and requests for correction and requests for reconsideration submitted to the EPA.
- Important Quality System Contacts. Provides contacts in EPA Regional Offices, National Program Offices and ORD National Research Laboratory and Centers responsible for developing and implementing individual quality systems in support of the EPA Quality System.
- Quality Training. The Environmental Quality Management Division develops training materials on quality assurance (QA) activities and the EPA quality system.
- Frequent Questions. Provides answers on all aspects of the Quality System including: goals, benefits, activities, relationship between the quality system and the Information Quality Guidelines, responsibilities and roles of managers and Offices in the QA/QC process.

The EPA Quality Program Policy and Procedure for Agency products and services, issued in October 2008, are available here: EPA Quality Program Policy – CIO 2106.0 and Procedure – CIO 2106-P-01.0.

Common Starting Points:

- If you are developing a quality management plan: Quality Management Tools – Quality Management Plans.
- If you are writing a QA project plan: Quality Management Tools – Quality Assurance Project Plans.
  Also see Quality Management Tools – Systematic Planning for information about planning your project before you document this planning in a QA project plan.
- If you are looking for a typical example of documentation for your specific-project, ask the QA Manager of the organization sponsoring the work. They might or might not provide examples, depending on their organization's policy.
- If you are looking for information about EPA's guidelines on information quality, see the EPA Information Quality Guidelines website.

General information on the Quality System is available at *Frequent Questions about EPA's Quality System*. Information on quality specifications for non-EPA organizations is available at *Quality Specifications for Non-EPA Organizations To Do Business with EPA*.

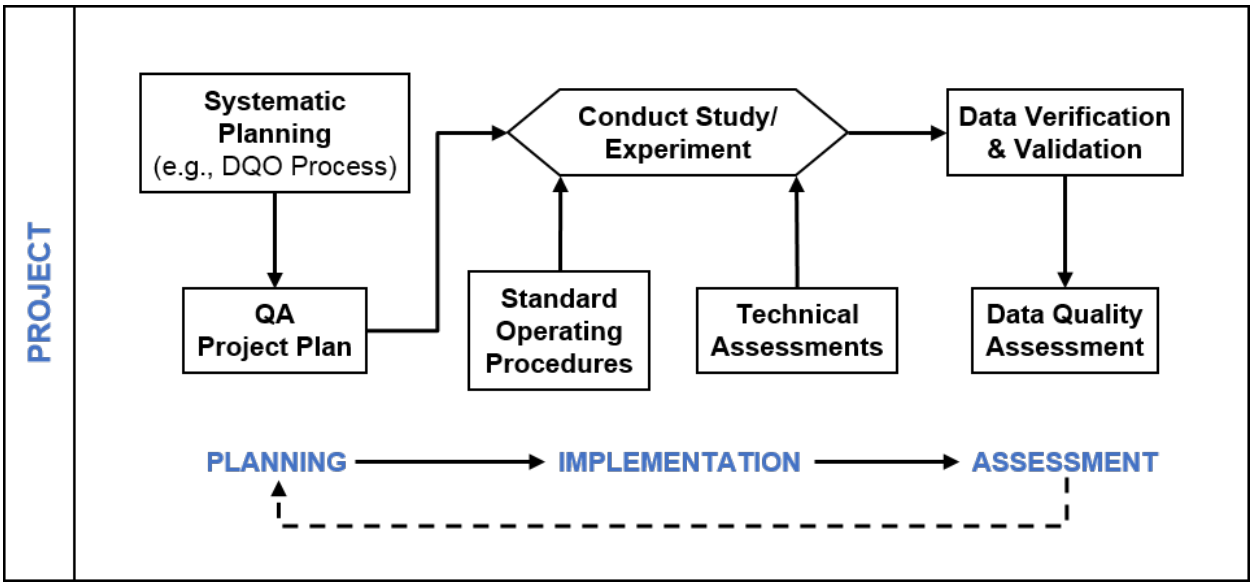
The Office of Management and Budget (OMB) issued government-wide guidelines that provide policy and procedural guidance to federal agencies for ensuring and maximizing the quality, objectivity, utility and integrity of information, including statistical information that federal agencies disseminate (OMB 2006). International agencies, such as the World Health Organization (WHO 2008) and the Canadian government have developed specific documents on data quality in exposure assessment. State agencies also have data quality programs, such as the

Department of Ecology of the State of Washington and the Texas State Soil and Water Conservation Board (see *Environmental Data Quality Management* website).

### 5.3.1. Data Quality System

EPA Order 5360.1, Policy and Program Requirements for the Mandatory Agency-Wide Quality System (U.S. EPA 2000e) defines EPA's quality system requirements. EPA's policy requires all EPA organizations and those that EPA funds to follow a quality system so data collected to characterize environmental processes and conditions are of the appropriate type and quality to support the decision. Agency policy, guidance, tools and guidelines are available at the EPA website, *How EPA Manages the Quality of its Environmental Data*; specific guidance is available at the *Agency-wide Quality System Documents* website. Figure 5-4 identifies the components and tools EPA's Quality System uses, including the project-specific components applied to individual projects (within a program) to ensure achievement of project objectives (U.S. EPA 2002e).

**Figure 5-4. EPA Quality System Components and Tools**




Source: U.S. EPA (2002e)

- **Planning:** Systematic planning, such as the data quality objectives (DQO) process, facilitates development of performance criteria for the data (i.e., the type, quantity and quality of data needed for a specific purpose), production of a sampling plan that satisfies those criteria and determination of the level of oversight and quality control activities needed to ensure the criteria are satisfied. The QA project plan and other planning materials document the systematic planning results. The *EPA Quality Manual for Environmental Programs* (U.S. EPA 2000c) details the process elements emphasizing the "specification of performance criteria for measuring quality" in the context of planning activities. Other guidance includes *EPA Requirements for Quality Assurance Project Plans* (QA/R-5) (U.S. EPA 2001c) and *EPA Requirements for Quality Management Plans* (EPA QA/R-2) (U.S. EPA 2001d).
- **Implementation and Oversight:** The approved methods and procedures documented in the QA project plan and *Guide for Preparing Standard Operating Procedures (SOPs)*

(U.S. EPA 2007c) govern data acquisition. Technical audits and assessments (such as product/service or process quality audits) comprise oversight, performed to determine whether data acquisition complies with requirements specified in the QA project plan and other planning documents. Audits and assessments initiate actions to correct any identified problems.

- **Assessment:** Project personnel use technical knowledge and statistical methods to determine whether the data meet the user's needs. Data verification and validation ensure the measured values are free of gross errors due to procedural or technical problems; data analysis determines whether the data meet the performance criteria documented in the QA project plan (data quality assessment).

### 5.3.2. Data Usability—Determining Whether Data Meet Assessment Factors

The quality of the data used in an exposure assessment drives the credibility of and confidence in the results. Any data used in an exposure assessment, existing or newly collected, need to be of sufficient quality to answer the exposure assessment questions credibly. From a quality perspective, "acceptance criteria" are specifications intended to evaluate the adequacy of one or more existing sources of information or data as being acceptable to support the intended use. "Performance criteria" represent the full set of specifications needed to design a data or information collection effort that, when implemented, generate newly collected data of sufficient quality and quantity to address the project's goals. Minimum performance and acceptance criteria are established during the planning and scoping stage of any assessment (see Section 3.1). EPA programs also might implement specific procedures, and exposure assessors need to consult with their programs and follow their SOPs.

The data needed for an exposure assessment depend on the assessment approach selected during planning and scoping and the assessment objectives (see Section 3.1.1). Therefore, in this stage of an exposure assessment process, an exposure assessor needs to:

- Determine what data are needed to conduct an exposure assessment and DQOs for those data
- For each data value needed, determine whether the data currently are available and if so, obtain them and evaluate their quality and appropriateness
- When appropriate data are not available, determine how crucial they are to the assessment and whether they can be estimated (e.g., collecting data, using models)
- When new data are collected, establish a QA project plan that documents the planning, implementation and assessment procedures and how specific QA/QC activities will be applied during a particular project (U.S. EPA 2001c).

Exposure assessment data present unique challenges when considering data quality. Whether implementing a sampling program or using existing data, an exposure assessor needs to determine that the resulting data meet QA/QC requirements. Upon receipt of data, an exposure assessor reviews their quality. The new data need to meet the five general assessment factors outlined in EPA's *Assessment Factors: A Summary of General Assessment Factors for Evaluating the Quality of Scientific and Technical Information* (U.S. EPA 2003a). Reviewing new and existing data for usability and determining whether the data meet the five general assessment factors involve considering the areas outlined in the following paragraphs.

**Aligning Data with Data Quality Objectives**

All exposure measurements are subject to some level of uncertainty and variability because of the inherent limitations of the sampling methods used and temporal and spatial differences in chemical concentrations. The measurement process, concentrations of specific chemicals measured in various media (e.g., soil, groundwater, sediment) and analytical measurement approaches can introduce uncertainty. DQOs describe the degree of uncertainty the project team is willing to accept based on the needs of the risk manager/decision maker. Setting realistic DQOs is essential because data of insufficient quality will have little value for problem solving, and data of quality that vastly exceeds what is needed to answer the exposure assessment questions provide few, if any, additional advantages. DQOs consider data needs, cost-effectiveness and the capability of the measurement process. In establishing realistic DQOs for the exposure assessment, the team considers the benefits of the additional information against cost, in both time and resources. These considerations need to include selection of analytical methods that meet the goals of the evaluation and minimize the number of non-detect samples in the range of interest in the exposure assessment. DQOs, established for an exposure assessment during planning and scoping (see Section 3.1), outline minimum performance and acceptance criteria. Determining whether existing data meet an exposure assessment's DQOs is critical to assessing whether the data are useful for the assessment. Often, existing data do not completely align with the DQOs but are sufficient to inform the assessment team on how to proceed. For example, air pollution sampling conducted as part of a network to track pollution trends is also useful in representing exposure concentrations at a regional or local level, depending on the locations of the samples. The assessor needs to consider potential exposure misclassification.

Using lower-quality data in an exposure assessment might be acceptable if the limitations in the data do not affect the results significantly in the absence of more accurate information. For example, sensitivity analyses or simulations can reveal whether different scenarios or assumptions lead to similar conclusions. In these cases, an assessor needs to explain in the exposure characterization why the limitations in the data do not invalidate conclusions. In some cases, considering inadequate or partially relevant data when they are the only data available might still yield some information. If these data are used, the exposure characterization needs to state the uncertainty and resulting limitations clearly.

**Establishing a Quality Assurance Project Plan**

Developing a sound QA project plan is critical to the success of any data collection effort. EPA defines a QA project plan as a written document that describes the QA procedures, QC specifications and other technical activities, the implementation of which ensures the results of the project or task will meet project specifications. QA project plans describe and document primary data collection, secondary data usage and data processing (such as modeling) activities that EPA funds (U.S. EPA 2018a).

EPA has compiled guidance and information about preparing a QA project plan on the *Quality Management Tools—QA Project Plans* website. This website includes links to guidance on preparing QA project plans for environmental data collection, modeling, secondary research data and other topics (U.S. EPA 1999a). The *EPA Requirements for Quality Assurance Project Plans* guidance document (U.S. EPA 2001c) outlines the specifications for QA project plans prepared for activities that EPA conducts or supports. In addition to discussing project management, assessment and oversight needs, this document details requirements for data generation,

acquisition, validation and usability. The website also provides several examples of QA project plans. Box 5-2 identified data quality resources, such as guidance for preparing QA project plans for environmental data collection, modeling, secondary research data and other topics, including example documents. Some individual Agency programs also might have information about preparing a QA project plan that considers quality concerns specific to their projects and missions. Agency exposure assessors are encouraged to consult with their programs to obtain specific procedures and guidelines including data submission and review procedures. As with the planning and scoping process, the QA project plan documents the implementation activities needed to ensure that the results of the project or task meet project specifications.

**Obtaining Peer Input to Data Review**

With few exceptions, data documentation (e.g., sampling and implementation plans, QA project plans, SOPs, data analysis plans) and data undergo some level of review, as *EPA's quality process* website describes. Various scientific and technical experts inside and outside the Agency provide input to the development of many Agency work products. EPA's *Peer Review Handbook, 4th Edition* (U.S. EPA 2015c) identifies the following categories of review in the evaluation of data:

- **Peer involvement.** A process whereby Agency staff involve subject matter experts from outside their program in one or more aspects of work product development. Peer involvement includes outreach to and participation by the broad scientific communities beyond the Agency (external) and within the Agency (internal).
- **Peer input.** Ongoing discussions during the development of the work product. Peer input is a form of peer involvement that generally connotes an interaction during the development of an evolving Agency work product, providing an open exchange of data, insights and ideas.
- **Peer review.** An evaluation of a work plan, preliminary draft or the final objective expert evaluation of the work product. Peer review is a documented critical review of a specific Agency scientific or technical work product.

Peer input, sometimes referred to as peer consultation, usually involves a one-time interaction or a limited number of interactions. Peer input is encouraged during the early stages of the project or as part of the culmination of the work product, as appropriate, or both. Evaluating potential peer input requirements early in the process helps ensure allocation of adequate resources. In addition, peer input considerations are integral to setting assessment milestones and schedules.

Major exposure assessments such as those involving controversial methodological or scoping issues are often subject to peer review. Other exposure assessment products that might warrant peer review include observational human exposure measurement studies (see Section 7.2.10), probabilistic exposure analyses (see Section 8.3.4), community-based exposure assessments, aggregate and cumulative exposure assessments and variability and susceptibility evaluations within populations.

**Evaluating Data Quality**

Upon receipt of data generated during sampling, an assessor and team members (e.g., the quality assurance staff) review the quality of the data following the same process used to assess existing data. These new data need to meet the same five general assessment factors outlined in EPA's

*Assessment Factors: A Summary of General Assessment Factors for Evaluating the Quality of Scientific and Technical Information* (U.S. EPA 2003a) and described above in the introduction to this section (see Section 5.3). The evaluation includes a data verification and validation process used to evaluate whether data have been generated according to specifications, satisfy acceptance criteria and are appropriate and consistent with their intended use. Data verification is a systematic process for evaluating performance and compliance of a set of data when compared to a set of standards to ascertain their completeness, correctness and consistency using the methods and criteria defined in the project documentation. Data validation occurs after the data verification process and uses information from the project documentation to determine the usability of the data in light of its measurement quality objectives and to ensure that results obtained are scientifically defensible.

**Validating Data and Reviewing Quality of Sample Collection and Analysis Methods**
EPA has developed several validated protocols for sample collection and analysis. Before using data, an exposure assessor needs to review the data collection and analysis protocols to determine if these methods have been validated. EPA's *Guidance on Environmental Data Verification and Data Validation EPA QA/G-8* explains how to implement data verification and data validation in the context of EPA's Quality System and also provides practical advice and references (U.S. EPA 2002e). If the use of validated methods is not possible, an exposure assessor needs to consider what effect having data of unknown quality has on the confidence in the conclusions.

Data validation is the process of reviewing laboratory data to identify potential QA/QC issues. During data validation, analysts might assign data qualifiers to values for individual chemicals. Examples of qualifiers used under EPA's *Contract Laboratory Program for the Superfund Program* (U.S. EPA 2010c) to indicate QA/QC issues include:

- B (blank): The analyte was found in blank samples.
- J (judgment): The analyte is present but the concentration value is estimated.
- U (undetected): The sample was analyzed but the analyte was not detected at the detection limit.
- R (reject): The quality control indicates that the data are unusable.

During a field study and subsequent analysis, several blank samples and duplicates are collected. Blank samples (e.g., trip blanks, field blanks, laboratory blanks) are samples known to be free of contamination that are carried through the sampling program. Trip blanks accompany the empty sample bottle(s) to the field and the laboratory for analysis. Field blanks, opened in the field, determine if field sampling procedures have contaminated samples. Laboratory blanks indicate potential sample processing contamination. Detection of the chemical in any of these blanks during analysis indicates that sampling or analytical processes have resulted in sample contamination.

Duplicate samples are two samples collected in one location using identical sampling techniques. Theoretically, analysis of these two samples would produce identical results. In reality, analysis results rarely are identical. Data validation, however, assesses the magnitude of the difference to identify possible quality issues. Duplicate laboratory samples demonstrate whether the laboratory achieves acceptable method precision at the time of analysis.

An assessor examines data quality concerns raised during validation because the data might be insufficient for use in an exposure assessment (e.g., a large number of rejected data can skew evaluations). The exposure characterization identifies any limitations with data use.

## 5.3.3. Assessment—Using Data to Evaluate Exposures

### Addressing Non-detect Values

All analytical methods have sensitivity limitations, referred to as the detection limit, quantification limit, method detection limit, reporting limit or other similar term. Analytical chemistry datasets often will include values that are lower than limits deemed reliable enough to report as numerical values (i.e., non-detects, sample quantitation limits). For these samples, the actual presence or concentration of the chemical in the medium is unknown. An assessor, therefore, determines how to represent these data in an exposure assessment including appropriate considerations of method(s) determined by program guidance and practice. Although the literature describes a variety of techniques, no single procedure is appropriate for all exposure assessment circumstances; thus, an assessor needs to decide on the appropriate method for a given situation. Techniques for analyzing non-detect datasets can be grouped into three classes (Helsel 1990): simple substitution methods, distributional methods and robust methods.

- **Simple substitution methods** involve using a single value as a surrogate for each non-detect value. Frequently used substitutions include the detection limit, half the detection limit or zero. In statutes requiring health protective standards, a worst-case approach might use the detection limit as a surrogate, which results in an upward bias in the data. On the other hand, assigning all non-detect values as zero biases the mean downward. Using half the detection limit as the surrogate seeks to balance the upward and downward biases. Depending on the number of non-detects, the overall distribution and standard deviation of the dataset might be severely biased, prompting evaluation by the exposure assessor.
- **Distributional methods** use the detected values in the dataset to extrapolate values for the non-detects. Several statistical analyses are available to extrapolate data, such as log-probit analysis. These methods are most useful for situations in which the dataset contains enough data points above the detection limit to define the distribution function (e.g., lognormal) for exposure values with an acceptable degree of confidence.
- **Robust methods** generally assume a distribution only for the non-detect values rather than the entire dataset. The non-detect values are extrapolated using regression techniques. These methods do not assume that data above the detection limit follow a defined distribution that then can be applied to the non-detect values. These methods involve somewhat more data manipulation than distributional methods.

*Data Quality Assessment: Statistical Methods for Practitioners (*EPA QA/G-9S) provides general guidance on assessing data quality criteria and performance (U.S. EPA 2006c). EPA developed ProUCL, a comprehensive statistical software package with statistical methods and graphic tools to address many environmental sampling and statistical issues. The ProUCL user's guide provides information on the evaluation of non-detects and a discussion of statistical methods (U.S. EPA 2013a). Additionally, the Office of Pesticide Programs developed specific guidance for dealing with non-detects in pesticide residues in food products (U.S. EPA 2000a).

An assessor needs to present a transparent analysis and avoid presenting only summary statistics (e.g., mean concentrations). Information characterizing the dataset (e.g., percentage of non-detect values, maximum detected value, standard deviation) provides additional context for the summary statistics. For complex statistical analyses, contacting a statistician for assistance might be appropriate.

**Evaluating Outlier Data**

The data analysis should not eliminate outlier data (i.e., data points that are numerically distant from the other data points in a dataset) unless these data points can be shown to differ from the other data points in the dataset. Very often, outliers provide useful information to an exposure assessor. Statistical tests such as the Dixon test are appropriate for determining the presence of outliers (Dean and Dixon 1951; Dixon 1950; Dixon 1953; Dixon 1960). The ProUCL software provides graphical techniques and programs to help identify outliers. EPA's *Guidance for Data Quality Assessment* provides detailed explanations of the procedures for conducting the two-sample tests for the evaluation of outliers (U.S. EPA 2000d).

**Combining Datasets and Modeling Data**

Combining datasets is not always possible and when done needs to be performed carefully. The circumstances under which each set of data was collected (e.g., receptor, sampling design, location, time, sampling methods, detection limits) and the quality (e.g., precision, accuracy, representativeness, completeness) need to be evaluated. Similarly, combining measured data with modeled data requires an understanding of the accuracy, representativeness and uncertainty of both datasets. An exposure assessor also needs to understand the implications of using combined datasets on resulting conclusions or exposure estimates. For example, differences in detection limits over time might result in older samples listed as non-detects and more recently acquired samples listed with detected levels. These changes could result in the need to determine whether to include the more recent detected levels or a combination of detected and non-detect concentrations that will affect the calculated exposures. Regardless of whether datasets can be combined, an assessor needs to provide sufficient background information to explain what was done and why, including clear documentation of the source of the data and any references.

**Bounding Estimates**

A bounding estimate is an estimate of exposure that is higher than the highest anticipated exposure to an individual, lifestage, group or population. Bounding estimates often are used during screening-level assessments to eliminate exposure pathways or chemicals of limited importance from further consideration or to determine whether more data and information are needed to evaluate other exposure pathways or agents.

**Calculating Exposure Point Concentrations**

Exposure point concentrations (EPCs) provide an estimate of exposure parameters in specific media (e.g., air, water, soil, sediment). For example, EPCs in the Superfund program assess chronic exposure scenarios (U.S. EPA 2002a); the calculation of the EPC depends on the number of samples and statistical analysis of the data (U.S. EPA 1992d; U.S. EPA 2013a). Sampling data and in some cases, modeling data, are used to calculate the media-specific EPCs. The EPC is determined for each exposure unit in which a receptor moves and is exposed to an environmental medium at a specific frequency (e.g., days/year) and for a specific duration (e.g., years). Exposure assessors need to consult with their specific programs for guidance on calculating an

EPC consistent with any legislative mandate. EPA recommends coordinating with an appropriate program because legislative mandates might require the use of the maximum concentration, mean concentration, upper confidence limit on the mean or other statistical value needed to represent exposures. Coordination with the program early in the process will inform data sampling and evaluation to ensure adherence to the statistical requirements.

## 5.4. Acquiring and Evaluating Data for an Exposure Assessment

When developing the analysis plan for an exposure assessment, an exposure assessor determines the type of data needed (see Section 3.3). This section provides information about existing data sources and methods for collecting new data. The information sources and the questions provided in the following paragraphs represent some of the many resources and concerns that an exposure assessor might encounter.

Each data type discussed in Section 5.1 has unique characteristics that need evaluation to determine their appropriateness for an exposure assessment. Sometimes data needed to support an exposure assessment are available from existing sources. An exposure assessor normally would consider the following issues before using existing data:

- Identify whether data are available to meet a data need
- Identify possible surrogate data
- Obtain and critically review the data to assess usability in an exposure assessment.

Numerous sources are available and accessible to assessors seeking data. These sources can provide data that characterize local, state, regional and national conditions (e.g., location-specific chemical concentrations, state cancer registries, U.S. census demographics). Data also might be available from peer-reviewed scientific literature (e.g., epidemiological studies considering exposures versus health effects). One resource useful in locating this information is EPA's Health and Environmental Research Online (HERO) database, which provides an easy way to access the scientific literature behind EPA science assessments.

An assessor can use one of many approaches to access existing data. For example, all federal agencies and departments that spend more than $100 million per year on research and development are required to increase public access to peer-reviewed scientific research publications and research data (OSTP 2013). That memorandum, "Increasing Access to the Results of Federally Funded Scientific Research," indicates that all federally funded scientific research should be available to the public, the scientific community and industry to the greatest extent feasible, consistent with the following: applicable law and policy; Agency mission; resource constraints; U.S. national, homeland and economic security; and the specific objectives of the memorandum. EPA's efforts to increase public access are detailed in *A Plan To Increase Access to Results of EPA-Funded Scientific Research* (U.S. EPA 2016c). Other federal agencies also have developed plans to make data available, including the U.S. Department of Health and Human Services (U.S. HHS 2016); the Food and Drug Administration (U.S. FDA 2015); and CDC (2015a). Table 5-6 (at the end of this chapter) highlights some of the more common data sources for exposure assessments EPA and other federal agencies develop.

EPA's *Guidance for Data Usability in Risk Assessment (Part A)* provides a foundation for rigorously reviewing and making nationally consistent decisions about the minimum quality and quantity of environmental data required to support a Superfund risk assessment (U.S. EPA 1992b) with specific guidance for federal facilities (U.S. EPA 2005i). These documents provide general concepts that can be useful beyond Superfund. EPA's OPPT recommends assessors consider the questions listed in Table 5-2 when evaluating any type of existing data for use in an exposure assessment (EPA's *Resources for Planning Projects that Use Existing Data* website).

**Table 5-2. Questions to Ask When Evaluating/Considering Data**

| Questions to Ask When Evaluating Existing Data | Questions to Ask When Considering New Data |
|---|---|
| What was the objective of the study or program that gathered the data (e.g., characterizing contamination, establishing baseline cancer rates)? Were the study objectives and designs suitable for the purpose of the exposure assessment? | Do the objectives, methods, scope and size of the proposed sampling program support the objectives of an exposure assessment (e.g., characterizing contamination)? |
| What were the data collection and analytical methods? Has an authoritative body adopted these methods (e.g., the National Institute for Occupational Safety and Health)? Do they meet project data quality objectives or does the scientific community consider them acceptable? | Are appropriate data collection and analytical methods available? Has the scientific community adopted or otherwise accepted those methods? Does EPA have standard operating procedures for the methods? How many samples will be needed to meet the study objectives? |
| What quality assurance/quality control procedures, if any, were used? | What quality assurance/quality control procedures are required? |
| What are the key uncertainties of the study or program data? | Will the uncertainty in the data substantially limit their usability in an exposure assessment? |
| | What will the sampling program cost? |
| What is the proximity of the contaminant source to the exposed individual? For example, if soil is a medium of concern, consideration is given to whether the contamination is located on the property or a road or at a location distant from the receptor. What is the groundwater direction and how does it influence the drinking water source? | Where do samples need to be collected in various media? What soil depths are appropriate to represent exposure? Where do groundwater samples need to be collected to represent impacts on drinking water sources? Are the data available for specific chemical species or are congener data needed to support the exposure assessment? |
| What chemicals in the existing dataset lack data, analytical sampling methods and standardized protocols for sampling? | Are new analytical sampling methods available? Can additional sampling be conducted within the needed timeframe? |

The data needed for an exposure assessment, as outlined during the planning and scoping process (see Chapter 3), are not always available from existing sources. When data are critical to an exposure assessment and no appropriate data are available, an assessor might consider implementing a sampling program to gather the required data.

Sampling often is a resource-intensive endeavor (i.e., requiring substantial time and money), necessitating evaluation of the costs and benefits of the sampling program. The questions listed in Table 5-2, modified from OPPT's *Considerations When Evaluating Exposure Assessments* (EPA's *Resources for Planning Projects that Use Existing Data* website), serve as a guide for assessing the cost-benefit implications of implementing a sampling program to provide data for an exposure assessment. Depending on the answers to those questions, an assessor might decide that:

- A sampling program cannot fill the data gaps (e.g., the appropriate sampling or analytical methods are unavailable, the uncertainty is too great to reduce the data gap satisfactorily)

- A sampling program sufficient to fill the data gaps clearly is more extensive than is possible within the resource, time and institutional constraints of an exposure assessment because, for example, the data collection or analytical methods necessary to meet the sampling program and assessment objectives require time, expertise or financial resources beyond the capacity of the organization
- A sampling program would provide valuable information to support an exposure assessment and would be feasible within the available time, resources and institutional framework.

Sections 5.4.1 through 5.4.5 discuss the unique aspects of conducting activities to gather data for an exposure assessment: characteristics of environmental data and environmental sampling; biomonitoring; compilation of exposure factor information; conduct of questionnaires, surveys and observations; and modeling. These discussions focus on sampling programs and methods applicable to exposure assessment. EPA programs have developed many guidance documents and compiled resources that detail the specifics of planning and implementing a sampling program specific to legislative mandates.

## 5.4.1. Environmental Data

Sources of environmental data include:

- Location-specific environmental sampling and summary documents
- Local, regional or national monitoring databases
- Regulatory submittals for new and existing products
- Local, state and federal agency studies
- Peer-reviewed scientific literature.

Researchers collect environmental data for many reasons using a variety of sampling methods. Table 5-3 describes some of the aspects of common environmental data measurements, including typical measurement objectives, typical target media and examples of sources of existing data.

For an exposure assessment, evaluation of environmental data focuses primarily on the spatial and temporal conditions that affect how well the existing data represent the conditions addressed in the assessment. Key evaluation questions include:

> **Were the data collected close to an exposure point of concern in space and time?** Media measurements collected close to the point of contact for the population or individual in space and time are preferable to measurements far removed geographically and temporally. In addition, considering the frequency and duration of exposure is important, for example, acute, subchronic and chronic; the age ranges of exposed individuals such as children, adolescents and adults; and the types of activities that could result in exposure such as children playing, adolescents trespassing, outdoor workers maintaining surface areas and construction workers digging to greater depths. The certainty with which the data represent the point of contact tends to decrease as the distance in space and time from the point of contact increases. For example, an outdoor air measurement alone cannot adequately characterize indoor exposure. Likewise, shelf studies of consumer products or market basket studies of foods that use regional or national sample groups can provide only a limited understanding of point-of-contact concentrations for localized areas or population groups.

**Table 5-3. Common Environmental Data Measurements**

| Type of Measurement | Typical Measurement Objectives | Typical Target Media | Examples of Sources of Existing Data |
|---|---|---|---|
| Fixed-location media monitoring | • Establish long-term trends at specific sampling locations<br>• Identify changes in existing conditions | • Air (indoor and outdoor)<br>• Vapor intrusion (indoor)<br>• Groundwater<br>• Soil/Indoor dust<br>• Surface water<br>• Sediment<br>• Biota (e.g., fish, crabs) | • National Stream Quality Accounting Network<br>• Water quality network<br>• Air Quality System (EPA)<br>• National Lakes Fish Tissue Study, National River and Streams Assessment Fish Tissue Survey, etc.[a]<br>• Remedial Investigation site-specific sampling under the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA) |
| Short-term media monitoring | • Characterize conditions at a location for a relatively short period of time | • Air (indoor and outdoor)<br>• Vapor intrusion (indoor)<br>• Groundwater<br>• Soil/Indoor dust<br>• Surface water<br>• Sediment<br>• Biota (e.g., fish, crabs) | • CERCLA – Removal Actions<br>• Resource Conservation and Recovery Act<br>• Special studies of environmental media<br>• Indoor air monitoring |
| Source monitoring | • Track chemical release rates to the environment from sources<br>• Characterize the relationships between release amounts and various source operating parameters<br>• Ensure regulatory compliance<br>• Identify disposal options for waste streams | • Air<br>• Groundwater<br>• Surface water<br>• Waste streams<br>• Drinking water<br>• Mobile sources | • National Emissions Inventory (EPA)<br>• Toxics Release Inventory (EPA)<br>• Stack sampling<br>• Effluent sampling<br>• Leachate sampling from landfills<br>• Incinerator ash sampling<br>• Fugitive emissions sampling<br>• Pollution control device sampling |

| Type of Measurement | Typical Measurement Objectives | Typical Target Media | Examples of Sources of Existing Data |
|---|---|---|---|
| Consumer product sampling | • Characterize chemical concentrations for exposure assessment<br>• Assess the quality of the food supply<br>• Ensure regulatory compliance | • Drinking water<br>• Food<br>• Consumer products[b] | • Tap water sampling<br>• Water supply sampling<br>• Prepared food diet sampling<br>• Shelf surveys<br>• Fish sampling from contaminated water bodies<br>• Sampling of crops and livestock associated with contaminated soils and surface water<br>• GIS (geographic information systems)<br>• Personal care products<br>• Household chemicals<br>• Pesticides |
| Microenvironmental sampling | • Evaluate ambient conditions in a defined area<br>• Identify exposure concentrations | • Indoor/Ambient air<br>• Dust<br>• Contaminated surfaces<br>• Residences, offices, commercial establishments<br>• Recreational (e.g., playgrounds, swimming pools) | • Special studies of residences<br>• Radon measurements<br>• Office building monitoring |
| Personal monitoring (e.g., breathing zone samples, skin patch samples) | • Assess exposure to airborne chemicals<br>• Characterize dermal exposure | • Ambient air<br>• Personal air breathing zone (active/passive)<br>• Indoor air<br>• Skin<br>• Duplicate plate for food | • Observational human exposure measurement study results published in the peer-reviewed literature<br>• Industrial hygiene studies<br>• Pesticide applicator surveys |

[a]https://www.epa.gov/fish-tech/fish-tissue-data-collected-epa
[b]https://www.epa.gov/stationary-sources-air-pollution/clean-air-act-guidelines-and-standards-solvent-use-and-surface

- **Under what environmental conditions were the data collected?**
  Data characterizing environmental conditions (e.g., groundwater flow, soil composition, prevailing wind direction) are more representative when measured closer to the point of contact. Again, as the distance from the point of contact or location increases, so does the uncertainty about how well the data represent local conditions. For instance, an aquifer might have an overall flow toward one direction, but local topography (e.g., streams, hills) might alter the direction of flow.
- **How might the chemical concentrations vary over space and time?**
  Chemical concentrations can vary considerably from place to place and over time because of changing use patterns, bioaccumulation, degradation and migration. Changes are of particular concern when using the measured data to extrapolate trends over long periods, such as a lifetime. Exposure assessors frequently use transport and dispersion models to understand how chemical concentrations vary over space and time.
- **How might the chemical concentration compare to background concentrations?**
  Background chemical concentrations might derive from naturally occurring or anthropogenic sources (U.S. EPA 2002e). Naturally occurring chemicals are those not influenced by human activity, while anthropogenic chemicals are natural and human-made substances present in the environment due to human activities (U.S. EPA 2002b; U.S. EPA 2007f). Program-specific guidance can influence the degree to which background is considered in the sampling design. The exposure assessor needs to consult the program for further guidance.
- **If data were collected from a microenvironmental study, do these data represent an exposure assessment population?**
  Microenvironmental measurement approaches are based on the concept that specific spaces are relatively homogeneous and a single measurement characterizes conditions in that zone. These zones are smaller than the room and typically closer in size to a personal breathing zone. For example, typical microenvironments include parts of a house or the entire house, an office or other indoor setting and an automobile. Microenvironments can be divided into time segments (e.g., kitchen-day, kitchen-night). This approach can produce measurements closely linked with the point of contact in both location and time. Because microenvironmental studies represent a very limited environment, an assessor needs to establish that the measurements are representative of the population of interest in an exposure assessment before generalizing them to a population.

Environmental sampling can fill data gaps associated with chemical concentrations or EPCs and physical conditions (e.g., geology, hydrology). These data can either help define an EPC (e.g., personal monitoring in the breathing zone) or support modeling efforts to characterize possible exposure routes (e.g., ingestion of groundwater at a distribution point based on groundwater direction and flow rates).

Questions an assessor might ask include:

- **What sample collection and analytical methods are appropriate?**
  Numerous methods for collecting and analyzing environmental samples exist. The most appropriate methods depend on the objectives of an exposure assessment regarding:
  - Media being sampled (e.g., physical location)
  - Biota type

- Required detection limits
- Target analytes
- Sampling program objectives.

- **What sample design is appropriate?**
  The sample design specifies the number of samples to be collected, sampling locations and sampling time or period (e.g., single samples at multiple locations, seasonal samples or multiple samples at various times in the year to establish trends) and the rationale or justification for each of these elements. The sampling design also includes appropriate QC samples, such as the number of duplicate samples, field blanks and laboratory blanks. A well-planned sample design ensures the data are representative and scientifically defensible for their intended use. Sample designs range from simple random sampling patterns to statistically stratified sampling patterns. As with the selection of the collection and analytical methods, the most appropriate sample design depends on the objectives of the exposure assessment and an understanding of the tolerable level of uncertainty (U.S. EPA 2002d). Section 7.2 presents more information on sampling and study designs.

## 5.4.2. Biomonitoring Data

Sources of biomonitoring data include location-specific studies; local, state or national surveys or registries; and peer-reviewed scientific literature. Table 5-4 describes some common biomonitoring measurements, including typical measurement objectives, media sampled and key sources for this type of data. Other considerations include: (1) differences in metabolic rate across individuals and effects on biomarker levels, (2) time between exposure and sample collection, (3) differences in metabolic rate depending on the route of exposure for rapidly metabolized compounds and (4) influences of body mass on biomarker levels in different fluids.

**Table 5-4. Common Biomonitoring Measurements**

| Typical Measurement Objectives | Typical Target Media | Examples of Sources of Existing Data[a] |
|---|---|---|
| • Confirm presence of a chemical in the body without establishing an exposure source<br>• Contribute to exposure assessments by measuring the internal concentration of a chemical<br>• Assess the relationship between biomarker concentrations and body burden<br>• Evaluate trends in concentrations of specific chemicals across populations<br>• Evaluate trends in chemical-specific concentrations over time, e.g., decreases in chemical concentrations in blood | • Adipose tissue<br>• Blood<br>• Breath<br>• Hair<br>• Nails<br>• Urine<br>• Breast milk | • NHANES<br>• Blood lead sampling in children<br>• ATSDR National Exposure Registry<br>• National Human Adipose Tissue Survey |

[a]NHANES = National Health and Nutrition Examination Survey available at http://www.cdc.gov/nchs/nhanes.htm; ATSDR = Agency for Toxic Substances and Disease Registry; National Human Adipose Tissue Survey available at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=55204

Evaluation questions specific to biomonitoring data include:

- **Are suitable biomarker and analytical methods available to evaluate exposures?**
  Biomarkers are available to assess exposures to several hundred chemicals. The exposure assessor needs to consider whether a biomarker is available for the specific chemical of interest and whether the analytical methods used to detect the chemical concentrations of concern in the media sampled (e.g., blood, serum, urine) are adequate. This information

is an important consideration in determining whether biomonitoring data are useful for the exposure assessment.

- **Are suitable reference levels available to interpret biomarker results?**
  Reference levels help interpret biomarker study results. Biomonitoring studies of chemical concentrations provide physicians and public health officials with reference values so they can determine if people have been exposed to levels of the chemical higher than found in the general population and whether actions are needed to reduce potential exposures (CDC 2012b; CDC 2017). Developing reference levels can require a determination of whether normalizing the results between participants will need additional measurements, for example, creatinine in urine or lipids in breast milk. Whether biomonitoring data need normalizing also is an important consideration during study design to optimize data collection.
- **Do confidentiality concerns restrict the access to or use of biomonitoring data?**
  Sometimes assessors cannot access or release biomonitoring data publicly due to concerns or requirements about maintaining the confidentiality of personal data. For example, assessors can access NHANES "public-use" datasets but not other datasets because of confidentiality restrictions. Section 7.2.10 discusses further considerations regarding data confidentiality. The National Center for Health Statistics (NCHS) has established Research Data Centers to allow researchers access to restricted data. The Research Data Centers host restricted data from a variety of groups within the U.S. Department of Health and Human Services. Release of the data follows strict protocols to protect participant confidentiality. For further information about Research Data Centers, see the *NCHS Research Data Center* website.
- **Are biomonitoring data the only data available to assess exposure?**
  Body burden or biomarker data represent the amount of a chemical inside the body of an exposed individual. These data can establish the presence of a chemical and quantify the concentration of the chemical or its metabolite in the sampled matrix. Biomonitoring data, however, do not identify a specific source of exposure or the period of exposure (e.g., years or days ago). Rather, exposure assessors have used body burden and biomarker data to supplement environmental monitoring data and modeling activities in estimating exposure. Increasingly, however, advances in science and research are making possible more robust reverse and forward dosimetry models that support evaluation of associations between biomonitoring data and exposures (see Section 6.2.3) (e.g., Morgan et al. 2008; Tulve et al. 2011).
- **What data quality information is available for the dataset?**
  EPA's general QA/QC procedures for collecting data can be applied to the collection of biomonitoring data. For example, for existing data such as NHANES, reviewing the study documentation to understand the QA/QC procedures is essential to ensure the data meet the study objectives (Berman et al. 2001; CDC 2016).

**Developing Data Quality Objectives and Identifying Sampling and Analysis Methods**

The objectives of an exposure assessment and the tolerable level of uncertainty will drive the selection of sample collection methods, analytical methods and study design. Consulting with experts in biomonitoring often is helpful in developing a scientifically sound biomonitoring study. Considerations for sample collection and analytical methods in biomonitoring studies are similar to those for environmental sampling. Special considerations apply, however, when

gathering data from people. EPA policy requires sampling programs that include gathering data from individuals to address confidentiality, ethical issues and protocol reviews and approvals, as detailed in Section 7.2.10.

Biomonitoring studies can address data gaps associated with:

- Possible exposures
- Baseline conditions
- Internal chemical or metabolite concentrations.

**Evaluating Biomonitoring Data**

Although biomonitoring data might not provide a direct link between an exposure source and a health effect, they can influence the outcome of an exposure assessment. For example, biomonitoring data that report chemical or metabolite concentrations can confirm that exposures are occurring, which can direct an exposure assessment. For some chemicals, these data also can provide information about internal doses, which can support modeling efforts. Box 5-3 lists useful guidelines and resources associated with conducting biomonitoring studies.

**Box 5-3. Guidance Documents and Resources for Planning and Implementing a Biomonitoring Program**

- CDC (2015b) *CDC Specimen-Collection Protocol for a Chemical-Exposure Event*.
- NRC (2006b) *Human Biomonitoring for Environmental Chemicals*.
- *Laboratory Systems and Standards* website. Association of Public Health Laboratories.
- *Publications and Products* website. *Division of Laboratory Sciences* website. CDC.
- *Publications and Products* website. *National Biomonitoring Program* website. CDC.
- *Publications and Products* website. *National Center for Environmental Health* website. CDC.

Biomonitoring is a rapidly advancing science. The available methods and data applications are evolving constantly; better and more sophisticated tools can quickly replace methods currently considered state-of-the-science. Consulting with experts in biomonitoring is critical to developing a scientifically defensible sampling program or study. Questions an assessor might ask these experts include:

- **When conducting biomonitoring, what sample collection methods, analytical methods and study design are appropriate?**
  Similar to environmental sampling, a biomonitoring project that involves collecting fluids, tissues, breath, hair or nails considers sample collection and analytical methods. Sample design considerations are similar for environmental and biomonitoring studies.
- **What special considerations apply when gathering data from people?**
  Sampling programs that include gathering data from individuals are subject to several considerations beyond sample collection, analysis and design. These programs also need to address confidentiality, ethical issues and protocol reviews. Section 7.2.10 provides a detailed discussion of the implications associated with conducting observational human exposure measurement studies.

### 5.4.3. Exposure Factor Information

Key sources of exposure factor information include:

- EPA exposure factors
  - EPA's *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011d)
  - EPA's *Child-Specific Exposure Scenarios Examples* (U.S. EPA 2014a)
  - EPA program, office or region default values that are transparent in their presentation of information, source of data and application in the absence of site-specific information [e.g., *Human Health Evaluation Manual, Supplemental Guidance: Update of Standard Default Exposure Factors* (U.S. EPA 2014g)].
- Datasets EPA has compiled
  - Consolidated Human Activity Database
- Datasets other federal agencies have compiled
  - American Time Use Survey
  - Food Commodity Intake Database
  - National Health and Nutrition Examination Survey (NHANES)
  - Continuing Survey of Food Intakes by Individuals
- Peer-reviewed scientific literature.

EPA's *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011d) is the most widely known source of exposure factor data. The basis of summary data and mean values cited in these documents is published data and information that provide general population data (e.g., food survey findings) or data collected from populations in a specific group or region (e.g., fish consumption by Native Americans, outdoor activity in the Northeast). EPA also presents confidence ratings that exposure assessors can use when evaluating data quality. A higher confidence rating indicates higher data quality.

Some EPA programs have derived default values for exposure factor data, used in the absence of location- or scenario-specific information. For example, the derivation of Maximum Contaminant Levels can use default drinking water intakes. The use of defaults in risk assessment raises concerns, however, and EPA's policies about using defaults have been the subject of scrutiny. Public commenters raised this issue, and the Office of the Science Advisor addressed it in their 2004 "Staff Paper," *An Examination of EPA Risk Assessment Principles and Practices* (U.S. EPA 2004c). In its 2009 publication, *Science and Decisions: Advancing Risk Assessment* (NRC 2009), the National Research Council (NRC) outlined several advantages and disadvantages of using default values. This document provides assessors with additional perspectives about the application of defaults in an exposure assessment.

Table 5-5 presents common exposure factor data, including typical measurement objectives and data collection methods and examples of each type of data. Selection of specific exposure factors needs to consider the ages of the exposed individuals, activity patterns, sensitive individuals such as pregnant women and consumption patterns (e.g., ingestion of fish, game).

**Table 5-5. Common Exposure Factor Information Measurements**

| Type of Measurement | Typical Measurement Objectives | Typical Data Collection Methods | Examples of Types of Exposure Factor Data |
|---|---|---|---|
| Physical characteristics | • Evaluate traits of individuals that could impact how chemical exposure affects their bodies | • Direct observation<br>• Surveys<br>• Questionnaires | Age-specific<br>• Body weight<br>• Height<br>• Skin surface area |
| Activity frequency and duration | • Identify how long and how frequently individuals engage in a particular activity<br>• Determine how often individuals engage in activities that could reduce/increase potential exposures | • Questionnaires<br>• Surveys | • Time spent indoors/outdoors<br>• Frequency of hand washing<br>• Duration of showering |
| Intake rates | • Determine the amount of a substance that individuals could take into their bodies from exposure | • Population surveys<br>• Questionnaires | Age-specific rates of<br>• Drinking water ingestion<br>• Fish consumption<br>• Incidental soil ingestion<br>• Inhalation rates |

When evaluating exposure factor data for use in an exposure assessment, key questions include:

- **When choosing to use default values because of a lack of location- or scenario-specific information, what is the basis for these values?**
  The use of default values needs careful and thoughtful consideration to ensure that default values are appropriate for the assessment. Because the use of default values in an exposure assessment often is unavoidable when specific exposure factor data are lacking, EPA has worked to provide transparency about the basis for choosing default values and evidence and policy supporting their use in exposure assessment (NRC 2009). The selection of exposure factors also needs to consider lifestages, sensitive populations such as pregnant women and other characteristics unique to the population.
- **Are the exposure factor data representative of the exposures being assessed?**
  Exposure factor data derive from studies of populations. The more the study population resembles the assessment population in size, age, race, sex, lifeways and socioeconomic status, the more representative exposure factor data are likely to be of the population being assessed. Conversely, the more the study population and assessment population differ, the less representative the exposure factor data likely will be.

## 5.4.4. Questionnaires, Surveys and Observations

Administering questionnaires and surveys or conducting observational human exposure measurement studies can help address data gaps in exposure factor information. Because exposure factor data contribute to the development of a conceptual model and exposure scenarios and the quantitative assessment of exposure, findings are useful to evaluate assumptions about exposure route, duration and frequency.

Data collected in an observational human exposure measurement study need to be of sufficient quality and quantity to support the study objectives, hypotheses or scientific questions. The most efficient way to ensure enough high-quality data is to establish the data quality criteria before the study begins and then develop a study design that incorporates these criteria. To facilitate this

approach, the Agency has developed the DQO process, a systematic planning tool based on the scientific method, for establishing criteria for data quality and developing data collection designs (U.S. EPA 2002c). Detailed guidance on the DQO process and other related information are available in EPA's report, *Guidance for Quality Assurance Project Plans: EPA QA/G-5* (U.S. EPA 2002c), and at the *EPA Quality System* website. Another resource is the EPA *Survey Management Handbook*, which provides guidance on conducting, designing and analyzing environmental surveys. The handbook provides practical advice on many aspects of survey research (U.S. EPA 2003h).

Box 5-4 lists useful guidelines and resources associated with designing and implementing questionnaires and surveys and conducting observational studies. Questionnaire and survey design is a complex process requiring experts in appropriate survey methods and techniques.

**Box 5-4. Examples of Guidance Documents and Resources for Conducting Questionnaires, Surveys or Observational Studies**

- U.S. EPA (1992a) *Consumption Surveys for Fish and Shellfish: A Review and Analysis of Survey Methods*. EPA/822/R-92/001.
- Dillman (1999) *Mail and Internet Surveys: The Tailored Design Method*.
- U.S. EPA (2003h) *Survey Management Handbook*. EPA/260/B-03/003.
- OMB (2006) *Questions and Answers When Designing Surveys for Information Collections*.
- U.S. EPA (2007g) *Guide for Measuring Compliance Assistance Outcomes*. EPA/300/B-07/002.

More information on observational human exposure measurement studies is found in Chapter 7.

Questions an assessor might ask these experts include:

- **What methods are available for implementing questionnaires and surveys?** Several approaches exist for conducting questionnaires and surveys. For exposure assessment, common methodologies include respondent estimates, third-party estimates and diaries.
  - **Respondent estimates** are the least expensive and most commonly used questionnaire alternative. Respondents are asked to estimate the time they spend at a particular activity. Questionnaires and surveys ask how many hours were spent doing a given activity, being at a given location or using a certain product. In exposure studies, respondents might be asked how often they use a chemical or product of interest or perform a specific activity.
  - **Third-party estimates** use essentially the same approach as respondent estimates, except that one person completes a questionnaire or survey for another. For third-party estimates, the questionnaire or survey asks how many hours per week the specific person spends completing a given activity, being at a given location or using certain products. The person completing the questionnaire or survey can obtain information by interviewing or observing the respondent (e.g., reviewing video monitoring data) (U.S. EPA 2012f).
  - **Diary** approaches provide a sequential record of a person's activities during a specified period. Typical time-diary studies follow activities across a day or a week. The design of diary forms facilitates respondents' reporting of all their activities and

locations for the specified period. Carefully designed forms are especially important for diary studies to ensure that the data each individual reports are comparable. The resulting time budget helps characterize an individual's behavior, activities or other features during the observation period. Sequential-activity monitoring forms the basis of an activity profile.

- **What methods are available for conducting observational studies?**
  Observational studies record activities, including location-time data, for an individual, lifestage, specific group or population. The person(s) under evaluation or an observer can record the activity. These studies sometimes use behavioral monitoring devices (e.g., accelerometers, GPS [global positioning system] applications). These methods probably are the most expensive approach to gathering activity data because they require the use or development of equipment, respondent agreement to use such equipment and technical help to install or adjust the equipment.
- **What are the clearance requirements for releasing questionnaires or surveys?**
  The Paperwork Reduction Act of 1995 requires each federal agency to obtain approval from OMB before collecting information from 10 or more people. The approval process ensures the quality and practical utility of the information collected. This process is time consuming and requires the publication of at least two *Federal Register* notices that an Information Collection Request—commonly known as an OMB clearance package—has been submitted. OMB's review of the request sometimes takes many months (i.e., at least 120 days) (OMB 2006).
- **What special considerations apply when gathering data from people?**
  Similar to biomonitoring studies involving individuals, an assessor considers confidentiality needs, ethical issues and protocol reviews associated with studying individuals. Questionnaires and surveys can be components of observational human exposure measurement studies; see Section 7.2.10, which provides a detailed discussion of considerations associated with gathering data from people.

## 5.4.5. Modeling

EPA defines a model as "a simplification of reality that is constructed to gain insights into select attributes of a particular physical, biological, economic or social system" (NRC 2007; U.S. EPA 2009d). Chapter 6 discusses model selection and use in exposure assessments.

In exposure assessments, assessors use models to reduce gaps in empirical data, extrapolate monitoring data to non-surveyed populations or predict future exposures. Models also serve as a framework to bring together various types of data to develop estimates of exposure that are consistent with all empirical data:

- Chemical release rates from sources
- Chemical fate and transport
- EPCs
- Exposure factors
- Internal chemical or metabolite concentrations
- Estimated doses.

The estimates generated by models can be used as variables for conducting quantitative exposure assessments. For example, a particular fate and transport model might estimate environmental

concentrations by predicting chemical migration through groundwater and concurrent loss by degradation. Model estimates also might serve as conclusions of an exposure assessment (e.g., estimates of the cumulative impacts of exposures to multiple chemicals).

Box 5-5 presents guidelines and resources associated with environmental models. Section 6.2 describes the process for selecting an appropriate model, which depends on the specific circumstances of an exposure assessment.

**Box 5-5. Guidance Documents and Resources to Support Modeling Efforts**

- WHO (2005) *Principles of Characterizing and Applying Human Exposure Models.*
- NRC (2007) *Models in Environmental Regulatory Decision Making.*
- U.S. EPA (2009d) *Guidance on the Development, Evaluation, and Application of Environmental Models.* EPA/100/K-09/003.
- *Center for Exposure Assessment Modeling (CEAM) website. U.S. EPA.*
- *Radiation Protection Document Library* website. *Radiation Protection* website. U.S. EPA.
- *Predictive Models and Tools for Assessing Chemicals under the Toxic Substances Control Act (TSCA)* website. U.S. EPA.

In addition, the following questions, set forth in the *Guidance on the Development, Evaluation, and Application of Environmental Models* (U.S. EPA 2009d) for consideration when using a model for regulatory or research purposes, provide a useful list for assessors to consider when evaluating empirical models for use in an exposure assessment:

- What are the project objectives?
- What are the type and scope of the needed model?
- What are the data criteria?
- In what situations does the model apply?
- What are the programmatic constraints?
- How does the empirical model fit with the conceptual model for the project?
- Has the model been peer reviewed?
- Has the model been evaluated with measured data?

The Agency has a community of practice that addresses environmental modeling. Modeling content, including databases and training, is available at EPA's *Environmental Modeling* website.

## 5.5. Data and Decision Uncertainty and Variability

An exposure assessment can have many sources of data uncertainty, data variability and decision uncertainty. This section highlights some general points about data and decision uncertainty and variability. Sections 8.1.1 through 8.1.3 present a detailed discussion of data uncertainty, decision uncertainty and variability, including processes and methodologies to evaluate and potentially reduce them. ExpoBox provides information on the concepts of uncertainty and variability in the form of questions and answers related to exposure assessment. Chapter 8 also provides a detailed discussion of the distinction between data uncertainty and decision uncertainty and the importance of distinguishing between the two. This section addresses

uncertainty and variability specifically associated with the data an assessment uses. An assessor needs to consider how data uncertainty and variability can influence the outcome of the assessment. Questions for an assessor to consider when reviewing the data include:

- **What are the sources of uncertainty in the data?**
  The term "data uncertainty" encompasses many concepts. Sampling uncertainty, also known as parameter uncertainty, stems from measurement errors, sampling errors, misclassification of data and surrogate data weaknesses. The degree to which the data are representative of actual conditions also introduces uncertainty. An assessor needs to review these factors when evaluating data sources for use in an exposure assessment. Many methods to address and reduce sampling uncertainty are available, ranging from classical statistical analyses to probabilistic uncertainty analyses (see Section 8.3). Qualitative or quantitative information about the level of uncertainty and variability (i.e., confidence) associated with a dataset sometimes is available or an assessor can estimate them. The *Exposure Factors Handbook: 2011 Edition* [(U.S. EPA 2011d) (pages 1-5 through 1-7] presents several factors a risk assessor needs to consider in evaluating data uncertainties and variability when selecting data to include. EPA provides confidence ratings for the data presented in the Handbook (U.S. EPA 2011d). A higher confidence rating typically is associated with data having fewer uncertainties. An assessor can conduct statistical analyses, such as standard deviation and upper confidence limit calculations, to represent uncertainty and variability quantitatively. For example, a larger standard deviation typically is associated with a greater level of uncertainty or variability in the data.
- **What are the sources of variability in the data?**
  All datasets introduce variability—the natural differences that occur in a sampling medium or population—into an exposure assessment. For example, environmental data represent the range of chemical concentrations in the environment, and activity information represents the range of possible activities that can occur in a population. EPA might address variability by selecting the data that represent a high-end exposure level (see Section 5.1.3).
- **How does decision uncertainty affect exposure assessment decisions?**
  Decision uncertainty includes data uncertainty and pertains to whether the analyses are adequate to better inform the exposure assessment decisions and help the risk manager/decision maker understand the relationships among the data and evaluate the potential decision options. This process includes evaluating data, including appropriate documentation of the approach used, to assess the adequacy of the data to support a decision. The assessment might consider the number of samples, spatial distribution of contaminants, detection limits, quantity and precision of measurements, number of duplicates and concentrations less than the detection level but above zero that could impact measured outcomes. The risk manager/decision maker might consider whether closing data gaps necessitates statistical evaluation. Can the data be deemed adequate for the decision at hand? Will uncertainty in the data or the manner in which they are used cause a risk manager/decision maker to change the decision? Do significant data gaps exist, making further data collection necessary? The confidence level assigned to the data during an uncertainty and variability evaluation can influence the decision making process. An assessor can use the confidence level to help determine data usability. Data

with a low confidence level (e.g., a mean exposure concentration or an activity pattern based on a small sample size) might be adequate to support screening-level exposure assessment DQOs. If these data are critical to meeting the DQOs, an assessor might decide that additional data collection efforts are necessary (WHO 2008).

## 5.6. Data Management

EPA's Office of Environmental Information maintains the *Data Standards* website, which features information relevant to the data management process. This website houses data standards, developed to ensure consistent data reporting across the Agency. Although these standards are not data requirements, they can serve as a starting point when assessing data management systems. An assessor needs to consider the unique data concerns and objectives for a data management system in the context of the particular exposure assessment and project team accessibility. Some individual programs within EPA have developed guidance and SOPs for managing data. Therefore, assessors need to consult their programs when developing a data management system. Useful questions for an assessor to ask when selecting a data management system include:

- **What technologies are available for managing data?**
  Many software programs are available for storing and managing data. Spreadsheet and database programs are two standard technologies and are available as standard desktop applications. GIS (geographic information system) applications are another tool for managing data, especially when data mapping is necessary. In selecting the best technology, an assessor reviews the data quantity and analysis needed and the technological limitations or requirements (e.g., software accessibility to multiple users, mapping functions). Information technology staff can provide guidance and assistance in selecting and building an appropriate data management tool. A basic understanding of the uses and limitations of each technology also is useful.
  - **Spreadsheets** organize data in simple tables and include functions to conduct statistical analyses, generate graphs and create charts. Most spreadsheet programs have a limited ability to query and extract data and have limited data storage capacity compared with more sophisticated database programs.
  - **Databases** provide functions that are more robust for conducting queries, extracting data and generating data reports compared with spreadsheet applications. Databases also have a greater data storage capacity and allow linkage of multiple tables within a database for establishing relationships between datasets. For example, a data analyst can link a table containing activity data for individuals to another data table housing biomonitoring results. Statistical analyses also are possible using databases. Users can share databases and access the data simultaneously.
  - **GIS** applications are sophisticated tools for depicting spatial relationships in data. Although historically considered to be mapping tools, current programs include the functionality to store and manage data, conduct statistical analyses, generate graphs and charts and map information spatially. Because GIS programs are complex, an assessor likely will need support from a GIS expert. Regardless of the data management system used, the data need appropriate annotation with supporting information so that future users can assess their quality and utility.

- Data managers need to consider the Agency's Records Management Policy. The assessor needs to coordinate with the program regarding specific legal and other constraints on releasing and sharing certain categories of information.

- **What are the implications of the Freedom of Information Act (FOIA) on data management?**
  Under FOIA, any person can submit a written request that EPA release Agency records. EPA releases these records unless they fall under one of the nine FOIA exemptions, such as trade secrets (e.g., pesticide formulations) or medical files (e.g., health information about an individual). Detailed information about FOIA, FOIA request forms and EPA's policies and procedures regarding FOIA are available at EPA's *Freedom of Information Act (FOIA)* website.
- **What are the restrictions on releasing data publicly?**
  Some types of data, such as data exempted under FOIA, are confidential, and assessors need to take precautions to avoid releasing them inadvertently. For example, the formulation of a pesticide under review for registration is an example of a trade secret or confidential business information. The U.S. Department of Justice's *DOJ Guide to the Freedom of Information Act* website provides more information about FOIA exemptions. The 1996 FOIA update identifies specific provisions for protecting privacy of personal information. Consultation with FOIA attorneys before the release of information is important to avoid potential violations of privacy.
- **What are the QA/QC requirements for data management?**
  QA/QC for data management needs to address data entry and verification and maintaining data as part of records management planning. Validation of data entry is a vital component of data management. Storing and retaining data is part of records management and is a requirement of all government employees.

Other data remain confidential under EPA's *Privacy Policy* (U.S. EPA 2005a), which establishes Agency requirements for safeguarding the collection, access, use, dissemination and storage of personally identifiable information.

## 5.7. Data Communication

Ongoing communication with project staff and stakeholders is an important part of an exposure assessment. Chapter 9 discusses communication needs. Several data-related topics are essential for effective communication with risk managers/decision makers and stakeholders about existing data reviews or data collection efforts (see Table 5-6 for example data sources):

- **Data presentation.** Outreach to stakeholders is important when evaluating existing data, identifying data for collection or using data to support decisions (U.S. EPA 2016e). Communication plans need to consider privacy and confidentiality of data (e.g., residential sampling), protection of personally identifiable information, how the data meet the DQOs and how to present the information in a format that participants, the community and stakeholders understand. Presentation considerations include length, content and format (e.g., website, social media site, fact sheets, flyers, informal meetings, briefings, formal meetings to meet regulatory requirements, informal availability

sessions, Community Advisory Group or virtual). Testing presentations and materials with colleagues to ensure the messages are understandable is helpful.

- **Data representation.** Quantitative data often are reported as a single point (e.g., average concentration of a chemical in soil) or represent one moment in time (e.g., concentrations in emissions from an incinerator). Rarely do these single data points represent the full range of actual conditions. For example, an average soil concentration does not indicate the highest or lowest detected value. An emissions sample from an incinerator does not represent changing conditions, such as increasing capacity or varying waste stream composition. Therefore, discussions about data indicate what the data do and do not represent. Presenting data in graphical formats is helpful in showing locations of concentrations, ranges of concentrations (e.g., minimum, maximum, average), outliers and other parameters.
- **Data limitations.** Data can help answer some but not all questions about exposure. Therefore, an assessor outlines the conclusions the data can and cannot support.
- **Data collection rationale.** In some cases, stakeholders might believe that data collection efforts will provide needed answers to their concerns. In other cases, stakeholders might believe that additional data collection is unnecessary. In both cases, an assessor states why existing data suffice for an exposure assessment or why additional data collection efforts are necessary. If collecting data, an assessor also explains the sample design (e.g., what and where samples will be collected, what analyses will be conducted) and the rationale for the sample design (e.g., why specific sample locations were selected).
- **Data uncertainty and variability.** Certain amounts of uncertainty and variability are associated with all data. An assessor needs to outline the uncertainty and variability associated with the data and show how these parameters affect the conclusions.

## 5.8. Summary

- Exposure assessments use a **variety of data**: environmental data, biomonitoring data and exposure factors. Some exposure assessments might use a combination of data types or supplement measurement data with modeling data.
- Identification of **data gaps and data needs** begins with understanding the conceptual model. When existing data are insufficient to satisfy exposure assessment needs, a sampling program is considered. Planning a sampling program requires careful evaluation of resource needs.
- The Agency has longstanding, established procedures for **ensuring data quality**, has published numerous guidance documents and provides a large body of resources that exposure assessors can consult when beginning an assessment.
    - EPA's policy requires all EPA organizations, and those funded by EPA, to follow a **quality system** to ensure that data collected to characterize environmental processes and conditions are appropriate to support the decision. EPA specifies a data quality system comprising seven iterative steps, spanning planning, implementation and assessment.
    - Reviewing new and existing data for **usability** and determining whether they meet the five general assessment factors (soundness, applicability and utility, clarity and completeness, uncertainty and variability and evaluation and review) involve (1) aligning data with data quality objectives, (2) establishing a QA project plan,

(3) obtaining peer input to data review, (4) evaluating data quality and (5) validating data and reviewing methods for sample collection and analysis.
    - When **using data for an exposure assessment**, the assessor needs to decide what methods to use in representing non-detects, how to handle outliers, whether and how to combine datasets or combine datasets with modeling outputs, how to make use of bounding estimates and how to calculate exposure point concentrations.
- **Acquiring and evaluating data for exposure assessment** informs assessors whether they can use existing data or need new data. During planning and scoping, assessors determine the data they need and how to obtain the data from existing sources, if available, or whether and how to gather new data. EPA provides many guidance documents for reviewing the quality of existing data and questions to guide an assessor's decision to use existing data. When critical data are not available, an assessor might consider implementing a sampling program to gather the required data. Each data type has unique characteristics that require evaluation.
    - Evaluation of **environmental data** focuses primarily on the spatial and temporal conditions that affect how well the data represent the conditions addressed in the assessment.
    - **Environmental sampling** can fill data gaps associated with chemical concentrations or EPCs and physical conditions such as geology or hydrology.
    - Evaluation of **biomonitoring data** determines whether biomarkers are appropriate for assessing exposure, reference levels are available and concerns exist regarding access or disclosure and what data quality measures are associated with the dataset.
    - Evaluation of **exposure factor information** determines the basis for any default values and whether exposure factors represent the exposure being assessed.
    - Acquiring data through **questionnaires, surveys or observational studies** involves considering the methods for implementing these approaches, the clearances required and what methods are available for observational studies.
    - **Modeling** fills data gaps for some exposure assessments. EPA and other organizations offer a large body of guidance for the application of models in exposure assessment.
- The key considerations for an exposure assessor regarding **data uncertainty and variability** are: What are the sources of uncertainty in the data? What are the sources of variability in the data? How does decision uncertainty affect exposure assessment decisions?
- An assessor needs to consider the unique data concerns and objectives for a **data management** system in the context of the particular exposure assessment and with regard to data accessibility for the project team.
- A fundamental requirement of effective exposure assessment is transparent and frequent **communication of data**, for which having a solid communication plan is key.

**Table 5-6. Examples of Sources of Non-Occupational Data for an Exposure Assessment from EPA and other Federal Agencies[a]**

| Source | Data Type | Scale | Description | Reference |
|---|---|---|---|---|
| U.S. EPA | | | | |
| EPA – *Exposure Factors Handbook: 2011 Edition* | • Exposure factors | • Local<br>• State<br>• Regional<br>• National<br>• International | The *Exposure Factors Handbook: 2011 Edition* provides information and recommendations on various factors used in assessing exposure to adults and children. The handbook summarizes data on human behaviors and characteristics that affect exposure to environmental contaminants and recommends values. This document summarizes the available statistical data on factors including consumption of drinking water, fruits, vegetables, beef, dairy products and fish; soil ingestion; inhalation rates; skin surface area; soil adherence; lifetime activity patterns; body weight; consumer product use; and building characteristics. Also see ExpoBox and ExpoFIRST. | U.S. EPA (2011d)<br>https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252 |
| EPA – ExpoBox | • Exposure factors | • Local<br>• State<br>• Regional<br>• National<br>• International | ExpoBox is a compendium of exposure assessment tools that links to guidance documents, databases, models, key reference materials and other related resources. Resources are organized into six Tool Sets, including modules designed to improve the accessibility and usability of data from EPA's *Exposure Factors Handbook: 2011 Edition*. EPA plans to add exposure assessment resources to EPA ExpoBox as they become available. Under the Media section, information on exposure assessment tools for consumer products is provided. | https://www.epa.gov/expobox |
| EPA – ExpoFIRST | • Exposure factors | • Local<br>• State<br>• Regional<br>• National<br>• International | ExpoFIRST – the Exposure Factors Interactive Resource for Scenarios Tool – uses data from EPA's *Exposure Factors Handbook: 2011 Edition* in an interactive tool that maximizes flexibility and transparency for exposure assessors. Users develop scenarios based on route of exposure, medium, receptor(s), timeframe and dose metric for a contaminant of concern. Assessors can modify initial parameters, as appropriate, to account for assessment-specific knowledge and calculate deterministic exposure estimates as point estimates. The tool enables users to define unlimited potential scenarios for various receptor populations and lifestages. Relies on the *Exposure Factors Handbook: 2011 Edition* and ExpoBox for updated information. | https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=322489 |

**Table 5-6. Examples of Sources of Non-Occupational Data for an Exposure Assessment from EPA and other Federal Agencies[a] (cont.)**

| Source | Data Type | Scale | Description | Reference |
|---|---|---|---|---|
| EPA – Consolidated Human Activity Database (CHAD) | • Exposure factors | • Local<br>• State<br>• Regional<br>• National | EPA's CHAD contains detailed data on human behavior from 22 separate exposure and time-use studies. The database includes more than 54,000 individual study days of data including age, sex, employment and education level, which allows researchers to examine specific groups within the general population and how their unique behavior patterns influence their exposures to chemicals. The database is continuously maintained and updated as new human activity data become available. | https://www.epa.gov/healthresearch/consolidated-human-activity-database-chad-use-human-exposure-and-health-studies-and |
| EPA – National Human Exposure Assessment Survey (NHEXAS) | • Observational human exposure | • Local<br>• State<br>• Regional | The purpose of NHEXAS was to evaluate comprehensive human exposure to multiple chemicals on a community and regional scale. These studies: (1) measured pollutant concentrations in air, water, soil, dust, food, blood, urine and hair and on surfaces and human skin using various sampling and analytical techniques; (2) determined direct exposure using personal exposure monitors; and (3) estimated human activity patterns using a series of questionnaires and diaries. | https://cfpub.epa.gov/si/si_public_record_report.cfm?Lab=NERL&TIMSType=&count=10000&dirEntryId=18200&searchAll=&showCriteria=2&simpleSearch=0&startIndex=70001 |
| EPA – Total Exposure Assessment Methodology Study (TEAM) | • Observational human exposure | • Local | TEAM, conducted from 1979 to 1985, developed methods for collecting individual exposure information and applying these methods, along with statistical analyses, to estimate exposures and body burdens for individuals living in several urban areas. Volume I is a summary and overview of the entire study. Volume II deals with studies in New Jersey, North Carolina and North Dakota. Volume III deals with studies in California. Volume IV presents the Standard Operating Procedures employed in the study. | U.S. EPA (1987b);<br>Handy et al. (1987)<br>https://cfpub.epa.gov/si/si_public_record_report.cfm?Lab=NERL&TIMSType=&count=10000&dirEntryId=50208&searchAll=&showCriteria=2&simpleSearch=0&startIndex=70001<br>https://cfpub.epa.gov/si/si_public_record_report.cfm?Lab=NERL&TIMSType=&count=10000&dirEntryId=44146&searchAll=&showCriteria=2&simpleSearch=0&startIndex=30001 |

**Table 5-6. Examples of Sources of Non-Occupational Data for an Exposure Assessment from EPA and other Federal Agencies[a] (cont.)**

| Source | Data Type | Scale | Description | Reference |
|---|---|---|---|---|
| EPA – Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants Study (CTEPP) | • Observational human exposure | • State<br>• Regional | CTEPP, completed in 2004, was designed to determine what commonly used chemicals are found in home or daycare environments and if children in these environments encountered those chemicals in the course of their regular, day-to-day activities. Chemicals included pesticides, cleaners and household products. Participants maintained normal daily routines during the study. The CTEPP website provides chapter-by-C hapterfiles of data, which also are available through HEDS (Human Exposure Database System). | https://archive.epa.gov/heasd/archive-dears/web/html/index-1.html. |
| EPA – Detroit Exposure and Aerosol Research Study (DEARS) | • Observational human exposure | • State<br>• Regional | DEARS was designed to collect data, from 2004 to 2007, to improve EPA's understanding of human exposure to various air pollutants in the environment. During a 3-year period, personal indoor and outdoor air monitoring data were collected to evaluate exposure to particulate matter and a set of air toxics. These data were correlated with information, such as blood pressure and heart rate, relevant to potential health effects. | https://archive.epa.gov/heasd/archive-dears/web/html/index.html |
| EPA – Air Toxics Risk Assessment Reference Library | • Reference on assessing exposures to air toxics | • Local<br>• National | EPA developed an air toxics risk assessment (ATRA) reference library for conducting air toxics analyses at the facility and community scales. This library provides information on the fundamental principles of risk-based assessment for air toxics and how to apply those principles in different settings, as well as strategies for reducing risk at the local level. | https://www.epa.gov/fera/risk-assessment-and-modeling-air-toxics-risk-assessment-reference-library |
| EPA – Air Exposure Guidelines Levels | • Information on the acute exposure guideline levels | • Local | Acute exposure guideline levels (AEGLs) describe the human health effects from once-in-a-lifetime, or rare, exposure to airborne chemicals. Used by emergency responders when dealing with chemical spills or other catastrophic exposures, AEGLs are set through a collaborative effort of the public and private sectors worldwide. | https://www.epa.gov/aegl |

**Table 5-6. Examples of Sources of Non-Occupational Data for an Exposure Assessment from EPA and other Federal Agencies[a] (cont.)**

| Source | Data Type | Scale | Description | Reference |
|---|---|---|---|---|
| EPA – Relationship Between Indoor, Outdoor and Personal Air Study (RIOPA) | • Observational human exposure | • Regional | RIOPA, completed in 2005, quantified indoor and outdoor inhalation exposures to agents in three areas of the United States. Integrated indoor, outdoor and personal air samples were collected both for gas-phase and fine particulate matter (2.5 µm or smaller) analyses, organic functional groups, elements, organic carbon, elemental carbon, gas- and particle-phase polycyclic aromatic hydrocarbons and chlordanes. Questionnaire and time activity information also were collected from residents.The study was funded by the National Urban Air Toxics Research Center with Dr. Clifford Weisel at the Environmental Occupational Health Sciences Institute (EOHSI) as Principal Investigator. One study was funded by the Health Effects Institute (HEI) with Dr. Jim Zhang of EOHSI as Principal Investigator. Another study was funded by HEI with Dr. Barbara Turpin of Rutgers University as Principal Investigator. | Weisel et al. (2005) https://cfpub.epa.gov/ncer_abstracts/index.cfm/fuseaction/display.highlight/abstract/8343 |
| EPA – ExpoCast Database | • Observational human exposure<br>• Environmental<br>• Biological | • Local<br>• State<br>• Regional<br>• National | ExpoCast quickly and efficiently examines multiple routes of exposure to provide exposure estimates and has been applied to almost 8,000 chemicals. ExpoCast uses two types of models to estimate exposure, farfield and nearfield. The database is updated on a continuing basis. | https://www.epa.gov/chemical-research/rapid-chemical-exposure-and-dose-research |
| EPA – Air Quality System (AQS) | • Environmental | • Local<br>• State<br>• Regional<br>• National | AQS contains ambient air pollution data collected by EPA, state, local and tribal air pollution control agencies from thousands of monitoring stations. AQS also contains meteorological data, descriptive information about each monitoring station (including its geographic location and operator) and data quality assurance/quality control (QA/QC) information. Data can aid in an exposure assessment of chemicals in air at varying geographic areas. Data are updated on an ongoing basis to inform EPA, state, local and tribal air pollution control agencies. | https://www.epa.gov/aqs |
| EPA – Monitoring the Occurrence of Unregulated Drinking Water Contaminants | • Environmental | • National | Nationally representative data on the occurrence of contaminants in drinking water, the number of people potentially exposed and an estimate of that exposure. These data provide the basis for future regulatory actions to protect public health. The database is updated on an ongoing basis. | https://www.epa.gov/dwucmr |

**Table 5-6. Examples of Sources of Non-Occupational Data for an Exposure Assessment from EPA and other Federal Agencies[a] (cont.)**

| Source | Data Type | Scale | Description | Reference |
|---|---|---|---|---|
| EPA – National Emissions Inventory | Air pollutants | • Local<br>• National | The National Emissions Inventory (NEI) is a comprehensive estimate of air emissions of criteria pollutants, criteria precursors and hazardous air pollutants from air emissions sources. The NEI is released every three years based primarily on data provided by state, local and tribal air agencies for sources in their jurisdictions and supplemented by data developed by EPA. | https://www.epa.gov/air-emissions-inventories/national-emissions-inventory-nei |
| EPA-Toxic Release Inventory Data (TRI) | Environmental | • Local<br>• State<br>• Regional | The TRI Program tracks the management of toxic chemicals that might pose a threat to human health and the environment. Facilities in certain industry sectors report annually on the volume of toxic chemicals managed as waste—recycled, treated or burned for energy recovery—and disposed of or otherwise released into the environment. | https://www.epa.gov/trinationalanalysis |
| Centers for Disease Control and Prevention (CDC) | | | | |
| CDC – National Health and Nutrition Examination Survey (NHANES) | • Observational human exposure<br>• Biological<br>• Biomonitoring | • Regional<br>• National | NHANES is a program of studies designed to assess the health and nutritional status of adults and children in the United States. The survey is unique in that it combines interviews and physical examinations. The sample for the survey is selected to represent the U.S. population of all ages. To produce reliable statistics, NHANES over-samples persons more than 60 years of age, African Americans and Hispanics. The survey has become a continuous program that has a changing focus on a variety of health and nutrition measurements to meet emerging needs. Data are summarized and published in National Reports on an ongoing basis. | http://www.cdc.gov/nchs/nhanes.htm<br>http://www.cdc.gov/exposurereport/ |
| CDC – National Center for Health Statistics (NCHS) – Surveys and Data Collection Systems | • Health characteristics | • National | NCHS provides data to evaluate national trends in health statistics on such topics as birth and death rates, infant mortality, life expectancy, morbidity and health status, risk factors, use of ambulatory and inpatient care, health personnel and facilities, financing of health care, health insurance and managed care and other health topics. Updates are developed on an ongoing basis. | http://www.cdc.gov/nchs/ |

**Table 5-6. Examples of Sources of Non-Occupational Data for an Exposure Assessment from EPA and other Federal Agencies[a] (cont.)**

| Source | Data Type | Scale | Description | Reference |
|---|---|---|---|---|
| CDC – NCHS – Research Data Centers (RDCs) | • Health characteristics | • National | RDCs allow researchers access to restricted data. Researchers are required to submit a research proposal outlining the need for these sensitive data. The proposal provides a framework for NCHS to identify potential disclosure risk. The RDCs also host restricted data from a variety of groups within the U.S. Department of Health and Human Services. Ongoing availability of data. | http://www.cdc.gov/rdc/index.htm |
| CDC – Behavioral Risk Factor Surveillance System (BRFSS) | • Biological<br>• Health-related behaviors<br>• Human activity | • State<br>• National | BRFSS is a telephone health survey system. It has tracked health conditions and risk behaviors in the United States yearly since 1984. Currently, data are collected monthly in all 50 states; Washington, DC; Puerto Rico; the U.S. Virgin Islands; and Guam. The BRFSS website makes its resources available to the public, including interactive databases, maps and raw annual survey data. The site also features data usage statistics by state. Updated annually. | http://www.cdc.gov/BRFSS/ |
| CDC – Agency for Toxic Substances and Disease Registry (ATSDR) | • Public health assessments<br>• Health consultations | • Local<br>• State<br>• Regional | ATSDR determines public health implications associated with hazardous waste sites and other environmental releases. ATSDR has developed a methodology for evaluating the public health implications of exposures to environmental contamination. Ongoing data development and availability. | http://www.atsdr.cdc.gov/hac/PHAManual/toc.html<br>http://www.atsdr.cdc.gov/hac/pha/index.asp |
| CDC – Agency for Toxic Substances and Disease Registry (ATSDR) | • Toxicological profiles | • National | ATSDR toxicological profiles characterize the toxicological and adverse health effects information for hazardous substances. Profiles include information on potential human exposures. | https://www.atsdr.cdc.gov/toxprofiledocs/index.html |
| U.S. Census Bureau | | | | |
| U.S. Census Bureau – American FactFinder | • Demographics | • Census tract<br>• State<br>• Regional<br>• National | The Census Bureau's American FactFinder is an interactive application that supports the Economic Census, the American Community Survey, the 1990 Census, Census 2010 and the latest population estimates. It provides fact sheets and data on population demographics, housing and businesses that can be useful in understanding sources of exposure. The website features downloadable Microsoft Excel sheets, maps and a search engine. Ongoing updates. | http://factfinder2.census.gov/faces/nav/jsf/pages/index.xhtml |

**Table 5-6. Examples of Sources of Non-Occupational Data for an Exposure Assessment from EPA and other Federal Agencies[a] (cont.)**

| Source | Data Type | Scale | Description | Reference |
|---|---|---|---|---|
| U.S. Census Bureau – Equal Employment Opportunity (EEO) Data Tool | Demographics | • Census tract<br>• State<br>• Regional<br>• National | The Census Bureau's Census 2000 EEO Data Tool is a web-based tool that enables users to select tabulations of residence or workplace information at varying levels of geographic specificity. The data present available information for a variety of occupations categorized by race/ethnicity and sex that can be used in assessing residence times in specific geographic areas. Ongoing updates. | https://www.census.gov/eeo2000/ |
| Bureau of Labor Statistics | | | | |
| Bureau of Labor Statistics – American Time Use Survey (ATUS) | Activity | • National | ATUS measures the amount of time individuals spend completing various activities, such as paid work, childcare, volunteering and socializing. These data can be used in an exposure assessment to estimate frequency and duration. Updated on an ongoing basis. | http://www.bls.gov/tus/ |
| U.S. Geological Survey (USGS) | | | | |
| USGS – Toxics Substances Hydrology Program | • Environmental | • Local<br>• Regional<br>• National | The USGS Toxics Substances Hydrology Program conducts (1) intensive field investigations of representative cases of subsurface contamination at local releases; and (2) watershed- and regional-scale investigations of contamination affecting aquatic ecosystems from nonpoint and distributed point sources. This type of information might be helpful in understanding geographical locations of water bodies and other factors that could contribute to exposures. The newsletter is updated on an ongoing basis. | http://toxics.usgs.gov/index.html) |
| USGS – National Water Information System | • Environmental | • Local<br>• Regional<br>• National | National Water Information System Mapper provides information on the geological locations of water bodies that might be sources of exposure. The website is updated on an ongoing basis. | http://waterdata.usgs.gov/nwis |

**Table 5-6. Examples of Sources of Non-Occupational Data for an Exposure Assessment from EPA and other Federal Agencies[a] (cont.)**

| Source | Data Type | Scale | Description | Reference |
|---|---|---|---|---|
| USGS – National Water Quality Assessment Program (NAWQA) | • Environmental | • Local<br>• State<br>• National | NAWQA provides data on water quality conditions, changes over time and how natural features and human activities affect those conditions. A consistent study design and uniform methods and analyses are used. Monitoring data are integrated with geographic information on hydrological characteristics, land use and other landscape features in models to extend water quality understanding to unmonitored areas. Data are used to design and implement strategies for managing, protecting and monitoring water resources in many different hydrologic and land-use settings across the nation. The website is updated on an ongoing basis. | http://water.usgs.gov/nawqa/ |
| USGS – Health Related Activities | • Environmental | • Local<br>• State<br>• National | The Human Consumption of Chemical and Pathogenic Contaminants portion of this website provides information on the occurrence of bioaccumulative contaminants in water, sediment and fish tissue that might be helpful in evaluating contaminant trends over time and sources of contamination in biota. The website is not being updated on an ongoing basis.<br><br>The USGS website (include second webpage link) on contaminants and pathogens provides information on chemical pollutants, human and animal pathogens, and the biological effects of chemical and biological contaminants on natural ecosystems. This webpage is updated on an ongoing basis. | https://archive.usgs.gov/archive/sites/health.usgs.gov/bioacc_cont/index.html<br><br>https://www.usgs.gov/centers/umid-water/science/contaminants-and-pathogens |
| USGS – National Stream Quality Accounting Network (NASQAN) | • Environmental | • Local<br>• Regional<br>• National | NASQAN's major objective is to report on the concentrations and loads of selected constituents delivered by major rivers to the coastal waters of the United States and selected inland subbasins in priority river basins to determine the sources and relative yields of constituents within these basins. These priority basins are significant in reducing delivery of constituents that contribute to adverse conditions in receiving waters. Other objectives include monitoring for climate change and describing long-term trends in the loads and concentrations of select constituents at key locations. The database is updated on an ongoing basis. | https://www.usgs.gov/centers/dakota-water/science/national-stream-quality-accounting-network-nasqan?qt-science_center_objects=0#qt-science_center_objects |

**Table 5-6. Examples of Sources of Non-Occupational Data for an Exposure Assessment from EPA and other Federal Agencies[a] (cont.)**

| Source | Data Type | Scale | Description | Reference |
|---|---|---|---|---|
| USGS – Sediment Data Portal | • Environmental<br>• Land use | • Local<br>• Regional<br>• National | This portal provides users with land use data, the ability to view the location of sediment sites in the context of various geospatial data layers and tools to enable users to select sites of interest. This website is updated on an ongoing basis. | http://cida.usgs.gov/sediment/ |
| USGS – Environmental Health Sciences | • Environmental data | • National | USGS provides information useful in characterizing the processes that affect the interaction among the physical environment, living environment and people, and the resulting factors that affect ecological and human exposures to disease agents. The *Environmental Health Science Strategy* summarizes national environmental health priorities that USGS is best suited to address and serves as a strategic framework to meet the USGS environmental health science goals, actions and outcomes for the next decade. Implementation of this strategy is intended to aid coordination of USGS environmental health activities with other federal agencies and to provide a focal point for disseminating information to stakeholders. This website is updated on an ongoing basis. | http://www.usgs.gov/envirohealth/ |
| U.S. EPA/USGS – Water Quality Portal (WQP) | • Environmental groundwater | • Local<br>• National | The WQP provides access to data stored in various large water quality databases. It provides information on location, site, sampling and date parameters to customize the returned results. WQP provides information (locations of sample collection) and sample results (analytical data of collected samples). The portal relies in part on STORET (STORage and RETrieval) and USGS's National Water Information System database. The website is updated on an ongoing basis. | http://www.waterqualitydata.us/ |
| USGS – Background levels of elements in soils and other surficial materials | • Environmental soil | • Local<br>• National | USGS developed a report on background concentrations of various chemicals, including metals, throughout the contiguous United States. Samples were analyzed for their content of elements in soils and other surficial materials. This website is updated on an ongoing basis. | https://www.usgs.gov/faqs/does-usgs-have-reports-background-levels-elements-soils-and-other-surficial-materials?qt-news_science_products=2#qt-news_science_products |

**Table 5-6. Examples of Sources of Non-Occupational Data for an Exposure Assessment from EPA and other Federal Agencies[a] (cont.)**

| Source | Data Type | Scale | Description | Reference |
|---|---|---|---|---|
| U.S. Department of Agriculture | | | | |
| USDA's Pesticide Data Program (PDP) | • Pesticide residue monitoring data | • National | The PDP is a national pesticide residue monitoring program that produces the most comprehensive pesticide residue database in the United States. The Monitoring Programs Division administers PDP activities, including the sampling, testing and reporting of pesticide residues on agricultural commodities in the U.S. food supply, with an emphasis on those commodities highly consumed by infants and children. The program is implemented through cooperation with state agriculture departments and other federal agencies. PDP data:<br>• Enable EPA to assess dietary exposure.<br>• Facilitate the global marketing of U.S. agricultural products.<br>• Provide guidance for the U.S. Food and Drug Administration (FDA) and other governmental agencies to make informed decisions.<br>Updated on an annual basis. | https://www.ams.usda.gov/datasets/pdp |
| U.S. Food and Drug Administration | | | | |
| U.S. FDA – Total Diet Study (TDS) | • Contaminant and nutrient data for food and beverages | • National | The TDS is an ongoing FDA program that monitors levels of about 800 contaminants and nutrients in the average U.S. diet; the number varies slightly from year to year. To conduct the study, the program purchases, prepares and analyzes about 280 types of foods and beverages from representative areas of the country, four times a year. Results of the TDS, from 1991 to the present, are available to the public in electronic form on this website. (Results prior to 1991 can be found in the publications listed on the publications page of the website.) Each section of the website explains a different aspect of the study, from a brief description of study design to a brief explanation of the organization of the results, including a link to zipped text files of the data. | https://www.fda.gov/Food/FoodScienceResearch/TotalDietStudy/ |
| U.S. FDA – Center for Food Safety and Applied Nutrition (CFSAN) | • Contaminant data for food and cosmetics | • National | The Center is one of six product-oriented centers at FDA that carry out FDA's mission. CFSAN provides services to consumers, domestic and foreign industry and other outside groups regarding field programs; agency administrative tasks; scientific analysis and support; and policy. | https://www.fda.gov/aboutfda/centersoffices/officeoffoods/cfsan/ |

**Table 5-6. Examples of Sources of Non-Occupational Data for an Exposure Assessment from EPA and other Federal Agencies[a] (cont.)**

| Source | Data Type | Scale | Description | Reference |
|---|---|---|---|---|
| National Oceanic and Atmospheric Administration | | | | |
| NOAA – National Center for Environmental Information | • Atmospheric, coastal, oceanic and geophysical data | • Local<br>• Regional<br>• National | NOAA's National Center for Environmental Information (NCEI) provides access to one of the most significant archives on Earth with comprehensive oceanic, atmospheric and geophysical data (approximately 25 petabytes). NCEI is the nation's leading authority for environmental information. | https://www.ncei.noaa.gov/ |
| NOAA – Weather Forecast | • Weather, water and climate data, forecasts and warnings; includes data for various timeframes for assessing exposures and model air concentrations | • Local<br>• National | NWS forecasts, warnings, data and products form a national information database and infrastructure used by other governmental agencies, the private sector, the public and the global community. This enables core partners to make decisions when weather, water or climate has a direct impact on the protection of lives and livelihoods. NWS forecasts and warnings are provided directly to decision makers in local communities and at state and federal levels to protect lives and property in neighborhoods and communities. This information is used in modeling concentrations from specific facilities, determining migration of air toxics, etc. | https://www.weather.gov/about/ |

[a]Not exhaustive

# CHAPTER 6. COMPUTATIONAL MODELING FOR EXPOSURE ASSESSMENTS

This chapter presents an overview of modeling in exposure assessments, highlighting basic concepts to consider when using models and providing a brief taxonomy of the types of models frequently encountered. Specifically, it:

- Provides the principles of the modeling process and key definitions (Section 6.1)
- Provides an overview of the process of identifying appropriate models based on exposure assessment goals (Section 6.2)
- Explains how an exposure assessor evaluates models that potentially are useful in the exposure assessment (Section 6.3).

Section 6.4 summarizes this chapter.

## 6.1. Principles and Definitions of Modeling

In EPA's *Guidance on the Development, Evaluation, and Application of Environmental Models* (U.S. EPA 2009d), the Agency adopted the National Academy of Sciences' definition of a model as "a simplification of reality that is constructed to gain insights into select attributes of a particular physical, biological, economic, or social system" (NRC 2007). Computational models are based on first developing conceptual models and then deriving mathematical models of the process defined by the conceptual model, with simplifying assumptions, as appropriate. In an exposure assessment, computational models are tools the assessor uses to analyze and characterize processes that are too complex for capturing completely by empirical data or for which empirical data are not available. Models help extrapolate monitoring data to non-surveyed populations, reconstruct past exposures or predict future exposures. Models also serve as a framework for assembling various types of data to develop estimates of exposure that are consistent with all available empirical data.

In general, the modeling process within an exposure assessment might include interactions among public policy processes, represented by the planning and scoping and problem formulation steps of an exposure assessment, model development and model application (U.S. EPA 2009d). Depending on the analysis plan developed during the problem formulation phase of an exposure assessment (see Section 3.3), exposure modeling might help estimate environmental concentrations, extend existing monitoring information to populations and locations without data, predict exposures under current and future scenarios and evaluate potential exposure reduction and associated environmental and health benefits resulting from risk management actions (Isakov et al. 2009; Jayjock et al. 2007; Lobdell et al. 2011; U.S. EPA 1989b; U.S. EPA 1992b; Williams et al. 2010). After the project team has identified the problem that modeling will address, they determine the specifications of the problem, including the model type that addresses the purpose of the assessment, meets the data criteria and considers the spatial, temporal and physical boundaries of the problem. This determination occurs while developing the analysis plan (see Section 3.3).

The process of developing and validating a new model or modifying and evaluating an existing model is beyond the scope of this document, but *Guidance on the Development, Evaluation, and Application of Environmental Models* (U.S. EPA 2009d) describes the steps in detail. This model guidance document recommends that model developers and users:

- Subject their model to a credible and objective peer review
- Assess the quality of the data used in the creation and evaluation of the model
- Corroborate their model by evaluating the degree to which it corresponds to the system being modeled
- Perform sensitivity and uncertainty analyses
- Document all aspects of a modeling project
- Communicate effectively with analysts and risk managers/decision makers.

Model applications also involve evaluating and refining the model and comparing the model results to assessment goals and data quality objectives to ensure that they are achieved (see Section 5.3.2). An assessor might need to refine the model further or use a new one if the model does not meet the criteria. The resources listed in Box 6-1 support EPA's continued efforts to ensure the quality, transparency and reproducibility of the information in models the Agency uses and disseminates.

**Box 6-1. Pertinent Resources for Modeling**

- U.S. EPA (2002f) *Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility and Integrity of Information Disseminated by the Environmental Protection Agency.* EPA/260/R-02/008.
- U.S. EPA (2006g) *System Life Cycle Management Policy.*
- NRC (2007) *Models in Environmental Regulatory Decision Making.* Reviews the evolving scientific and technical issues related to the development, selection and use of computational and statistical models at EPA.
- U.S. EPA (2009d) *Guidance on the Development, Evaluation, and Application of Environmental Models.* EPA/100/K-09/003. Provides a simplified, comprehensive resource on the principles of good modeling practice.
- WHO (2005) *Principles of Characterizing and Applying Human Exposure Models.*
- *Quality System for Environmental Data and Technology* website. U.S. EPA.
- *Predictive Models and Tools for Assessing Chemicals under the Toxic Substances Control Act (TSCA)* website. U.S. EPA.
- *Radiation Protection Document Library* website. *Radiation Protection* website. U.S. EPA.

## 6.2. Selecting the Type of Model for Exposure Assessments

The process of model selection first involves identifying the type of model needed to meet the risk management objectives of the assessment and then determining the complexity of the model necessary to reach a decision. After defining the type of model needed, the assessor and individuals with modeling expertise determine whether such a model exists to meet those needs or a new model needs to be developed.

Selection of an appropriate model is critical for accurately estimating exposure concentrations. Assessors generally choose from multiple models that are relevant for the populations and exposure sources of interest. The assessment should include documentation of the reasons for model selection.

When selecting and using models, assessors, in collaboration with individuals experienced in modeling, need to review the modeling literature. Several factors help an exposure assessor select an appropriate model for an exposure assessment: the study objectives, technical capabilities of the model, model availability and ease of use (U.S. EPA 1987a; U.S. EPA 1988b). An equally critical step in the process is to choose appropriate default values for exposure factors when data are missing or incomplete. The best model is less reliable without good data and appropriate default factors. Presentation of the rationale for selecting the model is essential to promoting transparency in the assessment (see Section 6.2.1). Table 6-1 lists environmental modeling-related inventories and clearinghouses.

**Table 6-1. EPA Exposure-Related Inventories and Clearinghouses**

| Source | Description | Types of Models and Information | URL |
|---|---|---|---|
| Registry of EPA Applications and Databases | Authoritative source of information about EPA information resources. | Models that EPA uses, supports or funds. | http://ofmpub.epa.gov/sor_internet/registry/systmreg/home/overview/home.do |
| Center for Exposure Assessment Modeling | Database designed to meet the scientific and technical exposure assessment needs of EPA, state environmental agencies and resource management agencies. | Models that provide predictive exposure assessment techniques for aquatic, terrestrial and multimedia pathways for organic chemicals and metals. Includes models of groundwater, surface water, food chains and multimedia. | http://www.epa.gov/ceampubl/ |
| Center for Subsurface Modeling Support (CSMoS) | Center that provides software and technical support to EPA and state risk managers/decision makers in subsurface model applications, including groundwater models and databases from EPA's National Risk Management Research Laboratory. | Models used for site characterization, conducting groundwater flow and transport simulations, determining wellhead protection areas and selecting groundwater remediation at Resource Conservation and Recovery Act and Superfund sites. | U.S. EPA (2012d) https://cfpub.epa.gov/si/si_public_record_Report.cfm?dirEntryID=19569 |
| Emissions Modeling Clearinghouse | Database that supports and promotes emission-modeling activities, both internal and external to EPA. | Emissions data, modeling platforms, emission modeling software resources and ancillary data. | https://www3.epa.gov/ttnchie1/software/ |
| *An Overview of Exposure Assessment Models Used by the U.S. Environmental Protection Agency* | Overview of exposure assessment models EPA supports and uses. | Includes 12 fate/transport models, 15 exposure models and 8 integrated fate/transport-exposure models. | Williams et al. (2010) |
| Model Clearinghouse Information Storage and Retrieval System | Single EPA focal point for reviewing the use of modeling techniques for specific regulatory applications. | Information about referrals from EPA regional offices involving the interpretation of modeling guidance for specific regulatory applications. | http://cfpub.epa.gov/oarweb/MCHISRS/ |
| Support Center for Regulatory Atmospheric Modeling | Website providing documentation of EPA's Air Quality Modeling Group modeling analyses that support policy and regulatory decisions in the Office of Air and Radiation. | Air quality models and other mathematical simulation techniques used in assessing control strategies and source impacts. | https://www.epa.gov/scram |
| Watershed and Water Quality Modeling Technical Support Center | Center that assists EPA programs and state and local governments in the implementation of the Clean Water Act. | Tools and approaches for use in developing Total Maximum Daily Loads, wasteload allocations and watershed protection plans. | https://www.epa.gov/tmdl/watershed-and-water-quality-modeling-technical-support-center-factsheet |
| Office of Pollution Prevention and Toxics | Website from which users can download or access tools and models the Office of Pollution Prevention and Toxics uses in its programs. | Models used for prioritization, screening and detailed assessment of chemicals. Includes hazard and exposure and fate models, tools and documents. | https://www.epa.gov/aboutepa/about-office-chemical-safety-and-pollution-prevention-ocspp |
| Office of Pesticide Programs | Website from which users can access exposure models, model-related resources (e.g., databases on exposures and guidance documents), and links to other models. | Models described at this site are used to predict exposures for a range of ecological receptors and to predict exposures for humans from dietary and non-dietary sources. | https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks |

Models range from simple to complex. Users typically begin with simpler models that, when combined with conservative inputs, can screen out exposures of low concern (see Section 6.2.2). Certain questions also are more amenable to simple models. For example, if the goal is to determine whether the level of a chemical in a product or the level of a chemical observed to occur in an environmental medium is of low concern, a bounding analysis using a deterministic model might be sufficient. Certain goals, by necessity, will require models that are more advanced. Questions concerning the fraction of the population a source affects or regarding the quantitative characterization of uncertainty immediately dictate the need for probabilistic models (see Section 6.2.3).

## 6.2.1. Setting the Objectives for the Modeling Effort

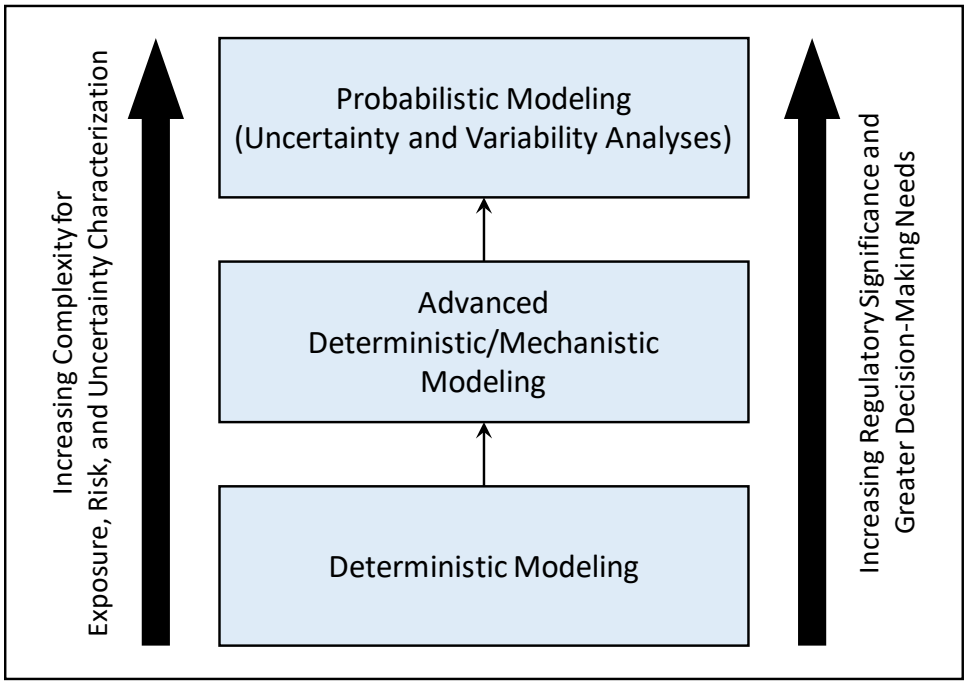
Before selecting a model to estimate an exposure, an exposure assessor defines the exposure assessment objectives(s) and describes how the model addresses assessment questions or hypotheses required to meet these objectives. The objectives include identifying the processes of greatest importance in the modeling effort (U.S. EPA 2009a). Identifying these processes is a key part of developing the conceptual model (see Section 3.2.2) and model selection.

An exposure assessor, in collaboration with other project team members, develops a clear statement of what information the model will estimate and how the assessment will use this estimate. Depending on program, office or regional guidelines, the exposure assessment plan, modeling approach document or a standard operating procedure (SOP) could include this statement. The modeling approach needs to be consistent with known project constraints (e.g., schedule or budget). The exposure assessment's analysis plan, discussed in Section 3.3, describes the information needs the model will address. Examples of such needs are identifying population groups of concern; determining whether to present outputs on an hourly, daily, quarterly, yearly or multiyear basis; deciding on the number of prediction years (e.g., lifetime or shorter timeframes) and location for modeling (e.g., on site, at the smoke stack, fence line, off site, indoor, in-vehicle, outdoor, residential); capturing variability over time, space or the population; and presenting results in a form appropriate for the intended purpose and audience. Exposure assessors need to be aware that many available modeling applications could make exposure-modeling simulations appear deceptively simple. EPA highly recommends a discipline expert conduct or participate in any statistical modeling to predict or estimate exposure.

## 6.2.2. Level of Model Complexity

The risk manager/decision maker, exposure assessor and modeler should work together to develop the problem statement and system conceptualization during the initial stage of the exposure assessment that forms the basis for developing a modeling methodology. This methodology stipulates the degree of model complexity. The computational models EPA uses in exposure assessment range from simple deterministic screening-level models to complex probabilistic models, based on both the complexity of the exposure process and regulatory considerations. Figure 6-1 illustrates that the complexity of the exposure and uncertainty characterization in an exposure assessment need to increase to meet greater decision making needs and regulatory significance, typically requiring selection of more complex models. The more sophisticated models provide more refined estimates of exposure that are useful for certain types of regulatory and decision making needs. Because of the higher levels of effort required to use and explain complex models, projects should make use of the simplest model that meets the project's needs.

**Figure 6-1. A Tiered Approach for Modeling Analysis**



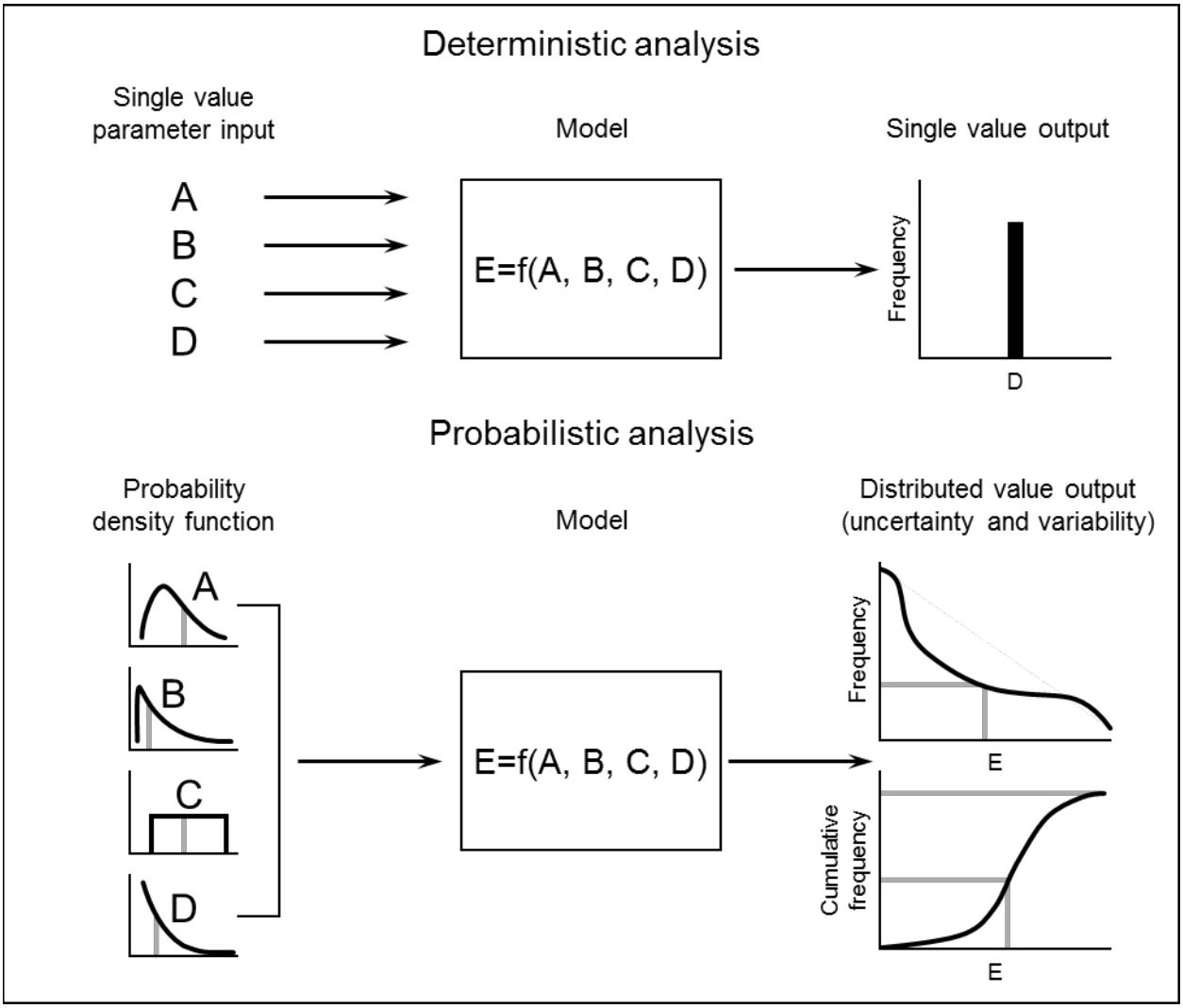

Adapted from Özkaynak et al. (2011)

EPA programs might implement specific procedures that vary from the basic process Figure 6-1 shows. In some cases, an exposure assessor might carry forward or eliminate a scenario for further evaluation based on community concerns, stakeholder input or other factors. Exposure assessors should consult with relevant EPA programs and make use of available SOPs. Assessors also are encouraged to consult the appropriate EPA programs to determine which screening-level models are used in their programs and to develop an understanding of their capabilities and limitations. Figure 6-2 illustrates the difference between deterministic and probabilistic models.

**Deterministic Models**

Deterministic models use single values for model parameters to predict a single output rather than a set of probabilistic outcomes. Because this type of model does not explicitly address variability or uncertainty associated with the values, changes in model outputs result solely from changes in model components or in the assumed boundary or initial conditions. Screening-level (often deterministic) models frequently are used first to assess whether an environmental agent is likely to pose a risk to human health and to rule out unimportant exposure pathways. Screening-level exposure assessments use the information considered most critical to predicting human exposures, often with default or conservative assumptions. Certain EPA programs routinely develop screening-level models for use in exposure assessments. These range from simpler, semi-empirical deterministic models to more advanced mechanistic models that capture the fundamental environmental and exposure processes of interest. An example of a simpler model is the Exposure and Fate Assessment Screening Tool (E-FAST) the Office of Pollution Prevention and Toxics uses to estimate the dermal, inhalation and ingestion exposure to chemicals in consumer products that occur as a result of product use (U.S. EPA 2014b). EPA's *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011d) provides other examples of deterministic models.

**Figure 6-2. Deterministic versus Probabilistic Analysis**




Adapted from Maslia and Aral (2004)

Assessors need to consult their programs to determine which screening-level models the programs use and to develop an understanding of the models' capabilities and limitations. Higher tier models provide estimates that are more refined for particular regulatory and decision making needs.

Deterministic models help establish the range of possible outcomes. Basing the input values for a deterministic model on the average value across a population yields a reasonable estimate of the average individual's exposures. When input values are conservative, but still realistic, the deterministic model will generate exposure estimates that fall on the high end of the expected exposure distribution. Several EPA programs routinely use screening-level models to screen out exposures of low concern rapidly and efficiently. Assessors compare exposure estimates from screening-level models to screening values. Screening values include health-based values expressed as a dose (e.g., reference doses) and chemical concentrations in a specific medium (e.g., soil screening values). (When using chemical concentrations as screening values, an exposure assessor usually can compare an exposure point concentration directly to the soil

screening value. In this case, estimating the exposure quantitatively would be unnecessary.) Typically, assessors carry forward those exposure estimates exceeding screening values for additional analyses. The additional analyses include in-depth evaluation of the problem by using a more sophisticated exposure model or by collecting additional monitoring data. Deterministic models can be the subject of sensitivity analyses, which can provide insight on which parameters should be the focus of additional data collection and refinement. Finally, if the cost of taking a risk management action is low or the cost of additional analyses is high, a screening assessment could trigger remedial action. Box 6-2 lists resources that support the use of screening-level models.

**Box 6-2. Examples of Resources for Screening-Level Models**

- U.S. EPA (2001f) *General Principles for Performing Aggregate Exposure and Risk Assessments.*
- Arnot (2009) *Mass Balance Models for Chemical Fate, Bioaccumulation, Exposure and Risk Assessment*.
- U.S. EPA (2009d) *Guidance on the Development, Evaluation, and Application of Environmental Models.* EPA/100/K-09/003.
- Williams et al. (2010) *An Overview of Exposure Assessment Models Used by the U.S. Environmental Protection Agency.*
- *Exposure Assessment Tools and Models* website. U.S. EPA.

**Probabilistic Models**

Probabilistic exposure modeling (e.g., Monte Carlo analysis, Latin hypercube) represents a higher tier assessment method that provides estimates of the range of probable exposures to agents of interest. Probabilistic risk assessment is employed when detailed statistical analysis (e.g., developing quantitative estimates of exposure or dose at upper percentiles) is necessary to support sensitive decisions and help risk managers/decision makers distinguish among possible alternatives. A probabilistic analysis considers the same exposure parameters (e.g., agent concentration, exposure duration, intake rate) as other types of exposure models but considers the range or distribution of exposures within a population rather than a single number. The output of a probabilistic assessment is a probability distribution of exposures that reflects the combination of the probability distributions of one or more of the model inputs or parameters. The distributions can help characterize variability, uncertainty or both, depending on the design of the model and its inputs. Probabilistic approaches also help identify data gaps, that is, cases for which additional data collection could significantly improve a decision by reducing uncertainty or better characterizing variability. If data gaps are identified, an exposure assessor can address them by collecting additional data or conducting additional statistical analyses, such as meta-analyses of existing data (Volstad et al. 2003; Weigel 2003). As an example, EPA conducted a probabilistic exposure assessment that evaluated potential exposure and risk to children from wood treated with chromated copper arsenate and a probabilistic multimedia exposure modeling analysis for children's lead exposure to inform public health decision making (Zartarian et al. 2006; Zartarian et al. 2017). These models typically require more resources than screening models, however, and they generally are used only when required. Box 6-3 lists examples of available resources for probabilistic assessments and models.

**Box 6-3. Examples of Resources for Probabilistic Assessments and Models**

- Finley and Paustenbach (1994) *The Benefits of Probabilistic Exposure Assessment: Three Case Studies Involving Contaminated Air, Water, and Soil.*
- U.S. EPA (1996e) *Summary Report for the Workshop on Monte Carlo Analysis.* EPA/630/R-96/010.
- U.S. EPA (1997b) *Guiding Principles for Monte Carlo Analysis*. EPA/630/R-97/001.
- Hansen (1997a) *Policy for Use of Probabilistic Analysis in Risk Assessment at the U.S. Environmental Protection Agency*.
- Hansen (1997b) *Use of Probabilistic Techniques (Including Monte Carlo Analysis) in Risk Assessment, and Guiding Principles for Monte Carlo Analysis*.
- U.S. EPA (1999b) *Report of the Workshop on Selecting Input Distributions for Probabilistic Assessments*. EPA/630/R-98/004.
- U.S. EPA (2001h) *Risk Assessment Guidance for Superfund. Volume III: Part A, Process for Conducting Probabilistic Risk Assessment.* EPA/540/R-02/002.
- U.S. EPA (2005g) *Review of the National Ambient Air Quality Standards for Particulate Matter: Policy Assessment of Scientific and Technical Information.* EPA/452/D-03/001.
- U.S. EPA (2014i) *Risk Assessment Forum White Paper: Probabilistic Risk Assessment Methods and Case Studies.* EPA/100/R-14/004.

Monte Carlo analysis is a widely used probabilistic method that uses a computer program to combine multiple probability distributions. The methodology is applicable to simplistic models with few input variables or to complex models involving dozens or hundreds of inputs. The simulations use values of model inputs selected randomly from relevant distributions that describe uncertainty or variability in model inputs to produce a quantitative estimate of exposure. This process repeats, generating a series of exposure estimates that can be statistically analyzed. Monte Carlo models can consider correlations between input values using correlation coefficients or can assume independence. In more complex simulations, selection parameter values can be linked by conditional distributions, for example, as in Zartarian et al. (2017). A Monte Carlo analysis can characterize uncertainty, variability, or both, in a population. The data reflected in the distributions of inputs (U.S. EPA 2001h) determine the inclusion of uncertainty and variability.

Probabilistic exposure assessment is not necessary for every situation, and the complexity of a probabilistic assessment can vary depending on the nature of the assessment performed. Monte Carlo analysis is one of the simpler probabilistic approaches.

**Advanced Methods for Probabilistic Modeling**

Advanced modeling methods employ complex statistical analyses to characterize uncertainty and variability either jointly or separately. In Appendix D of *Risk Assessment Guidance for Superfund. Volume III: Part A, Process for Conducting Probabilistic Risk Assessment* (U.S. EPA 2001h), EPA highlights several advanced modeling methods, introduces terminology and basic concepts of advanced modeling and provides resources for more information. Advanced models or methods introduced in that document include:

- **Microexposure Event (Microenvironmental Exposure) Analysis.** The basic exposure equation (see Section 2.4.1) assumes exposures are constant over time. Exposures at any given moment, however, tend to fluctuate as the impacts from sources in an environment vary over time or as individuals move from one microenvironment (e.g., outdoors, kitchen, bedroom) to another. Microexposure event analysis separately models the doses

an individual receives while in each microenvironment for a sufficiently short period during which exposures are reasonably constant. The sum of these individual doses gives daily or longer-term doses (Price et al. 1996).

- **Two-dimensional Monte Carlo analysis.** This analysis, which also is a probabilistic risk assessment method, separately characterizes the data uncertainty and variability of one or more parameters in an exposure estimate. In the basic case, nested computational loops (MacIntosh et al. 1995) sample distributions that represent variability and data uncertainty. Varying parameter values over many iterations (e.g., 5,000 times) results in probability distributions for further statistical analyses (e.g., evaluation of confidence limits surrounding the base-case variability distributions). In more advanced, separate probabilistic modeling of variability and uncertainty, EPA has used the bootstrap-based uncertainty analysis techniques described in Xue et al. (2006) for the Stochastic Human Exposure and Dose Simulation (SHEDS) model application to chromated copper arsenate exposures.
- **Geospatial Statistics.** This specialized branch of statistical analyses, relying on a multivariate statistical tool, explicitly considers the geospatial location of data points in the analysis of exposure. Geospatial statistics incorporate information about the spatial distribution of chemical concentration inputs and modeled exposure predictions (e.g., cities, states, regions).
- **Elicitation of Expert Judgment.** Expert elicitation is the process by which the judgments of experts in multiple fields are quantified and documented. Experts characterize the relationships, quantities, events or parameters of interest based on their professional judgment and expertise, typically expressing the characterizations as probabilities. Expert elicitation can be sought individually (i.e., each expert acts alone) or as a group (i.e., experts meet and provide a collective response). An individual approach typically is used when uncertainty characterization is needed. A group approach is appropriate when a consensus or best estimate of uncertainty is needed (U.S. EPA 2009a; U.S. EPA 2009b). Information from such elicitations can be used to characterize data uncertainty and to fill data gaps in an exposure assessment when traditional scientific research is not feasible or data are unavailable. Expert elicitation also can support probabilistic approaches when data are scarce or lacking. In Bayesian analyses, experts in a field construct distribution probabilities based on professional judgment and experience, updating the distributions as new data become available. Statistical analyses help quantify the value of the information stemming from the Bayesian analysis and the impact on uncertainty and variability analyses (Bates et al. 2003; Gronewold et al. 2008).

To select among advanced modeling methods, an exposure assessor examines the rationale for selecting a particular model, including the questions being addressed, data requirements of the model, availability of the existing data, resources required to obtain additional data, scientific integrity of the model, uncertainty and variability the model addresses and uncertainty the model introduces. Note that more complex models are not necessarily more accurate than simpler models. Accuracy depends on the availability of data and model-specific uncertainties. Also, requirements for additional parameters might necessitate the use of more default values, leading to greater uncertainty.

## 6.2.3. Categories of Models Used in Exposure Assessments

Different types of models are used during different stages of the continuum between source and dose (see Figure 2-1).

- **Fate and transport models.** Assess the movement and transformation of pollutants in the environment and yield predicted ambient pollutant concentrations in different environmental media. The outputs of these models are concentrations of chemicals in media that are relevant to specific receptors. These estimates often serve as proxies, or surrogates, for actual exposures or serve as inputs to human exposure models.
- **Human exposure models.** Incorporate information on environmental concentrations and exposure factors and yield predictions of exposures based on actual or assumed contact between a receptor and the concentration of contaminants in the environment.
- **Integrated fate/transport-exposure models.** Yield both predicted ambient pollutant concentrations and predicted exposures.
- **Dose estimation models.** Used to predict internal doses at target tissues, organs or toxicity pathways that result from exposure to an agent. In the case of reverse dosimetry, dose estimation models reconstruct exposure levels that are consistent with measurements inside an organism or in biological material.

The above list focuses on deterministic or probabilistic quantitative mass-transfer models. Statistical models such as regression models based on available or empirical data also help estimate the distribution of exposures within a population, including central tendencies and percentiles or help quantify the relative significance of factors that can influence exposure levels. Section 6.2.6 (on high-throughput exposure models) discusses examples of these models.

In addition, a class of "sub" models can provide the input parameters for the mass transport models described above. Such models include programs of indoor air concentrations such as iSVOC, Params and MCCEM (Multi-chamber Concentration and Exposure Model). Other examples of such submodels include models of exposure-related parameters such as dermal absorption (IHA (American Industrial Hygiene Association) Exposure Assessment Committee 2000).

**Fate and Transport Models**

Exposure assessors use fate and transport models to estimate the movement and alteration of contaminants as they are transported through environmental media (e.g., air, soil, water, groundwater) (U.S. EPA 2019a). These models aid in the understanding of natural systems and the way in which systems react to varying conditions, including the spread of toxic substances in various media and the short- and long-term effects of exposure to hazardous substances. Model outputs can include current and future media concentrations and concentrations at specific locations (e.g., fence lines, locations for permit compliance, on site, off site). The EPISuite™ model can be used to estimate environmental fate and transport for certain chemicals.

Fate and transport models describe the impact of the physical, chemical and biological processes on the predictions of exposures from specific sources of environmental release. Physical processes include bulk transport in the movement of air, surface or groundwater flows or soil transport; movement between media such as volatilization and sorption to solids; and dispersion in a medium such as air or water. Chemical processes considered in the models include chemical

oxidation and reduction, reactions with solid material and photodegradation in air and water. Microbial degradation also can affect concentrations of chemicals in the environment and change the chemical nature of contaminants.

Atmospheric fate and transport models the Agency uses range from simple to complex. Simple models are appropriate when substantial amounts of monitoring data are available. These modeling approaches include models for inverse distance weighting that interpolate between locations with monitoring data. Land use regression is another simple approach used to approximate ambient air concentrations by combining land use information and monitoring data in a multiple regression model and applying the model to areas having limited monitoring data. More complex models include the spatially resolved point- and line-source-oriented AERMOD model with limited consideration of chemistry or removal processes and the more complex multisource and larger spatial scale CMAQ (Community Multiscale Air Quality) model that incorporates physical-chemical processes influencing the concentrations of various pollutants and their species. Examples of commonly used models of fate and transport in water are PRZM3, BASINS and AQUATOX. The resources listed in Table 6-1 provide additional information on the use of fate and transport models.

**Human Exposure Models**

Human exposure models simulate and predict population exposure and dose distributions and assess variability in model inputs. The website, *An Overview of Human Exposure Modeling at the U.S. EPA's National Exposure Research Laboratory*, and journal publications (Furtaw Jr. 2001; Williams et al. 2010) provide overviews of these models. Table 6-1 also provides resources on where to obtain detailed information on human exposure models. EPA and other organizations have developed human exposure models that range from deterministic screening models for assessing specific sources to probabilistic models of aggregate and cumulative exposures across populations and over time. Screening models that address specific environmental sources and a range of consumer products include E-FAST (U.S. EPA 2014c) and the more recent Consumer Exposure Model (U.S. EPA 2016a). EPA and other organizations have developed several human exposure models suited for inhalation exposure modeling. Examples of more complicated models include SHEDS-Air, Air Pollutants Exposure Model (APEX) for criteria air pollutants and Hazardous Air Pollutant Exposure Model (HAPEM) for other hazardous air pollutants. In addition, EPA and other organizations have developed similar but more complex probabilistic multimedia human exposure and dose models for aggregate and cumulative pesticide exposures (e.g., SHEDS-Multimedia, Cumulative and Aggregate Risk Evaluation System, LifeLine™, Calendex™) to accommodate additional chemicals (Price et al. 2001; Young et al. 2012). These models are examples of microexposure event models.

**Integrated Fate/Transport-Exposure Models**

Integrated fate/transport-exposure models combine measured or modeled concentrations in different media (e.g., air, water, soil, indoor surfaces, food) with pertinent exposure factors to estimate human exposures at modeled locations. For example, both atmospheric transport and diffusion models and human exposure models combine ambient pollutant concentrations, location-specific representative human or demographic data and relevant exposure factors (e.g., breathing rates, times spent indoors and outdoors) to estimate or predict human exposures. Examples of such models include SHEDS-Air, APEX and HAPEM. These models focus on integrating data on fate and transport parameters with information on human physiology and

exposure-related behaviors for complex assessments of exposures to air toxics. In addition, many integrated fate/transport-exposure assessment models provide estimates of potential or absorbed dose (U.S. EPA 2015b; U.S. EPA 2016d; U.S. EPA 2017a; U.S. EPA 2017b).

Although EPA designed many of its exposure models as standalone models, ongoing efforts in the Agency have focused on developing integrated modeling approaches. One effort is the development of integrated air quality and exposure models to identify those sources and microenvironments that contribute to the greatest portion of personal or population exposures and determine optimum risk management strategies (Isakov et al. 2009). Advanced approaches that combine regional and local models have been proposed as a future direction for air quality modeling of hazardous air pollutants to address the spatial variability of air concentrations and allow for better treatment of chemically reactive air toxics (Touma et al. 2006). EPA's *White Paper: Integrated Modeling for Integrated Environmental Decision Making* recommends the Agency adopt a systems thinking approach and consistently and systematically implement integrated modeling approaches and practices to inform Agency decision making (U.S. EPA 2008d). NRC (2012b) states, "systems thinking considers the cumulative effects of multiple stressors, evaluates a range of alternatives, analyzes upstream and downstream life-cycle implications, involves a broad range of stakeholders and uses interdisciplinary scientific approaches."

As indicated by these examples, integrated fate/transport-exposure models generally are for a specific purpose (e.g., aggregate human inhalation exposures from hazardous air pollutants or fumigants, cumulative exposures to multiple chemicals). Table 6-1 provides resources on where to obtain detailed information on integrated fate/transport-exposure models.

**Dose Estimation Models**

Models are available that estimate dose (the mass of a chemical that crosses the exposure barrier over a defined period) from exposure data or estimate both exposure and dose from environmental data (U.S. EPA 2011d). The models include parameters that address the uptake of chemicals across the gut (for ingestion), the dermis (for dermal exposures) and the lung surface (for inhalation). Many of these models address uptake and determine both the applied and the absorbed doses.

## 6.2.4. Estimates of Exposure Using Scenario Evaluation

In the planning and scoping phase of an exposure assessment, an assessor develops exposure scenarios of interest, as Section 3.1 described. A conceptual model identifies potential exposure media and receptors for developing exposure scenarios. An exposure scenario is a combination of facts, assumptions and inferences that define a discrete situation in which exposures occur. An assessor determines chemical concentrations in a medium or location and combines this information with information on the relevant physiology and exposure-related behaviors of the exposed individuals. Characterization of an exposure scenario consists of the collection of environmental measurement data (e.g., soil, dust, air, diet) and exposure factor information (e.g., contact rates, activities), which then are combined according to the applicable conceptual model structure. For an exposure scenario, an assessor usually characterizes the chemical concentration and the time of contact separately.

For the chemical concentration characterization, an assessor typically estimates an exposure concentration indirectly by measuring, modeling or using existing data on concentrations in the bulk medium rather than at the point of contact. A chemical assessor's assumption that the concentration in the bulk medium is the same as an exposure concentration can introduce uncertainty in an exposure estimate. Section 6.3.4 on model uncertainty analysis discusses this assumption. Generally, the closer to the point of contact (in both space and time) the concentration in the medium is measured, the less uncertainty exists in an exposure concentration characterization. Estimating the change in concentration over time helps calculate an exposure estimate more accurately.

For the time-of-contact characterization, the assessor estimates the frequency and duration of exposure for the activities related to that exposure (as Section 6.2.2 on microexposure event analysis mentioned). Some electronic means of recording locations and activities are available, including personal data recorders, automated global positioning system-based recorders, videography-based microactivity diaries and smart phones. As Chapter 5 discussed, several methods are being explored to characterize the locations and activities of individuals. Paper time-activity diaries, however, are still the most common means to collect location and activity information from participants in observational human exposure measurement studies. When participant-specific activity information is not collected, time and activity are estimated using available databases, for example:

- *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011d)
- Consolidated Human Activity Database
- American Time Use Survey.

In the absence of more substantive information, an assessor acquires participant-specific activity information by making assumptions about behavior. Estimating dermal exposure, for example, might involve combining assumptions about activity patterns based on observations, surface sampling data for the chemical of interest and a dermal transfer rate. Likewise, estimating inhalation exposure could involve linking databases of indoor and outdoor environmental pollution concentrations with time-activity diary and inhalation rate information.

In 2001, EPA published the *Draft Protocol for Measuring Children's Non-Occupational Exposure to Pesticides by All Relevant Pathways*, which details a systematic, measurement-based approach to evaluating exposure by each route (i.e., inhalation, dermal, ingestion) using a series of algorithms (U.S. EPA 2001b). Each algorithm mathematically expresses exposure for a specific route as a function of chemical concentration in an environmental medium and selected exposure factors. The algorithm's inputs explicitly identify the data requirements. Estimating aggregate exposures using these algorithms requires complete datasets for each pathway. Similar to the 2001 Draft Protocol, EPA's Office of Pesticide Programs (OPP) uses a set of SOPs to estimate post-application exposures to pesticides for toddlers (through dermal contact and hand-to-mouth activity) from treated residential surfaces. These SOPs are used for product registration or reregistration in the United States and provide a screening-level assessment to estimate exposures when data are limited and exposure estimates beyond the day of application are desired. OPP has finalized an updated set of SOPs (U.S. EPA 2012f). Another example of a scenario-based approach is EPA's *Example Exposure Assessment Scenarios Tool and Associated Report* (U.S. EPA 2005b), which is designed to assist in developing estimates of exposure, dose

and risk. The purpose of the *Example Exposure Scenarios* document (U.S. EPA 2003c) is to outline scenarios for various exposure pathways and demonstrate how data from the *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011d) might be applied for estimating exposures.

The outcome of the scenario evaluation often is an exposure estimate that results from combining concentrations with exposure factors. The assumptions or boundary conditions limit the estimates, however (see Section 5.3.3, which discussed boundary conditions). To address this limitation, an assessor (1) evaluates an exposure equation under conditions for which the limiting assumptions hold true or (2) addresses the uncertainty caused by the divergence from the boundary conditions. An example of the first approach is the microenvironment method. The term microenvironment refers to surroundings (e.g., home, office, automobile) treated as homogeneous or well characterized in the concentrations of an agent. In a given microenvironment, the pollutant concentration is assumed uniformly distributed spatially during the contact time, although the pollutant concentration might vary over time. Therefore, this method evaluates an individual's exposures as a series of time segments and locations in which the assumption of uniform concentration is approximately true and then sums results for the segments to estimate total exposure over longer periods (Price et al. 1996). This effectively removes some of the boundary conditions. For example, in determining inhalation exposure to acute toxicants, the estimated ventilation rate changes depending on the activities performed during an exposure event. This process avoids much of the error that using average values causes when concentration varies widely along with time of contact. Several researchers have reported the uncertainty that relying on deterministic bounding estimates introduces (Finley and Paustenbach 1994; Simon 1999). Section 6.3.4 presents additional discussion of variability and uncertainty analysis in probabilistic modeling.

## 6.2.5. Exposure and Dose Estimation Using Biomonitoring Data

Biomonitoring is the measurement or tracking of an agent or its biomarker in an organism or in biological material to characterize the organism's exposure to an agent. Chemical agents investigated using biomonitoring include organic compounds, metals and anions (CDC 2009). Biomarkers of exposure confirm that an individual has been exposed to a chemical and function as an important tool for understanding the linkages between external chemical exposures, internal doses and potential health outcomes in humans (Clewell et al. 2008; NRC 2006b). In addition, such measurements provide an integrated measurement of exposure to a chemical from all sources and routes. The measurements are also one of the few available ways of characterizing the total internal doses of agents that occur as a result of exposures from multiple sources (aggregate exposures). Biomonitoring data reflect both current and past exposures of the individual. Depending on the persistence of the agent, or its biomarker, the observed concentrations might reflect exposures from the prior day or exposures that occurred decades earlier (Chen et al. 2013; Clewell et al. 2008).

A limitation of most biomarkers of exposure is that they cannot be used alone to identify specific sources and quantify the contribution of individual exposure pathways. As a result, biomonitoring data collected in isolation are best used as a surveillance tool [e.g., baseline exposure levels, trends over time, identifying populations with higher chemical exposures (CDC 2005; Hays et al. 2007; Sobus et al. 2010; Tan et al. 2005)]. The value of biomonitoring data increases if collected in combination with demographic data and exposure data. In these cases,

biomonitoring data confirm the estimates of absorbed doses that exposure modeling produces (Hinderliter et al. 2011).

Chemicals or their metabolites frequently serve as biomarkers of human exposure. The chemicals are measured in samples of body fluids and tissues such as urine, blood, breath, hair and saliva. Maternal biomonitoring provides information on in utero exposures. Measurements in cord blood, amniotic fluid and meconium characterize perinatal exposures (Barr et al. 2007). Urine is a frequently used matrix for biomonitoring for exposure to nonpersistent chemicals because these contaminants generally have short half-lives (e.g., <24 hours) in the body. For persistent chemicals, blood is a commonly used matrix for biomonitoring because, for these compounds, levels are higher in blood than urine.

**Forward Dosimetry**

Forward and reverse dosimetry are two approaches for using biomonitoring data to provide quantitative estimates of human exposure to chemicals. Forward dosimetry uses measurements of environmental concentrations and supplemental data (such as exposure factors) in conjunction with simple pharmacokinetic (PK) or more complex physiologically based pharmacokinetic (PBPK) models to estimate internal doses of a chemical that are consistent with measured biomonitoring data. The forward dosimetry approach provides valuable information on the important sources, pathways and routes of human exposure to chemicals. It also provides a quantitative measure of an integrated internal dose from multiple sources and routes over a specified period. For instance, this approach showed the importance of dust pathways in exposures to polybrominated diphenyl ethers (Stapleton et al. 2014). Ideally, the forward dosimetry estimates are similar to the measured biomarker estimates, as was the case for polybrominated diphenyl ethers (Lyons et al. 2008). Tulve et al. (2011) published cumulative exposure estimates using forward dosimetry approaches. Tan et al. (2007) and Clewell et al. (2008) present illustrative examples and further discussion of the interplay between exposure estimation, biomonitoring data and these modeling methodologies. Table 6-2 presents examples of dose estimation using forward dosimetry.

**Table 6-2. Example Publications on Modeling Exposure and Dose from Biomonitoring Data**

| Agent | Dosimetry Approach | Studies |
|---|---|---|
| Chlorpyrifos | Forward | Morgan et al. (2005); Edlmann et al. (2016) |
| Dioxins and dioxin-like compounds | Forward | Lorber et al. (2009); NRC (2006a) |
| Phthalates | Forward | Clark et al. (2011); Lorber et al. (2010) |
| Polybrominated diphenyl ethers | Forward | Lorber (2007) |
| Chloroform | Reverse | Lyons et al. (2008) |
| Glyphosate | Reverse | Acquavella et al. (2004) |
| Malathion | Reverse | Dong et al. (1994) |
| Perchlorate | Reverse | Blount et al. (2007); Huber et al. (2011) |
| Pesticides | Reverse | Mage et al. (2004); Mage et al. (2008) |
| Phthalates | Reverse | Koch et al. (2003) |
| Trihalomethanes | Reverse | Tan et al. (2007) |

**Reverse Dosimetry**

Reverse dosimetry (i.e., exposure reconstruction) models estimate an external exposure to a chemical that is consistent with, and based on, biomonitoring data. Reverse dosimetry is distinct from forward dosimetry in that forward dosimetry considers all components and pathways of exposure that comprise an individual's total exposure, whereas reverse dosimetry seeks only to arrive at the total dose responsible for the measured biomarker. Reverse dosimetry modeling, however, can incorporate basic PK information known about the chemical in the application process. PK and PBPK models are applicable in reverse dosimetry analyses by rearranging parameters to estimate intakes based on biomarkers and modeling parameters. Other simple reverse dosimetry approaches assume steady-state exposures and measure exposure based on urinary excretion rates. Urine accumulation in the bladder and differences in hydration across individuals complicate measurements of urinary excretion, necessitating having data on the timing of the accumulation period and urine volumes or normalized creatinine production rates (LaKind et al. 2014). Creatinine correction is the most common method for adjusting for variable dilutions in spot urine samples (Barr et al. 2005) and has been used in assessments of perchlorate (Blount et al. 2007), phthalates (Koch et al. 2003) and pesticides (Mage et al. 2004; Mage et al. 2008).

Table 6-2 presents examples of exposure estimation using reverse dosimetry. Forward and reverse dosimetry approaches are complementary because the hypotheses one analysis raises can be tested by the other [e.g., Georgopoulos et al. (2009)].

**Simple PK Models**

In some cases, human PK data are available for environmental chemicals, and given the information on external dose, these data are useful for predicting concentrations of the chemical in an easily sampled body matrix such as urine or blood. PK data, such as first-order elimination rates (often described by human half-lives), can be used. Depending on the nature of the PK data, simple one-, two- and even three-compartment models are appropriate for this purpose (Gabrielsson and Weiner 2000). In dosimetry, a "compartment" can be physiologically defined (e.g., the volume of body lipid) or not physiologically defined (e.g., "volume of distribution"). The simplest PK model is a mass-balance model, which implicitly assumes the organism is at steady state with its environment. Often, the goal of simple PK models is to compare predictions of concentrations in body matrices with analogous measurements the literature reports. The standard one-compartment, first-order absorption model, however, makes inherent assumptions about the absorption, distribution, metabolism and elimination (ADME) processes that could limit its use (Neubig 1990).

**PBPK Models**

PBPK models represent an important class of dosimetry models that assessors can use to predict the internal dose at target organs for risk assessment applications. PBPK models consist of a series of mathematical algorithms that represent biological tissues and physiological processes in the body and simulate chemical ADME. The internal dose replaces the administered dose for the derivation of quantitative dose-response relationships. When the PBPK modeling is reliable, the move to the internal dose improves inter- and intraspecies extrapolations because differences in ADME across species and across individuals are removed from the assessment. This reduces the uncertainty in predictions of human dose-response and is one reason for the growing use of PBPK models in scientific and regulatory assessments. Characterizing uncertainty in risk

assessments based on PBPK model results compared with uncertainty in results based on administered dose is an important and active research area (U.S. EPA 2006a). In some cases, the Agency might incorporate exposure and dose modeling uncertainties within a hierarchical Bayesian framework in some of the exposure evaluations (Tornero-Velez et al. 2010). EPA suggests considering the following questions when using PBPK models in risk assessments.

- Are data available on tissue-specific kinetics (e.g., distribution) for all relevant tissues, physicochemical properties of the chemical and chemical-specific ADME?
- Does the PBPK model contain a compartment associated with the target tissue, contain the target tissue or identify a surrogate for the target tissue?
- Are the physiological parameter values defensible (i.e., within the known plausible range of the organism)?
- Have the models undergone a thorough evaluation of their structure, implementation, appropriate application domain and predictive capability (U.S. EPA 2006a)?

PBPK models have been developed to address age-related changes in physiology (Loccisano et al. 2013; McLanahan et al. 2014; Wu et al. 2016). These models, often referred to as lifestage models, address physiological changes associated with pregnancy (McLanahan et al. 2014) and the growth and development of infants and children (El-Masri et al. 2016; Luecke et al. 2007). These modeling efforts also seek to address the issue of age-related changes in the activity of enzymes associated with Phase I and Phase II metabolism of chemicals (Hines 2013). An example of a model with age-related changes in ADME is the IEUBK (Integrated Exposure Uptake Biokinetic) model (U.S. EPA 1994a).

### 6.2.6. High-Throughput Exposure Models

The recently developed ToxCast program has resulted in the generation of in vitro toxicity and bioactivity data on thousands of chemicals in commerce. The ToxCast data have been used to set screening levels of systemic dose associated with minimal levels of bioactivity (Thomas et al. 2013). These emerging findings form the basis for potentially prioritizing the need for animal testing or the need for refined exposure estimates. Using these dose-bioactivity datasets to prioritize requires screening estimates of the aggregate exposures to the chemicals. To meet this need, a new type of human exposure model is being developed that generates high-throughput screening estimates of aggregate exposures (Isaacs et al. 2014; Shin et al. 2015; Wambaugh et al. 2013; Wambaugh et al. 2014). The hallmark of the high-throughput screening models is that they trade a reduction in model complexity with an increase in model uncertainty for models that can be applied rapidly to thousands of chemicals (many of which have minimal exposure-related information).

The SHEDS-High Throughput model (SHEDS-HT) is an example of this type of model. Based on probabilistic methods and algorithms developed for earlier models in the SHEDS family of software, the algorithms in SHEDS-HT reduce the input data demands and run times of the earlier SHEDS models, while maintaining critical features and inputs that influence variation in exposure (Isaacs et al. 2014). An initial effort applied SHEDS-HT to 2,507 organic chemicals associated with consumer products and agricultural pesticides. The model addressed exposure associated with the use of commercial products (nearfield sources) and dietary exposures from agricultural pesticide use. The SHEDS-HT approach has the advantage of generating estimates of the distributions of aggregate exposures across populations of different ages.

In addition to SHEDS-HT, Wambaugh et al. (2014) have proposed high-throughput screening heuristic models of exposure. This approach has produced predictive models of the median aggregate exposures to chemicals in the general population based on chemical use information and the physical and chemical properties of the chemicals. EPA (U.S. EPA 2014e) also proposed a framework for using estimates of exposures inferred from the National Health and Nutrition Examination Survey biomonitoring program to evaluate and calibrate estimates from multiple high-throughput models to form consensus high-throughput exposure predictions.

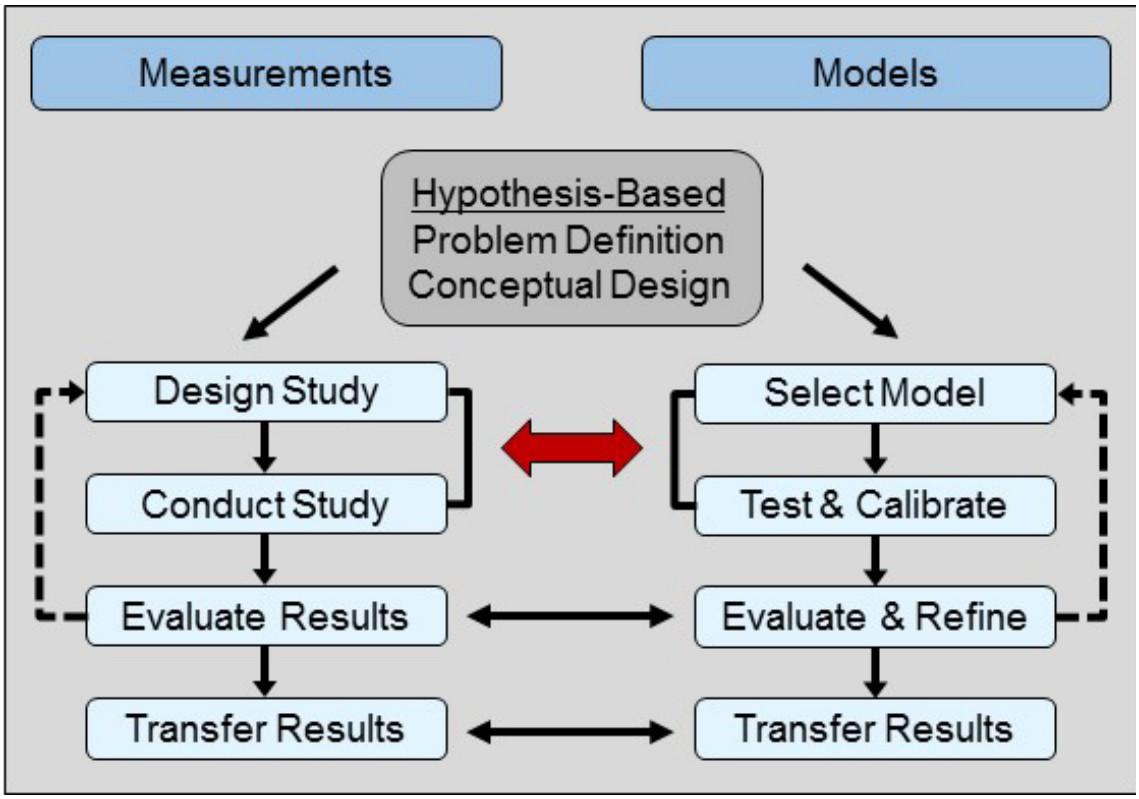
## 6.3. Evaluation of Models

The Agency defines model evaluation as the process that generates information during model application to determine whether the model and its analytical results are of sufficient quality to serve as the basis for a decision (U.S. EPA 2009d). Similarly, the National Academy of Sciences defines model evaluation as the process of deciding whether and when a model is suitable for its intended purpose. The Academy stipulates this process is not a strict validation or verification procedure. Instead, it provides an objective assessment of the model's performance for the stated purpose and increases the understanding of model strengths and limitations (NRC 2007). EPA's *Guidance on the Development, Evaluation, and Application of Environmental Models* (U.S. EPA 2009d) discusses model evaluation versus validation versus verification.

Model evaluation is a multifaceted activity including peer input, corroboration of results with data (e.g., other model predictions, actual measurements or other proxies such as biomonitoring data), quality assurance/quality control (QA/QC) checks and uncertainty and sensitivity analyses (NRC 2007). This process compares the accuracy of model results with data as an independent test of how well the model represents the actual conditions. One consideration is how close the predicted values (based on either deterministic model estimates or various statistics and percentiles of more advanced probabilistic models) are to observational data. Evaluation also considers the degree to which the basis of the model is generally accepted science and computational methods. Whether the model fulfills its designed task and how well it approximates observed conditions are also components of model evaluation. For example, evaluating a fate and transport model that estimates concentrations at an exposure point might include verifying that model equations appropriately represent the transport and transformation concepts, the computer code is free from error (by comparing the model output with data from laboratory microcosms) and modeling results are comparable to field data under various conditions and for various chemicals.

Figure 6-3 illustrates the iterative use of models along with monitoring data from observational human exposure measurement studies to evaluate and refine study designs and to inform planning of future observational human exposure measurement studies. The single-headed arrows indicate steps in the two processes (modeling and monitoring) while the double-headed arrows denote the exchange of information between the two activities.

**Figure 6-3. Iterative Use of Measurements and Models**




Source: Özkaynak (2009)

Although complex computational models typically cannot be validated, module-specific predictions can be evaluated against available measurements or alternative model predictions (NRC 2007). Consequently, many key components of EPA's exposure assessment models have been evaluated using various approaches and comparing results to available measurements. Approaches include comparing (1) the structure, model inputs and results of one model to another, (2) modeled estimates with measured or field data and (3) modeled estimates with biomonitoring data. Comparing predictions against field data can reveal uncertainties and identify missing pathways, leading to the subsequent refinement of model selection and helping design field studies to fill critical data gaps (Özkaynak 2009).

Model evaluation makes possible the identification of the model's strengths and limitations and the most critical model parameters and assumptions. Such an evaluation not only indicates the conditions under which a simulation will be acceptable and accurate for its intended purpose, but also the conditions under which using the model is unacceptable.

### 6.3.1. Soundness of Assumptions, Methods and Conclusions, Appropriateness

Peer input provides an independent evaluation and review of models used in an exposure assessment. The purpose of model peer input is to evaluate the assumptions and whether sound scientific principles underlie the methods and conclusions derived from models and to check the scientific appropriateness of a model for informing a specific regulatory or risk management decision (U.S. EPA 2009d). The latter objective is particularly important for applications of existing models for purposes other than those intended in their initial design. Researchers and

practitioners in academia, consulting, private industry and state and local governments—both nationally and internationally—frequently use models and sometimes collaborate in their development. A critical consideration in using models is transparency, including providing rigorous model documentation and promoting unfettered communication among an exposure assessor, modeler and risk manager/decision maker in the application of the model to a specific problem.

### 6.3.2. Attainment of Quality Assurance Objectives

For a chosen model, an exposure assessor determines whether the inputs the model requires are available and all parameters the model requires are obtainable or reasonable default values are accessible. After running the model, an exposure assessor needs to evaluate whether the model outputs meet the exposure assessment goal(s) and data quality objectives. If they do not, the model parameters might need adjustment or a different model selected and tested. All input data need to meet data quality acceptance criteria (see Section 5.3.2).

The exposure assessor also conducts a data quality assessment to assess the type, quantity and quality of data to verify that the planning objectives, QA project plan components and sample collection procedures are satisfied and to confirm the data are suitable for their intended purpose. EPA's *Quality Management Tools – Data Quality Assessment* website describes EPA's five-step process for data quality assessment.

### 6.3.3. Qualitative and Quantitative Model Calibration

As a standard practice, an exposure assessor verifies model operation and results. Some models might need precalibration for use in subsequent exposure assessments. Calibration is the process of adjusting selected model parameters within an expected range until the differences between model predictions and field observations are within selected criteria (U.S. EPA 2009d). Calibration accounts for spatial variation and temporal variation that the model formulation does not represent; functional dependencies of parameters that are unquantifiable, unknown or not included in the model algorithms; and extrapolation of laboratory measurements to field conditions.

### 6.3.4. Model Uncertainty and Sensitivity Analyses

An exposure assessor acknowledges and characterizes important sources of uncertainty in modeled estimates, either qualitatively, quantitatively or both. Uncertainty is the lack of precise knowledge, either qualitative or quantitative, and can refer to the limited knowledge about the factors affecting exposure and adequacy of model outputs for decision making. An exposure assessor characterizes the quality of the input data and the resulting limitations on the uses of the model results. Chapter 8 presents a broader discussion of issues on uncertainty in exposure assessment.

Models are mathematical representations of processes that quantify how a system behaves in response to changes in its inputs. Exposure model development entails several choices regarding what to include and at what level of detail. Model inputs and parameters typically include various sources of uncertainty. Important sources of uncertainty are measurement error, statistical sampling error, nonrepresentativeness of data and structural uncertainties in scenarios and formulations of models.

Scenarios are assumptions regarding the factors that define the scope of the assessment, such as the averaging time, geographic and temporal scales and the exposed population of interest (Özkaynak et al. 2008). Omitting any elements of the scenario of interest from the modeling approach can bias the estimates. Uncertainty also might stem from extrapolating beyond conditions for which the model was constructed or calibrated. The extent of verification and validation, whether the model is extrapolated beyond the range of its evaluation and whether alternative theories exist upon which alternative modeling approaches could be developed all influence model uncertainty (Cullen and Frey 1999).

Assessments of input and parameter uncertainty can use advanced statistical methods (e.g., Bayesian techniques), conventional Monte Carlo methods or two-dimensional Monte Carlo methods. Such assessments iterate model simulations using alternative sets of variability distributions for key inputs and parameters. Typically, the simulations generate a few hundred alternative exposure prediction distributions that depict the uncertainty around the initial exposure distribution; for example, the cumulative distribution function for exposures or dose (WHO 2008). Most Monte Carlo applications performed for predicting exposures capture the combined variability and uncertainty associated with each input and variable in the model runs. These results typically represent the variability in the predictions and the extremes in the alternative uncertainty cumulative distribution functions by capturing the variability and uncertainty bounds within a one-dimensional simulation (WHO 2008). In models that are more refined, using two-dimensional Monte Carlo methods distinguishes variability from uncertainty. Simplified two-dimensional Monte Carlo methods, as MacIntosh et al. (1995) describe, are appropriate, provided one ignores the potential correlations between the statistical parameters of the variability distributions (e.g., if one were to assume independent uncertainty distributions for the means and standard deviations of normal distributions). These correlations can be captured, however, by the use of bootstrap-based uncertainty analysis techniques used in Xue et al. (2006).

Some of the fate and transport, human exposure and integrated fate/transport-exposure models can simulate stochastic processes, which enables assessment of the variability and uncertainty in modeled estimates and input parameters. Variability refers to the heterogeneity or diversity of potential exposures in a population. The models, which can simulate stochastic processes, tend to be higher tier exposure models and some of the integrated fate/transport-exposure models. For these models, such assessments usually involve performing univariate or multivariate Monte Carlo analyses, sensitivity analyses or exposure pathway contribution analyses (i.e., analyses to understand the relative importance of different pathways), or a combination. The most common model input parameters varied to address variability or uncertainty are exposure factors and chemical residue values in different environmental media. A key challenge for integrated fate/transport-exposure models is the quantification of coupled model uncertainties resulting from propagation of errors from the different model components, linked during an integrated analysis. Selected case studies have evaluated the impact of this problem (Özkaynak et al. 2009).

In the context of an exposure assessment, EPA defines sensitivity analysis as “any systematic, common sense technique used to understand how risk estimates and, in particular, risk-based decisions, are dependent on variability and uncertainty in the factors contributing to risk” (U.S. EPA 2001h). In other words, for understanding and addressing data uncertainty, the sensitivity analysis is a process of determining which parameter(s) in an exposure assessment drive the results. An exposure assessor uses these analyses to decide when to stop collecting data or

performing more time-consuming probabilistic analyses. Identifying the parameter(s) that most influence uncertainty and variability in an exposure assessment's results enables an exposure assessor to:

- Prioritize sources of data uncertainty, model uncertainty and variability
- Inform risk managers/decision makers and stakeholders about the potential impacts of risk management decisions
- Support a cost-benefit analysis that weighs the cost of additional analyses or data collection efforts against the benefit of having a more refined exposure assessment
- Target additional analyses or data collection efforts
- Assist in model development and refinement by highlighting key input parameters.

Sensitivity analyses can range from simple to more complex analyses, including modeling and regression analysis. Simpler analysis typically involves a one-at-a-time fixed or percentile scaling approach. Fixed approaches, for instance, might test the variation of results by varying each input up and down by a factor of 2. In the percentile scaling approach, first a reference or base (e.g., mean) value of the chosen variables is selected. Then, the modeler conducts two more runs for each input at lower (e.g., 5th) and upper (e.g., 95th) percentiles of their distributional range. For each run and simulated individual, modelers determine the mean outputs for each lower and upper percentile simulation and compare them to the reference or base case results. In addition, high/low ratios (e.g., the ratio of the 95th percentile result to the 5th percentile prediction) are calculated. These ratios or ranges provide assessors with the impact and significance of each influential variable on the exposure modeling predictions. A more complicated sensitivity analysis approach relies on multivariate methods, whereby, in probabilistic simulations, the modeler retains each simulated individual's means of input variables and outputs. The modeler then uses this information in stepwise regression models to examine the relationship between inputs and outputs of the model to determine the impact of the key variables in the presence of others that influence the results.

The type of sensitivity analysis needed for each situation depends on the complexity of the exposure assessment question (U.S. EPA 2001h). The essence of the analysis, however, remains the same: evaluating how changes in the input parameters change the output. Several methodological tools and approaches are available for conducting sensitivity and uncertainty analysis (Cullen and Frey 1999; Mokhtari et al. 2006; Saltelli et al. 2004; WHO 2008). For example, global sensitivity analysis methods (such as regression, analysis of variance, categorical and regression trees), the Fourier amplitude sensitivity test and Sobol's method identify key sources of variability, uncertainty, or both, when many inputs are varied simultaneously. Appendix A of EPA's *Risk Assessment Guidance for Superfund. Volume III: Part A, Process for Conducting Probabilistic Risk Assessment* (U.S. EPA 2001h) and the World Health Organization's *Uncertainty and Data Quality in Exposure Assessment* (WHO 2008) provide detailed guidance on conducting sensitivity analyses. EPA programs might implement specific procedures for conducting sensitivity analyses; therefore, assessors need to consult with their programs and follow their SOPs.

This section has focused on sensitivity and uncertainty analyses within a selected model. Performing sensitivity analyses across different models is also appropriate to determine whether some models are less sensitive to certain critical parameters. Uncertainty across models is also

appropriate, for example, to quantify ranges of outputs that reflect the uncertainties of model assumptions for a given set of inputs (Cullen and Frey 1999; Young et al. 2012).

## 6.4. Summary

- EPA has adopted the National Research Council **definition of a model**: "a simplification of reality that is constructed to gain insights into select attributes of a particular physical, biological, economic, or social system."
- **Model selection** involves identifying the type of model needed to meet the risk management objectives of the assessment and determining the complexity of the model necessary to reach a decision. The assessor determines whether a model to meet those needs is available or if a new model needs to be developed.
    - Before selecting a model, an exposure assessor defines the **assessment objective(s)** and describes how the model addresses assessment questions or hypotheses required to meet them.
    - Based on the problem statement and system conceptualization, an assessor develops a modeling methodology that stipulates the degree of **complexity of the selected model**. Models range in complexity from deterministic to probabilistic to advanced probabilistic modeling.
    - Various categories of models are appropriate for application in exposure assessment: **fate and transport** models, **human exposure** models, **integrated fate/transport-exposure** models and **dose estimation** models.
    - In the planning and scoping phase, an assessor develops **exposure scenarios** from which to estimate exposure. The scenarios incorporate environmental measurement data and exposure factor information. The outcome of the scenario evaluation is an exposure estimate that results from combining concentrations with exposure factors.
    - **Biomonitoring data can be used to estimate exposure and dose.** Forward and reverse dosimetry are two approaches for using biomonitoring data to provide quantitative estimates of human exposure to chemicals. Both simple PK models and PBPK models can estimate exposure.
    - **High-throughput screening models** rapidly generate estimates of aggregate exposures to typical individuals for large numbers of chemicals. The hallmark of the **high-throughput screening models** is that they trade model complexity and a possible increase in model prediction uncertainty for applicability to thousands of chemicals.
- **Model evaluation** is the process that generates information during model application to determine whether the model and its analytical results are of sufficient quality to serve as the basis for a decision.
    - An exposure assessor typically verifies model operation and results both qualitatively and quantitatively through calibration.
    - Important sources of **uncertainty** include measurement error, statistical sampling error, nonrepresentativeness of data and structural uncertainties in scenarios and formulations of models. **Sensitivity** analysis is "any systematic, common sense technique used to understand how risk estimates and, in particular, risk-based decisions, are dependent on variability and uncertainty in the factors contributing to risk."

# CHAPTER 7. PLANNING AND IMPLEMENTING AN OBSERVATIONAL HUMAN EXPOSURE MEASUREMENT STUDY

Observational human exposure measurement studies quantify people's exposures to chemical, physical or biological agents or other stressors found in their everyday environments during their normal daily activities. Such studies involve measurements of these agents in environmental media (e.g., air, dust, soil, water); collection of information about the study participants and their homes, work environments and activities (e.g., use of personal care products, cleaning activities); and collection of personal exposure (e.g., duplicate diet, dermal) and biomarker samples (e.g., blood, urine) (Lioy et al. 2005; Sheldon 2010; U.S. EPA 2008c; U.S. EPA 2009a; Zartarian et al. 2005). These types of studies do not intentionally introduce agents or other stressors into people's environments.

After a brief overview (Section 7.1), this chapter discusses the major aspects of planning and implementing an observational human exposure measurement study:

- Designing a study (Section 7.2)
- Planning and executing a pilot study (Section 7.3)
- Planning and executing a full field study (Section 7.4)
- Conducting peer review and completing a final report (Section 7.5).

Section 7.6 summarizes this chapter.

## 7.1. Overview

Observational human exposure measurement studies enable exposure scientists and risk assessors to identify agents to which people are exposed; exposure concentrations; important sources, routes and pathways of exposure; and factors that have the greatest influence on exposure. Observational human exposure measurement studies also can be conducted within the context of an epidemiological investigation. Results from observational human exposure measurement studies support the regulatory work of Agency programs and contribute significantly to our understanding of human exposures and risks from environmental agents. In addition, results from these studies have identified major stressors and determined whether mitigation measures have been successful and whether exposures exceeded regulatory standards. These studies evaluate exposures; they do not examine absorption, distribution, metabolism and elimination (ADME) parameters or dose-response. Box 7-1 lists examples of observational human exposure measurement studies.

Data from an observational human exposure measurement study also can be used to evaluate and refine exposure and dose models. The data collected in the study, however, need to be compatible with the data needs of the model of interest. An iterative relationship exists between the information derived from observational human exposure measurement studies and exposure and dose models (see Section 6.2). Model evaluation and optimization use the measured data as model inputs. Exposure and dose models then help identify key data needs that observational human exposure measurement studies can provide.

**Box 7-1. Examples of Observational Human Exposure Measurement Studies**

- U.S. EPA (1987c) *The Total Exposure Assessment Methodology (TEAM) Study*.
  - Measured the personal exposures of 600 residents of 7 U.S. cities to toxic and carcinogenic chemicals in air and drinking water.
- Eskenazi et al. (1999) *Exposures of Children to Organophosphate Pesticides and Their Potential Adverse Health Effects*
  - Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS Study). Investigated in utero and postnatal organophosphate pesticide exposure and its relationship to neurodevelopment, growth and symptoms of respiratory illness in children.
- Weisel et al. (2005) *Relationship between Indoor, Outdoor, and Personal Air Study (RIOPA)*.
  - Large urban air toxics project comprising three studies.
- U.S. EPA (2005f) *A Pilot Study of Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants (CTEPP)*.
  - Investigated the aggregate exposures of 257 preschool children and their primary adult caregivers to pollutants commonly detected in their everyday environments.
- U.S. EPA (2003f) *National Human Exposure Assessment Survey (NHEXAS)*.
  - Examined the range of environmental pollutants and chemicals (volatile organic chemicals, metals, pesticides) to which humans are exposed in daily life.
- U.S. EPA (2011a) *Detroit Exposure and Aerosol Research Study (DEARS)*.
  - Evaluated how air quality information collected at community monitors represents what people living in neighborhoods are exposed to every day.

Table 5-6 presents more information about these and other data sources.

In the exposure assessment process, biological measurements often are combined with environmental, personal and activity pattern data (Bouvier et al. 2005). Use of biological measurements in exposure assessments is limited because the potential clinical significance of biomonitoring results (e.g., association with a health effect) has been established for relatively few chemicals (ECETOC 2005; NRC 2006b). Barr et al. (2006) presented an overview of the concepts that need to be considered when using biomonitoring data. Sections 5.1.2, 5.4.2 and 6.2.5 presented additional information about the uses and limitations of biomonitoring data.

Although this chapter focuses on observational human exposure measurement studies, exposure assessments can use other types of research. All research on human subjects that EPA scientists conduct or the Agency supports must go through several levels of approval. Although the specific path for review differs slightly depending on the origin of the research, the Human Subjects Research Review Official (HSRRO) must approve all research projects on human subjects before any such work can begin. The HSRRO's responsibility is to ensure that all research studies EPA supports comply with EPA regulations concerning research with human subjects (40 Code of Federal Regulations [CFR] 26), EPA Policy Order 1000.17 Change A1 and best practices in ethics. A review and approval by an Institutional Review Board must precede a review request to the HSRRO.

Requests for all third-party research involving intentional exposure of a human subject to any substance, submitted to EPA or considered in connection with any EPA decision under the

Federal Insecticide, Fungicide, and Rodenticide Act[13] or section 408 of the Federal Food, Drug and Cosmetic Act,[14] must meet the additional standards specified in 40 CFR 26. Among other provisions, these regulations might require review by the Human Studies Review Board, an advisory board established under the Federal Advisory Committee Act, depending on the purpose and initiation date for the research. More information can be found at the Office of the Science Advisor *Human Studies Review Board* website. Questions related to third-party pesticide research may be directed to the Office of Pesticide Programs' Human Research Ethics Review Officer.

## 7.2. Study Design

An adequately developed technical study design will address all parts of a study—from identifying data needs to reporting the results to the study participants. As such, a study design might include planning that considers

- Budget and logistics
- Data elements
- Sample size
- Criteria for selecting study location
- Eligibility criteria for study participants
- Data quality objectives and sampling and analytical protocols
- Chain of custody, storage and data management
- Community involvement
- Engaging stakeholders
- Human subjects guidelines, informed consent and recruitment
- Sample collection
- Sampling schemes
- Data analysis and database design.

This section addresses these aspects of the study design. Many other published articles and reports can assist when developing the technical study design (Buckley et al. 2000; Daston et al. 2004; Fenske et al. 2005; Morgenstern and Thomas 1993; Özkaynak et al. 2005; Rice et al. 2003; U.S. EPA 1998; U.S. EPA 2001b; U.S. EPA 2005d).

### 7.2.1. Budget and Logistical Planning

Availability of resources is an important consideration in planning an observational human exposure measurement study. Available resources, participant burden, types of sampling methods and specificity of the measurements that need to be collected strongly influence the number of participants and the types of samples collected and analyzed. Sufficient resources need to be available to obtain sample sizes sufficient to meet the study objectives. At some point, the researchers might need to consider how to balance data needs against limited resources. Achieving such a balance could entail reducing the number of study participants, eliminating selected analytical procedures or modifying other study elements. When altering the study plan

[13]Federal Insecticide, Fungicide, and Rodenticide Act, 7 U.S.C. ch. 6 § 136 et seq.
[14]Federal Food, Drug and Cosmetic Act, 21 U.S.C. ch. 9 § 301 et seq.

to meet resource constraints, the researchers weigh whether the modified study plan is likely to provide the quality of information necessary to meet the study objectives against other options for filling data or informational needs.

Planning also needs to consider burdens to both the participants and field technicians. Field studies typically are complex and might require many field staff and extensive travel. Logistical planning is essential for conducting the study within a specified period and using available resources most efficiently.

### 7.2.2. Identifying Critical Data Elements

For each specific study objective, hypothesis or scientific question, the critical data elements are those pieces of information that need to be collected to achieve the objective, test the hypothesis or to answer the question. For example, a study objective might be to determine the associations between concentrations measured at central site monitors and outdoor residential, indoor residential and personal exposures for selected air toxics, particulate matter (PM) constituents and PM from specific sources. To achieve this objective, the following measurements are required: personal, indoor, outdoor and central site measurements for fine PM (2.5 μm in diameter and smaller); coarse PM (diameter larger than 2.5 μm and smaller than 10 μm); air toxics; and other pollutant variables. These measurements need to be stratified by site, season, housing stock, geographic location and primary source (U.S. EPA 2011a). In addition, models also might be used for identifying critical data elements and testing hypotheses.

### 7.2.3. Determining Sample Size for Each Data Element

The sample size needed to address the study objectives, hypotheses or scientific questions is determined statistically based on the desired outcome. Estimations of sample size (i.e., power calculations) are necessary to ensure the probability of missing an important difference is small and to reduce unnecessary cost and waste (Devane et al. 2004). The number of participants enrolled in a study and the frequency of sample collection from participants often are a compromise between the available budget and the statistical power the study can achieve (Dupont and Plummer Jr. 1990; Kulldorff et al. 2004; Woodward 1999).

Estimating effect size helps determine the appropriate sample size for a study. Effect size is a measure of the differences between or within populations used to assess whether the differences are statistically significant. If the effect size is large (e.g., the difference in average fish consumption between recreational anglers and the general population), the differences are easier to establish, and identifying statistically significant results would require a smaller study population. Conversely, if the effect size is small (e.g., the difference in fish consumption between men and women in the general population), establishing the differences is more difficult, and identifying statistically significant results would require a larger study population. If the true effect size were known already, variable parameters (e.g., average fish consumption) would be known and a study would be unnecessary. Data from a pilot study could help determine the predicted effect size (Devane et al. 2004).

The variability within the defined population also needs consideration when determining sample size. Much information is available in the peer-reviewed literature on sample size estimations for studies (Baguley 2004; Dell et al. 2002; Devane et al. 2004; Dupont and Plummer Jr. 1990;

Dupont and Plummer Jr. 1998; Kampman et al. 2003; Kieser et al. 2004; Kraemer et al. 2006; Rippin 2001; Salganik 2006; Vaeth and Skovlund 2004).

### 7.2.4. Developing Criteria and Identifying Potential Study Locations

Study location is an integral part of the technical study design and needs to be based on the study objectives, hypotheses or scientific questions. Criteria can include the location of the population group of interest, geographic or built environment considerations, the size of the cohort and the time of year for the study. For example, a study objective to determine exposures to vehicle exhaust in an urban area requires selection of a study location in an urban environment.

### 7.2.5. Developing Eligibility Criteria for Study Participants

Eligibility criteria also are essential to the technical study design. Eligibility criteria determine the type of person selected for an observational human exposure measurement study based on the study objectives, hypotheses or scientific questions. For example, an observational human exposure measurement study seeking to understand the variety of fruits and vegetables consumed by the older adult population in the United States would have very different eligibility criteria from an observational human exposure measurement study evaluating exposure to vehicle exhaust associated with bicycle use as a means of transportation in urban areas. Some studies might be designed to sample a representative portion of some larger population (i.e., random or probability sampling). Other studies might select participants based on particular activities or other lifestyle characteristics (i.e., convenience sampling). More information on scientific and ethical approaches for observational human exposure measurement studies can be found at the EPA *Scientific and Ethical Approaches for Observational Exposure Studies* website. Information also is available in the peer-reviewed literature on design issues for these types of studies (Adgate et al. 2000; Buck et al. 1995; Callahan et al. 1995; Lebowitz et al. 1995; Marshall 1996; Pellizzari et al. 1995; Quackenboss et al. 2000; Vojta et al. 2002; Whitmore et al. 2005).

### 7.2.6. Developing Data Quality Objectives and Identifying Sampling and Analysis Methods

After the exposure assessor establishes the data quality criteria (see Section 5.3), the assessor identifies methods available to meet these criteria. Observational human exposure measurement studies need to follow sampling and analytical protocols that are sufficiently accurate, precise and sensitive to meet the study objectives, test the hypotheses or answer the scientific questions. Selected analytical and sample collection methods will have demonstrated and acceptable performance parameters. Many standard operating procedures (SOPs) are publicly available in various Agency databases. If existing or adequate methods are not available, study implementation could depend on additional method development and testing. If method development is required, an assessor determines acceptable performance parameters and evaluation criteria before deeming an analytical or sample collection method ready for implementation.

Sample collection methods are tested and evaluated in small-scale pilot studies either in the laboratory or in the field. Evaluating the sample collection methods in a pilot study prior to full study implementation provides an opportunity for an assessor to ensure that the sampling methods will be accurate, precise and sensitive and to reevaluate modifications, if necessary. Evaluation of analytical protocols uses reference standards or previously analyzed samples, if

available. A comparison of the known results from a reference standard or previously analyzed sample with the results of the analytical protocol can help determine the likelihood of success when following the protocol.

## 7.2.7. Developing Chain-of-Custody, Storage and Data Management Procedures

Chain-of-custody forms, storage of materials associated with a study and data management procedures are all associated with the quality assurance (QA) project plan (U.S. EPA 2001c; U.S. EPA 2012a). In combination, these procedures accurately track the movement of samples before, during and after analyzing, storing and transferring the results.

Chain-of-custody forms (e.g., paper or electronic format) document all collection, shipment, receipt, analysis, processing and handling steps that a sample undergoes. A chain-of-custody record, initiated in the field, captures the field collection information for the sample and all subsequent actions performed. EPA provides the *Air Pollution Training Institute* website for training on chain-of-custody procedures for samples and data.

Proper sample storage procedures ensure adequate and appropriate storage space for samples (e.g., freezer, ultra-cold freezer, laboratory space). Storage procedures need to ensure minimal analyte loss, contamination or degradation during shipment and minimize holding times prior to analysis. Adequate storage space also might be required for paper forms collected during a study. Ideally, sample and record storage is secure, with access limited to authorized personnel.

Researchers establish data management procedures to process data effectively so that relevant data descriptions (e.g., sample numbers, locations, procedures, methods) are readily accessible and accurately maintained (U.S. EPA 2003a). EPA's Forum on Environmental Measurements maintains a website with information relevant to the data management process. Section 7.2.13 contains more information on the data analysis plan and database design. Section 5.6 provided additional guidance on data management.

## 7.2.8. Engaging the Community

Community involvement is the process of engaging in dialogue and collaborating with members of the community where the study will take place. Researchers need to define the community for a particular study clearly and consider the extent of the community involvement for the study. Involving the community is one way to increase respect for the study participants and to shape research that addresses the needs and priorities of the community (NRC and IOM 2005; U.S. EPA 2008c). Community involvement is founded on the belief that people need to know what the Agency is doing in their community and be able to have input into the decision making process (U.S. EPA 2001i). Information and suggestions regarding community involvement in the Superfund process (U.S. EPA 2016e) might be generally applicable to community involvement in observational human exposure measurement studies. EPA's *Superfund Community Involvement Handbook* (U.S. EPA 2016e) provides specific information.

Involving a community offers many advantages. Community representatives bring perspective, value and competence to a research project. Community representatives also provide a study with knowledge of community concerns, needs, values and priorities; a history of activism, leadership and coalition building; and a network of community contacts (NRC and IOM 2005).

Community leaders can help researchers increase acceptance of the study in their community, ensure that data collection instruments are culturally appropriate, promote enrollment and increase retention in the study (NRC and IOM 2005). *Ethical Considerations for Research on Housing-Related Health Hazards Involving Children* (NRC and IOM 2005) presents more details on the importance of community involvement.

Community-based participatory research is an approach in which community members are active partners in all aspects of the study, from the formulation of research questions to the application of findings. Community members use their knowledge and experience in the community to help specify the issues for study, develop research questions that are culturally sensitive and apply study results to help support relevant program and policy development (NRC and IOM 2005). Community residents can be involved in the research process as participants, parents of participants, research staff, community consultants, reviewers or members of community advisory boards (Hough et al. 2006; NRC and IOM 2005; U.S. EPA 2008c; Williamson et al. 2005). Making community involvement a priority helps ensure the research addresses the concerns, needs and priorities of the community and leads to actions and changes that benefit the community.

Communication between the research staff and the community is key. The research staff needs to have a clear understanding of the type of community involvement needed for the particular study they have proposed and clearly communicate with the community about the benefits of the study. Although communication with the community is important, it also can be challenging. Many investigators have published articles on developing and implementing an effective communication plan (Brauer et al. 2004; Deck and Kosatsky 1999; White et al. 2004; Williamson et al. 2005). Section 3.1.3 discussed community involvement in the planning and scoping phase of an exposure assessment.

## 7.2.9. Engaging Stakeholders

Engaging other stakeholders in addition to community members is necessary when planning an observational human exposure measurement study. A stakeholder is defined as anyone who has a stake in the study but is not directly involved in it. Examples of stakeholders include community residents not involved in the research, community groups, advocacy groups, interested members of the public, medical organizations, university partnerships, industry groups, nonprofit organizations, nongovernment and government organizations, states, tribes and the media. The researchers and the community jointly decide which stakeholders to invite as participants in the planning process. Beierle (2002) reported that including stakeholder points of view can improve decisions. Determining which stakeholders to engage in planning an observational human exposure measurement study depends on the objectives, hypotheses or scientific questions of the research study and the persons recruited to participate. Stakeholders engaged in planning one observational human exposure measurement study might not be the same as those engaged in planning another. The Agency's *Stakeholder Involvement & Public Participation at the U.S. EPA: Lessons Learned, Barriers, & Innovative Approaches* reviews how EPA handles stakeholder involvement and public participation (U.S. EPA 2001i).

During the planning of an observational human exposure measurement study, meetings take place between the researchers and community members and other stakeholders. These meetings gather input from the stakeholders and explain the purpose and approach of the study.

Researchers send study announcements sufficiently ahead of planning an observational human exposure measurement study so that the stakeholders can prepare and actively participate. In addition, the schedule for developing the technical study design allows ample opportunity for stakeholder participation. Factoring time into the schedule to allow for public/stakeholder participation is essential for the success of an observational human exposure measurement study. EPA's *Environmental Justice* website presents information on incorporating stakeholders in the research planning process.

## 7.2.10. Human Subjects Considerations

EPA has a history of conducting observational human exposure measurement studies to assess the contact that people have with agents while completing routine activities in their homes and work environments. Observational human exposure measurement studies often provide the strongest data available to support regulatory action. Such studies can be complex in their design and implementation, addressing many scientific and ethical considerations. In conducting these studies, all scientists (regardless of affiliation) should endeavor to apply the most current scientifically valid approaches, while recognizing the special responsibilities regarding the ethical issues that sometimes arise when conducting these studies.

EPA's document, *Scientific and Ethical Approaches for Observational Exposure Studies* (U.S. EPA 2008c), provides a template for EPA scientists to conduct scientifically valid observational human exposure measurement studies, while addressing personal concerns and ethical issues. The document, developed with guidance and input from experts outside the Agency, addresses such issues as ensuring the protection of vulnerable groups, protecting the privacy of participants, maintaining confidentiality, ensuring fair and equitable participant selection, obtaining informed consent, involving the community and designing strategies for effective communication. EPA's advisory committee, the Human Studies Review Board, reviewed the document. Implementing the approaches the document outlines ensures that scientists conduct observational human exposure measurement studies with attention to the concerns of the participants. The document contains more information on the history of human subjects research [see Section 1.2 in (U.S. EPA 2008c)], as do numerous peer-reviewed publications (Emanuel et al. 2008; Emanuel and Menikoff 2011; Moreno and Sisti 2015; Ndebele 2013; Presidential Commission for the Study of Bioethical Issues 2011a; Presidential Commission for the Study of Bioethical Issues 2011b; Resnik 2012; Reverby 2009; Wertheimer 2011).

In addition to complying with 40 CFR Part 26 for studies involving human subjects, the appropriate Institutional Review Board (IRB) needs to approve the study protocol and all associated documentation. As EPA Policy Order 1000.17 Change A1 directs, approval normally involves an IRB from each participating organization and final approval by HSRRO, located in the EPA Office of the Science Advisor. The HSRRO is responsible for reviewing and approving human subjects research at EPA before the recruitment of participants into a study. The *Office of the Science Advisor* website provides more information on this process. Additional information on human subjects research and IRBs is available on the U.S. Department of Health and Human Services' *Office for Human Research Protections* website and on the National Institutes of Health's *Bioethics Information Resources* website. When the number of participants in an observational human exposure measurement study is 10 or greater, Office of Management and Budget (OMB) review also is required. More information on the OMB process is available on the HHS *Office of the Chief Information Officer* website.

Effective recruitment is essential to the success of a study. Recruitment methods vary, depending on the study design and the targeted participants, especially when English is not the primary language of the participants. In representative, population-based sample designs, conducting in-person or telephone recruitment for all selected households or individuals might be necessary. For study designs that are not population based, recruitment methods include but are not limited to advertisements in newspapers or magazines, advertisements on radio or television, word-of-mouth, social media, endorsements from community leaders and message boards at grocery stores, religious establishments or community centers (U.S. EPA 2008c). Recruitment plans and materials are subject to IRB and HSRRO review and approval. Recruitment is most effective when community leaders are engaged in the recruitment process (NRC and IOM 2005). Many published papers discuss the recruitment process (Cabral et al. 2003; Sexton et al. 2003).

In addition, researchers need to obtain informed consent before a person can participate in a research study. The appropriate IRBs need to approve the informed consent documents and process prior to their use in the field. In studies where children old enough to have some understanding of the study are the participants, researchers need to obtain their assent in addition to the consent of their parents or guardians. The age at which a child can provide assent to participate in a research study varies on a case-by-case basis and the study principal investigator is advised to consult the IRB and HSRRO. Many peer-reviewed publications address the challenges associated with informed consent (Crowhurst and Dobson 1993; IOM 2004; Mammel and Kaplan 1995; Miller et al. 2004; Wendler 2006; Wendler and Shah 2003; Whittle et al. 2004).

Confidentiality and privacy also are key considerations in studies involving human subjects. The Privacy Act of 1974,[15] the E-Government Act of 2002,[16] the Federal Information Security Management Act,[17] the Health Insurance Portability and Accountability Act (2003 Privacy Act)[18] and OMB policy and guidance outline restrictions and requirements associated with using personally identifiable information. EPA developed the Agency's *Privacy Policy* (U.S. EPA 2005a) to ensure compliance and outline Agency requirements for safeguarding the collection, access, use, dissemination and storage of personally identifiable information. The Agency's *Privacy Policy* defines personally identifiable information as "any information about an individual maintained by an agency, which can be used to distinguish, trace, or identify an individual's identity, including personal information which is linked or linkable to an individual" (U.S. EPA 2005a). As such, researchers must safeguard data collected during an observational human exposure measurement study and linked or linkable to an individual. More information and resources are available at the *EPA Policy 2151.0: Privacy Policy* website.

Determining appropriate compensation or incentives for participants in a research study can be complex. Compensation or incentives can include offering to pay people for their time and effort for participating in a study, but little guidance exists regarding an appropriate level of compensation (U.S. EPA 2008c). Compensation or incentives can take various forms, including monetary payments (e.g., cash, gift certificates), nonmonetary payments (e.g., gifts, valuable information, study-related services), reimbursement for expenses associated with participating in

[15]Privacy Act of 1974, 5 U.S.C. ch. 5 § 552a.
[16]E-Government Act of 2002, 44 U.S.C. ch. 36 § 3601 et seq. 44 U.S.C. ch. 35, subch. III § 3541 et seq.
[17]Federal Information Security Management Act, 44 U.S.C. ch. 35, subch. III § 3541 et seq.
[18]Health Insurance Portability and Accountability Act, Pub.L. 104–191.

the study (e.g., mileage, parking) or nothing (i.e., altruistic approach). Compensation and incentives for participants are subject to IRB and HSRRO review and approval. Numerous research articles address the issues associated with compensating research participants (Ackerman 1989; Dickert et al. 2002; Erlen et al. 1999; Fry et al. 2005; Grady et al. 2005; Iltis et al. 2006; NRC and IOM 2005; Russell et al. 2000; VanderWalde 2005; Weise et al. 2002).

### 7.2.11. Samples To Be Collected—Environmental, Biological, Personal, Exposure Factors and Questionnaires

Researchers collect environmental, biological, personal and exposure factor data and questionnaire information to understand potential exposures. They select environmental samples that account for exposure through the relevant routes and pathways based on the study objectives, hypotheses or scientific questions. In some cases (e.g., pesticides), measuring all relevant media is important, including air, water, food, dust and soil. In other cases, measuring different types of analytes in one medium might be important (e.g., PM and other criteria pollutants in air). The method needs to capture the appropriate timeframes of interest, be sufficiently sensitive and be specific for the analytes of interest at anticipated or potential exposure levels. Field data collection sheets are used to document supporting information about each sample collected (e.g., temperature, humidity, time of day, day of week, sample collection location).

In addition to environmental samples, collecting biological, personal, exposure factor data and questionnaire information also might be necessary. Personal samples directly relate to the individual participant, resulting in an individualized sample. For example, a personal air monitor collects an air sample from a participant's breathing zone. A duplicate diet sample is a personal sample that collects an exact copy of all foods and beverages the participant consumes. Exposure factor information includes information on contact rates and time-activity information. Time-activity information captures all locations where the participant has spent time and all activities in which the participant has engaged during the period of interest that could account for exposures. Researchers should be cautious to ensure they do not influence participant behavior during sample collection (e.g., additional cleaning of house, eating foods different from usual diet). Table 5-6 presented a discussion of EPA's Consolidated Human Activity Database and other data sources. Measurements on biological samples determine the absorbed dose of the chemical of interest. Sections 5.1.2, 5.4.2 and 6.2.5 provide more discussion of the uses and limitations of biomonitoring.

Questionnaires collect information on parameters that researchers cannot measure any other way, such as household demographic information or occupation (see Section 5.4.4). The *Draft Protocol for Measuring Children's Non-Occupational Exposure to Pesticides by All Relevant Pathways* (U.S. EPA 2001b) describes methods and approaches for estimating exposure. This protocol document is helpful for identifying the environmental, biological and personal samples; activity pattern data; and questionnaires needed for an observational human exposure measurement study. Two other frameworks that might be useful tools for developing the technical study design for an observational human exposure measurement study include EPA's National Center for Environmental Assessment's *A Framework for Assessing Health Risk of Environmental Exposures to Children* (U.S. EPA 2006d) and the International Life Sciences Institute's framework for children's risk assessment (Olin and Sonawane 2003).

## 7.2.12. Sampling Scheme

Researchers develop the sampling scheme after identifying the study objectives, hypotheses or scientific questions, writing the technical study design and specifying the types of samples to collect. The sampling scheme systematically details the samples to collect in the field and usually includes the time, location and any other sample collection logistics (such as sample collection order and preservation methods). The sampling scheme might include information for both field samples and QC samples (see Section 5.3.2). The QC samples normally collected in a field study include field blanks, field controls and duplicates. Field blanks are prepared in the field to assess sample contamination from materials and handling methods. Field controls are prepared in the laboratory, taken to the field, returned to the laboratory and analyzed to assess potential losses of target compounds resulting from materials and handling methods. Duplicate samples serve to assess collection and analytical precision. The QA project plan contains the details on the QA associated with the field study, including the QC samples and procedures for assessing the accuracy and precision of the sample collection and laboratory analysis. General information on the QA project plan can be found on EPA's website; Section 5.3.2 presented more details about these requirements).

## 7.2.13. Data Analysis Plan and Database Design

The data analysis plan describes how researchers analyze the collected data to address the objectives, hypotheses or scientific questions of the research study. The data analysis plan includes the objectives, hypotheses or scientific questions; the data relevant for evaluating each objective, hypothesis or scientific question; and the statistical analyses that will be performed on the data. Researchers write the data analysis plan in conjunction with the technical study design and sampling scheme. They also use the plan to design the database to house the sampling information, raw data and analysis results. Overall, details about the data requirements needed to address the objectives, hypotheses or scientific questions are essential to data analysis and necessitate comprehensive documentation.

The database houses the measurement data and all supporting documentation associated with sample collection and analysis. Its development is a critical component of the study, completed as part of the planning and scoping process (see Section 3.1). The Agency provides general guidance on designing, implementing and using databases (U.S. EPA 2018c; U.S. EPA 2018d), but in general, a database is specifically designed for each study with the help and guidance of the study's database manager. EPA's *Developer Central, Data* website and EPA's *Forum on Environmental Measurements, Collection of Methods* website include Agency guidance.

To be an effective source of information, the database needs to be relational and searchable, with sufficient documentation to identify samples, corresponding measurements and any annotations associated with sample collection and analysis. Other database requirements depend on the type of data the database will include and the purpose of the database. Little published information exists in the peer-reviewed literature on relevant database design elements; however, a handful of papers suggests the need for well-organized databases (Detenbeck et al. 2005; Mills et al. 2001; Sexton et al. 1994; Van Dyke et al. 2001).

Usually, researchers test the database design with the data generated during the pilot study (described in Section 7.3). Testing the database before the full field study is imperative because making design changes before attempting to populate the database with numerous data points is

easier than making changes to a populated database. Testing the database with the pilot study data also ensures that the database is designed to meet the study specifications (e.g., relational, searchable).

## 7.3. Planning and Executing a Pilot Study

In preparing for an observational human exposure measurement study, planning and executing a pilot study are crucial. A pilot study is subject to the same requirements for obtaining informed consent, and IRB and HSRRO review and approval, as the full field study. The purpose of the pilot study is to evaluate all methods selected for use in the field study, including the recruitment strategy, field collection and analytical methods. Typically, the pilot study includes only a few participants and serves to evaluate the field readiness of the research personnel. The results and lessons learned from the pilot study also identify needed changes in the implementation plan before the full field study starts. Researchers address any special concerns or issues raised during the pilot study so that they do not affect the full field study. Conducting a pilot study improves the chances for success of the field study. For example, the research team conducted multiple pilot studies before implementing the Total Exposure Assessment Methodology Study (U.S. EPA 1987b), and pilot studies preceded the National Children's Study, as described at the *National Children's Study* website.

### 7.3.1. Community and Stakeholder Involvement in the Pilot Study

Once the researchers engage the community and stakeholders in planning, they define their roles and responsibilities in the pilot study. Examples of roles and responsibilities include serving as a consultant in planning the study, contributing to the communication plan, reviewing the pilot study results and providing resources.

Implementing the communication plan (see Section 7.3.3) is a critical component of the pilot study. Research staff, the community and other stakeholders planning the design of an observational human exposure measurement study collaboratively develop the communication plan. The communication plan includes the opportunity for a debriefing after the pilot study is completed. A debriefing provides all members of the field study team (e.g., research staff, community members, other stakeholders) an opportunity to give direct feedback about their experiences with the pilot study, including an in-depth view of what went well and any needed changes. A debriefing with the community, other stakeholders and research staff identifies the lessons learned and offers details needed for the implementation plan for the full study.

### 7.3.2. Implementation Plan for the Full Study

The study design delineates the study components and the implementation plan. The implementation plan describes the study execution and contains all the details for conducting a full observational human exposure measurement study successfully. The pilot study provides the necessary information for refining both documents prior to the full study.

### 7.3.3. Communication Considerations

A communication plan is essential for successfully disseminating information about the pilot study and the full study. As with communication in other exposure-related activities, the study organizers need to involve the communication staff early in the planning process (see

Section 3.1.3 and Chapter 9). The communication plan details what information to exchange, with whom and in what format. For example, the communication plan addresses the timely reporting of results to the study participants. Numerous references discuss the importance of reporting results to the study participants and the usefulness of communicating with research participants in the format they specify (Ackerman and Proffit 1995; Brauer et al. 2004; Collins et al. 2004; Covello 1989; Herrier and Boyce 1995; Hoffrage et al. 2000; Kasperson 1986; Keeney and von Winterfeldt 1986; Parkin 2004; Payne-Sturges et al. 2004; Quandt et al. 2004; Schulte and Singal 1989; Sharlin 1986; Slovic 1986).

The communication plan also specifies how research staff will discuss information with the community, the media, public health officials, members of the scientific community and other stakeholders, as they deem appropriate. Researchers need to consult the community and stakeholders about what information they would like to receive and in what format.

Chapter 9 provides guidance on developing a comprehensive communication plan for exposure assessments, including how to present data and results effectively.

## 7.4. Planning and Executing a Full Field Study

All components of the pilot study discussed in this chapter help in planning and executing the full field study. Each component, as refined based on pilot study findings, is necessary for the full field study:

- The study goals and objectives, and the data quality objectives, sampling needs, data management guidelines, location and participant criteria and human subjects considerations and needs, are detailed in the study design
- Data quality and data deliverables for the full field study are specified in the technical study design and implementation plan
- Sampling and analysis methods are outlined in the method protocols and SOPs
- QA/QC issues are specified in detail in the QA project plan (see Section 5.3.2)
- A relational database is used to organize the collected data (multimedia samples and questionnaire information) for analysis
- The data analysis plan specifies the analyses of the collected data in relation to the study objectives, hypotheses or scientific questions
- The communication plan—developed by the project team, community members and other stakeholders—specifies what data to convey, to whom and in what format.

## 7.5. Peer Review and Completion of the Final Report

Peer review is an integral component of the design, implementation and completion of an observational human exposure measurement study. The peer-review process ensures the data generated and information disseminated about the study meet the highest quality and ethical standards (U.S. EPA 1998; U.S. EPA 2000b; U.S. EPA 2015c). Any documents associated with the study are subject to peer review, but only the study design and final documents, such as reports and journal articles, typically are peer reviewed. EPA's *Peer Review Handbook, 4th*

*Edition* (U.S. EPA 2015c) provides a comprehensive guide for organizing and conducting peer reviews in accordance with EPA's updated peer review and peer involvement policy statement.

## 7.6. Summary

- **Observational human exposure measurement studies** enable exposure scientists and risk assessors to identify agents to which people are exposed; exposure concentrations; important sources, routes and pathways of exposure; and factors having the greatest influence on exposure. The studies can help evaluate and refine exposure and dose models.
- An adequately developed technical **study design** addresses all parts of a study. It might include planning that considers budget and logistics; data elements; sample size; criteria for selecting study location; eligibility criteria for study participants; data quality objectives; chain-of-custody, storage and data management; community and stakeholder involvement; human subjects guidelines; informed consent; recruitment; sample collection; sampling schemes; and data analysis and database design.
- **Planning and executing a pilot study** can be crucial when preparing for an observational human exposure measurement study. A well-executed pilot study that **involves communities and stakeholders**, communicates the **full study implementation plan** and articulates a carefully considered **communication plan** for successfully disseminating information about the pilot study and the full study greatly increases the odds of successful completion of the full study.
- **Peer review** is integral throughout the design, implementation and completion of an observational human exposure measurement study.

# CHAPTER 8. UNCERTAINTY AND VARIABILITY FOR EXPOSURE ASSESSMENTS

Distinguishing between the uncertainty and variability in the data and the uncertainty in the decisions is critical when conducting an exposure assessment and communicating its results. Data uncertainty refers to incomplete or incorrect information. Variability refers to true differences in attributes stemming from heterogeneity or diversity in an individual or population. Decision uncertainty includes all uncertainties due to the data and to other choices that affect the exposure assessment or influence the decisions made. Data uncertainty and variability are components of decision uncertainty (NRC 2009).

Evaluating uncertainty and variability is essential for developing a robust exposure assessment that provides information risk managers/decision makers need. Such evaluations can range from using simple screening methods to conducting complex statistical analyses. The information from these evaluations can inform decisions to reduce uncertainties in an exposure assessment further.

Effectively communicating the uncertainties in an exposure assessment is a challenging but critical part of any exposure assessment. Ensuring that stakeholders understand the various uncertainties and the compounded effects of the uncertainties on the results and the decisions made facilitates communication between groups.

To help an assessor evaluate uncertainties and their effects on an exposure assessment, this chapter:

- Defines data uncertainty and variability, describes their differences and distinguishes them from decision uncertainty (Section 8.1)
- Outlines the basic considerations that influence an uncertainty and variability evaluation (Section 8.2)
- Describes a process for conducting such an evaluation using a tiered approach (Section 8.3)
- Introduces considerations for effectively communicating information about uncertainty and variability to risk managers/decision makers and stakeholders (Section 8.4).

Section 8.5 summarizes this chapter.

EPA consistently has acknowledged the need to characterize uncertainty in exposure and risk estimates. This history is described in more detail in National Research Council (NRC) and EPA documents (Executive Order No. 13045 1997; Hansen 1997a; NRC 1983; NRC 1989a; NRC 1994; NRC 1996; U.S. EPA 1986a; U.S. EPA 1986b; U.S. EPA 1986c; U.S. EPA 1986d; U.S. EPA 1986e; U.S. EPA 1992c; U.S. EPA 1995a; U.S. EPA 1996e; U.S. EPA 1997a; U.S. EPA 2001h; U.S. EPA 2004c; U.S. EPA 2011g; U.S. EPA 2014i; U.S. EPA 2019d). In addition, the World Health Organization's International Programme on Chemical Safety developed guidance for characterizing and communicating uncertainty in exposure assessment and has emphasized the importance of addressing both data and decision uncertainty in its 10 guiding principles for an uncertainty evaluation (WHO 2008). These documents focus on reducing and characterizing

data uncertainties, while the emphasis of the 2013 Institute of Medicine report, *Environmental Decisions in the Face of Uncertainty* (IOM 2013), addresses the need to understand and characterize uncertainties that derive from the many other components of an environmental assessment. Such components include those pertaining to subjective judgments and choices about how risks are calculated and expressed.

This chapter discusses uncertainty and variability concerns associated with the entire exposure assessment. Chapter 5 briefly described uncertainty and variability concerns associated with the datasets used in an exposure assessment. Chapter 6 briefly described uncertainty and variability concerns associated with models. Other chapters mention uncertainty and variability specific to the topic of discussion.

# 8.1. Terminology

Many types of uncertainty exist. Sections 8.1.1, 8.1.2 and 8.1.3 discuss data uncertainty, decision uncertainty and variability, respectively, in detail. Box 8-1 lists uncertainty and variability terminology relevant to this document. Table 8-1 elaborates on the errors that can result from these types of uncertainty.

## 8.1.1. Data Uncertainty

EPA defines data uncertainty as "a lack of precise knowledge as to what the truth is, whether qualitative or quantitative" (U.S. EPA 2004c). Using more complete or "better" data in an exposure assessment often reduces data uncertainty. Uncertainty analysis is the process of identifying the sources of data uncertainty in an assessment and the magnitude and direction of the resulting error (WHO 2004). Uncertainty analyses range from qualitative discussions of the uncertainty to analyses that use quantitative techniques, such as probabilistic analysis, to describe uncertainty by presenting a range of possible exposures and risks.

## 8.1.2. Decision Uncertainty

Regardless of whether an exposure assessor can reduce data uncertainty, decision uncertainty remains for risk managers/decision makers. Data uncertainty is a scientific problem; decision uncertainty involves both the uncertainties of the scientific problem and the uncertainties involved when risk managers/decision makers choose how to formulate and execute the exposure assessment. When combining multiple pieces of data to produce a single exposure assessment or choosing appropriate alternatives among decision options, the decision maker/risk manager wants to understand the compounded effect of all pieces of data. The compounded effect can result from (1) how the assessor formulated the problem, (2) the expert and stakeholder contributions to problem formulation and (3) the extent to which expert and stakeholder input could change the assessment result. In decision uncertainty, the risk manager/decision maker seeks to know, "How sensitive is a particular change (in data values or modeled result, problem scoping/formulation, stakeholder values, expert judgments) to the outcome?"

**Box 8-1. Terminology**

- Data uncertainty
  - A component of decision uncertainty describing how well the data used in the assessment are understood. Data uncertainty can lead to inaccurate or biased estimates of exposure. Additional information can reduce uncertainty and increase the accuracy of exposure estimates. A perfect model producing perfect results is an example of zero uncertainty.
- Decision uncertainty
  - Compounded effect of total uncertainty and variability on the exposure assessment. Total uncertainty includes those uncertainties pertaining to the data and models used, uncertainties regarding how to formulate the problem, selection of data/model inputs and outputs, etc. It includes the extent to which experts agree about how to use those data to describe the exposure assessment problem (e.g., uncertainty about the values/judgments used to reach the exposure assessment conclusions). Risk managers/decision makers cannot always reduce decision uncertainty, but they can work to understand the decision context better and determine the robustness of choosing one alternative over another.
- Expert elicitation
  - A process that gathers input from experts to characterize uncertainty and fill data gaps when traditional scientific research is not feasible or data are not available.
- Exposure scenario uncertainty
  - Uncertainty in an exposure assessment occurs when the information regarding the exposure scenario is limited or inadequate. For example, using an exposure assessment that relies on information from a study conducted in the southwestern United States to evaluate activity patterns in New England can introduce uncertainty. WHO (2008) defines scenario uncertainty as the "uncertainty in specifying [an] exposure scenario that is consistent with the scope and purpose of the assessment."
- Monte Carlo analysis
  - A probabilistic technique used in exposure assessment that provides a probability function of an estimated exposure using repeated random sampling from probability distributions for input parameters.
- Observational or model uncertainty
  - Gaps in the scientific theory required to make predictions based on causal inferences result in observational or model uncertainty. Model uncertainty is unavoidable and difficult to quantify because modeling relies on mathematical or statistical formulas to capture complex processes (e.g., chemical releases, environmental fate and transport, biological activity).
- Probabilistic exposure assessment
  - A range of techniques (e.g., Monte Carlo analysis, Latin hypercube) that rely on statistical distributions of input data in place of point values for key parameters resulting in a distribution of possible exposure estimates and greater ability to characterize variability and uncertainty.
- Sampling or measurement uncertainty
  - Uncertainty in sampling or measurement data is associated with data collection or analysis methods. Systematic sampling error, sample location, sample number and analysis methods are sources of sampling uncertainty. Sampling methods and analyses are unlikely to produce the same reading every time, even when measuring the same sample, which adds to the overall uncertainty of an exposure assessment. Using surrogate data to represent an exposure or using data not representative of the exposures also introduces sampling uncertainty. Other organizations use the term "parameter uncertainty" for this type of uncertainty (WHO 2008).
- Sensitivity analysis
  - An analysis conducted on a multivariate model to understand the degree to which a result changes due to uncertainty or variability. In a sensitivity analysis, the analyst changes one variable while holding the others constant to determine that variable's effect on the result. This procedure compares exposure results when varying a parameter's input values between, for example, its credible lower and upper bounds (holding all others at their nominal values, such as medians). The results help identify the variables having the greatest effect on exposure estimates and help focus further information-gathering efforts.
- Variability
  - Real differences in data, even when knowledge is complete, for example, the heterogeneity in daily water consumption by an individual or population, which varies based on age, residence and activity patterns. Variability can be understood more completely—but not reduced—with additional information.

Source: U.S. EPA (2009b); U.S. EPA (2017c)

**Table 8-1. Types of Uncertainty and Contributing Errors**

| Type of Uncertainty | Type of Error Causing Uncertainty | Description or Example |
|---|---|---|
| Exposure scenario | Misclassification | Failure to identify exposure routes, exposure media and exposed populations adequately |
| Sampling or measurement (Parameter uncertainty) | Measurement, random | Random errors in analytical devices (e.g., imprecision of continuous monitors that measure stack emissions) |
| | Measurement, systemic | Systemic bias (e.g., estimating inhalation from indoor ambient air without considering the effect of volatilization of contaminants from hot water during showers) |
| | Surrogate data | Alternative data used for a parameter instead of direct analysis of exposure (e.g., using number of people as a surrogate for population exposure) |
| | Misclassification | Incorrect assignment of exposures of subjects in historical epidemiological studies resulting from faulty or ambiguous information |
| | Random sampling error | Result of using a small sample of individuals to estimate risk to a larger population |
| | Nonrepresentativeness | Result of developing exposure estimates for a population in a rural area based on exposure estimates for a population in a city |
| Observational or model | Relationship errors | Result of incorrectly inferring the basis of correlations between environmental concentrations and urinary output |
| | Oversimplification | Misrepresentations of reality (e.g., representing a three-dimensional aquifer with a two-dimensional mathematical model) |
| | Incompleteness | Exclusion of one or more relevant variables (e.g., relating a biomarker of exposure measured in a biological matrix without considering the presence of the metabolite in the environment) |
| | Surrogate variables | Alternative variables used for variables that cannot be measured (e.g., wind speed at the nearest airport used as a proxy for wind speed at the facility site) |
| | Failure to account for correlations | Not accounting for correlations that cause seemingly unrelated events to occur more frequently than expected by chance (e.g., two separate components of a nuclear plant are missing a particular washer because the same newly hired person assembled them) |
| | Model disaggregation | Extent of (dis)aggregation used in the model (e.g., separately considering subcutaneous and abdominal fat in the fat compartment of a physiologically based pharmacokinetic model) |

Source: U.S. EPA (2004c)

Decision uncertainty pertains to comprehending the decision context. Understanding the decision context includes deciding whether the analysis has been adequately characterized to answer the question(s) (e.g., Were the appropriate data used?) and understanding the relationships among the factors relevant to the decision options. To understand these relationships, two distinctions are essential. The first, which requires analytical expertise, is determining how significant those decision factors are to a specific exposure assessment. For example, an exposure assessor determines the relative significance of the route of exposure and the exposure concentration. The second distinction is determining the relative importance of those decision factors, which is the role of a risk manager/decision maker. Determining relative importance means explicitly and transparently expressing how to balance those factors. The relative importance of decision factors reflects the values of the risk manager/decision maker and the input of stakeholders and is determined by the risk manager/decision maker through a process that includes stakeholder input.

Table 8-2 provides information about how to consider and evaluate decision uncertainty. Note that although some of the risk management/decision making questions pertain to data (and hence, data uncertainty), the issue in addressing decision uncertainty is that of understanding the data (or data gaps) and other factors relative to the choice of decision options within the resource constraints of the decision.

**Table 8-2. Examples of Questions Asked to Examine Decision Uncertainty**

| Risk Management Questions and Issues | Questions/Approaches Responding to Risk Management Questions/Issues |
|---|---|
| Do the analytical design and current data answer the decision question? | Using a sensitivity analysis, discuss the decision/analytical question with risk managers/decision makers and stakeholders. |
| Will the decision be different if uncertainty is better characterized? | Conduct a sensitivity analysis to determine whether a change in data values could alter the risk manager's/decision maker's decision. |
| Are data gaps a problem for the decision? | How sensitive are the decision options to the data? That is, is the risk manager/decision maker able to make a decision with the currently available data? |
| Will using a different dataset be a problem? | If the data were different, would the risk management decision change significantly? |
| Does the risk manager/decision maker need to understand the current data more completely? | What is the relationship between the currently available data and the management decision options under consideration? For example, are the conditions expected to change significantly in the future? How does variability affect the decision options? |
| How is the relative acceptability of decision options influenced by the choice of data compared with how those data are combined and used? | With sensitivity analyses, use "what if" scenarios to experiment with different data and values (e.g., look at the ends of uncertainty bands) to examine the relative merits of the decision options. |
| Uncertainty matters: The risk manager/decision maker needs to reduce uncertainty to make a decision. | What are the key exposure parameters that need to be addressed in this analysis, and how will the additional data influence the decision? |

### 8.1.3. Variability Impacts on Uncertainty

EPA defines variability as the "inherent heterogeneity across space, in time, or among individuals. Variability cannot be reduced with additional investigation, only better understood or characterized" (U.S. EPA 2004c). In exposure assessment, variability embodies the range of possible outcomes representing an individual's or a population's exposures based on specific characteristics (e.g., age group, socioeconomic status) or activities (e.g., the amount of water or fish consumed on a daily basis, residence in particular geographic areas). Variability affects the precision of exposure estimates and the degree to which results are generalizable. The need to select a generalized result that has multiple sources of variability for an exposure assessment contributes additional uncertainty to the assessment. Types of variability encountered in exposure assessments include human, spatial and temporal variability. Variability adds another level of unavoidable complexity when addressing uncertainty in exposure assessments.

**Human variability** describes person-to-person differences in biological susceptibility or exposure (U.S. EPA 2004c). Human variability consists of intra- and interindividual variability. Intra-individual variability refers to the changes that occur in one person over time, which can be physiological (e.g., body weight, age) or behavioral (e.g., ingestion rates, activity patterns). Interindividual variability refers to the differences among individuals within a population (e.g., physiological or behavioral characteristics).

**Spatial variability and temporal variability** describe differences that occur in space and time, respectively. Spatial variability can occur at regional (i.e., macroscale) or local (i.e., microscale) levels; for example, the percentage of drinking water from groundwater compared with surface water sources varies from state to state and city to city. Temporal variability can occur over long or short periods. For example, a change in outdoor exercise can occur seasonally or even daily, depending on weather conditions (e.g., rain, snow, sun).

## 8.2. Considerations for Conducting an Uncertainty and Variability Evaluation

Conducting an evaluation of uncertainty and variability provides the assessor with an opportunity to evaluate the accuracy and effectiveness of the whole exposure assessment, as well as its individual components (e.g., conceptual models, modeling approaches). An uncertainty evaluation will not eliminate all uncertainty, but it will help an assessor address questions that arise about the results of the exposure assessment and its impact on risk management decisions. For example, an uncertainty and variability evaluation enables an assessor to determine how a risk management decision (e.g., requiring the removal of contaminated soil) could change potential exposures (e.g., eliminating exposure via direct contact with soil).

An uncertainty and variability evaluation can answer many questions that arise during an exposure assessment (e.g., What are the sources of uncertainty?) and can influence the methods selected for conducting the evaluation (e.g., Does one specific exposure scenario contribute substantially to the total exposure?). Section 8.2.1 discusses this consideration and provides examples of questions for an assessor to consider for each step of the exposure assessment: planning and scoping, implementation and presentation of results.

### 8.2.1. Planning and Scoping for Characterizing Uncertainty and Variability

As described in Section 3.1, the planning and scoping step of an exposure assessment involves determining the purpose, scope, approach, participants, level of effort and resources for the assessment. During this step, an assessor considers how to characterize uncertainty and variability for the assessment. Essential for this step, and throughout the exposure assessment process, are transparent and open discussions with stakeholders and risk managers/decision makers about the possible influence of assumptions, spatial and temporal scale (e.g., individual versus population, immediate versus future timelines) and other factors on the resulting exposure assessment. Stakeholders and risk managers/decision makers can use their understanding of decision uncertainty to determine when they believe the exposure assessment is adequate. U.S. EPA (2004c) provides a sample of questions to ask during planning and scoping to characterize uncertainty and variability. U.S. EPA (2004c) primarily addresses data uncertainty. This list of sample questions is applicable to both data uncertainty and decision uncertainty. We present the questions in groups as those likely directed to assessors, to managers and to both assessors and managers.

Questions directed to assessors might include:

- Who is being exposed (e.g., an individual, group or lifestage), and what are the routes of exposure?
- What are the major sources of uncertainty?
- What are the major sources of variability within the individual, lifestage, group, population?
- Have the weaknesses and strengths of the methods involved been identified?

Questions directed to managers might include:

- What time and resources are available for conducting an evaluation?
- What level of effort is warranted for this project?
- Are the essential skills (e.g., statistical expertise) and experience available to perform the analysis?
- What is the timeframe within which a decision is needed?

Questions appropriate for joint discussions between assessors and managers might include:

- Will a quantitative estimate of uncertainty improve the assessment or the decision? That is, will a quantitative estimate of uncertainty reduce decision uncertainty for the risk manager/decision maker and inform stakeholders?
- Will a quantitative estimate of the variability of a specific exposure parameter improve the assessment or the decision?
- How will the uncertainty and variability analyses affect the results of the exposure assessment or the regulatory decision?
- How will the uncertainty analysis be communicated to the risk managers/decision makers and stakeholders?

Communicating with risk managers/decision makers and stakeholders during the planning and scoping phase also can identify questions that might influence the uncertainty and variability evaluation and the outcome of the exposure assessment. Communication between an assessor and risk manager/decision maker (see Section 9.3.5) is critical for identifying potential areas where additional research or resources might be useful in an exposure assessment. Anticipating these concerns during the planning and scoping and problem formulation phases can help an assessor be responsive to the needs of the risk manager/decision maker and stakeholder.

## 8.2.2. Assessing the Impact of Uncertainty

Understanding whether uncertainties due to data uncertainty or variability contribute more to the exposure assessment is informative for assessors. The use of statistical or other means could help resolve data uncertainties, while data variability needs to be understood, and, if possible, quantified. Considering decision uncertainty when designing and conducting an exposure assessment can help assessors better understand and explain the relative influence of data uncertainty and variability on the assessment outcome. Understanding specific data concerns can highlight some limitations of the estimated exposures and help assessors determine whether to spend additional resources on reducing uncertainties related to those data. Reducing or otherwise addressing these concerns also can strengthen an exposure assessment.

In some cases, location- or project-specific data are available to support an exposure assessment. In the absence of such data, an assessor might rely on existing datasets, such as those in the *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011d). Existing data can serve as an important reference for evaluating potential exposure factors for various segments of the population. Regardless of the data source, an assessor considers how data uncertainty and variability in the datasets used affect estimated exposures and decisions based on an exposure assessment.

A data uncertainty and variability analysis is an iterative process. The extent of the evaluation depends on many factors, including the type of assessment, data quality objectives and data availability. In the planning stage, an assessor balances the cost of conducting uncertainty and variability evaluations that are more advanced (e.g., probabilistic assessment, advanced modeling) with the benefits reaped from the information. Likewise, evaluating decision uncertainty is iterative, which can help stakeholders provide input regarding whether more resources could reduce uncertainty and provide consequential benefits. In most instances, spending more resources to obtain data that are more certain is important only if the new information would change the choices a risk manager/decision maker makes. Whether a particular level of uncertainty is acceptable is a matter of context (e.g., regulations for which the decision is made), the timeframe within which the decision is needed and regulatory policy (Jamieson 1996a; Stahl and Cimorelli 2005).

## 8.2.3. Conveying Uncertainty When Presenting Results

Transparency in the communication of information about an exposure assessment increases the common understanding of exposure assessment results and limitations (NRC 2009). Clearly communicating information about an uncertainty (data and decision) and variability evaluation, however, can be difficult. Risk managers/decision makers and stakeholders might ask questions about how uncertainty shapes decisions, affects confidence in an exposure assessment or influences the application of the results to specific groups or populations. When risk

managers/decision makers determine which uncertainties contribute the greatest influence on the exposure assessment results (e.g., which data or which judgments), they can focus on the most consequential individual uncertainties in their communication plan. Determining and evaluating decision uncertainty can facilitate communication because stakeholders will be able to explain the influence of the compounded uncertainties on the resulting exposure assessment (Stahl and Cimorelli 2005). *Risk Assessment Guidance for Superfund, Volume III: Part A,* Chapter 6 (U.S. EPA 2001h) provides specific information on communicating uncertainty and variability to many audiences, such as risk managers/decision makers and stakeholders. Section 6.4 of the Superfund guidance discusses key factors for successfully communicating probabilistic risk assessment, including early and continuous involvement of stakeholders, a well-developed communication plan, effective graphics, a working knowledge of the factors that might influence perceptions of risk and uncertainty and a foundation of trust and credibility (U.S. EPA 2001h). EPA's *Risk Characterization Handbook* (2000g) is another resource for information about communicating results to risk managers/decision makers and stakeholders (e.g., community groups). Section 8.4 and Chapter 9 in this document provide additional information about communication considerations for exposure assessments.

## 8.3. A Tiered Approach to Data and Decision Uncertainty and Variability Evaluations

Data uncertainty and variability evaluations are increasing in complexity as evaluation tools (i.e., modeling capabilities) become more sophisticated. Not all exposure evaluations, however, require the most complex evaluation possible. The level of complexity of the evaluation relates to the complexity of the assessment and the potential use of the exposure information in the risk management decision. EPA has emphasized the use of a tiered approach for conducting data uncertainty and variability evaluations. In its simplest form, the tiered approach to understanding the effects of data uncertainty and variability on the exposure assessment outcomes involves starting with basic screening methods and then sequentially employing more sophisticated methods as needed to support the decision (U.S. EPA 2004c). This section describes the tiered approach and discusses the methods most commonly used for each tier. Some evaluation methods are appropriate for use in more than one tier. Assessors need to identify and use the methods that best meet their needs and coordinate with their programs for specific guidance.

In addition to data uncertainty and variability, uncertainties related to agreements about planning, scoping and problem formulation, data and model selection, what role expert judgment plays and how stakeholders intend to use the data need evaluation to understand the compounded effect of all these aspects on the resulting exposure assessment. Although traditional statistical tools and methods can be useful in reducing data uncertainty and better understanding variability, other, more stakeholder-focused approaches need to be engaged to determine and evaluate decision uncertainty (Belzer et al. 2001; IOM 2013; Stahl 2014; Verweij and Thompson 2006).

In moving through each tier, from simple to complex, an assessor determines whether additional, case-by-case evaluations are needed or whether the uncertainty (data and decision) and variability have been addressed or reduced to acceptable levels. This process involves:

- Selecting input parameters for an exposure assessment (data uncertainty and variability)
- Developing a deterministic analysis to identify potential exposures to provide a baseline for a sensitivity and more sophisticated analyses (data uncertainty and variability)
- Conducting a sensitivity analysis to characterize decision uncertainty that includes the compounded impacts of uncertainty or variability on exposure assessment outcomes (data uncertainty, variability and decision uncertainty)
- When high decision uncertainty is an issue, implementing further analyses to refine the input parameters to an exposure assessment and reduce uncertainty and better understand variability in the assessment (data uncertainty, variability and decision uncertainty).

This process is iterative. The information generated when refining input parameters at one tier of the evaluation (e.g., screening) overlaps with selecting input parameters at the next tier (e.g., one-dimensional Monte Carlo analysis). Figure 8-1 illustrates EPA's tiered approach to data uncertainty.

Figure 8-1 provides examples of commonly used methods for each tier. Assessors are encouraged to consult with their programs to identify preferred evaluation tools and default input parameters (e.g., drinking water intake, body weight). Assessors proceed iteratively to understand more fully how each component of the exposure assessment influences the assessment's decision uncertainty. Data uncertainty and variability are just two of the many possible contributors to an exposure assessment's decision uncertainty. Discussions of several methods that can help an assessor evaluate the importance of uncertainty within the risk management/decision making process are available in the literature (Ducey 2001; Fischhoff 1976; Fischhoff 1988; Frey and Patil 2002; Greenland 2001; IOM 2013; Jamieson 1996b; Renn 1986; Stahl and Cimorelli 2005).

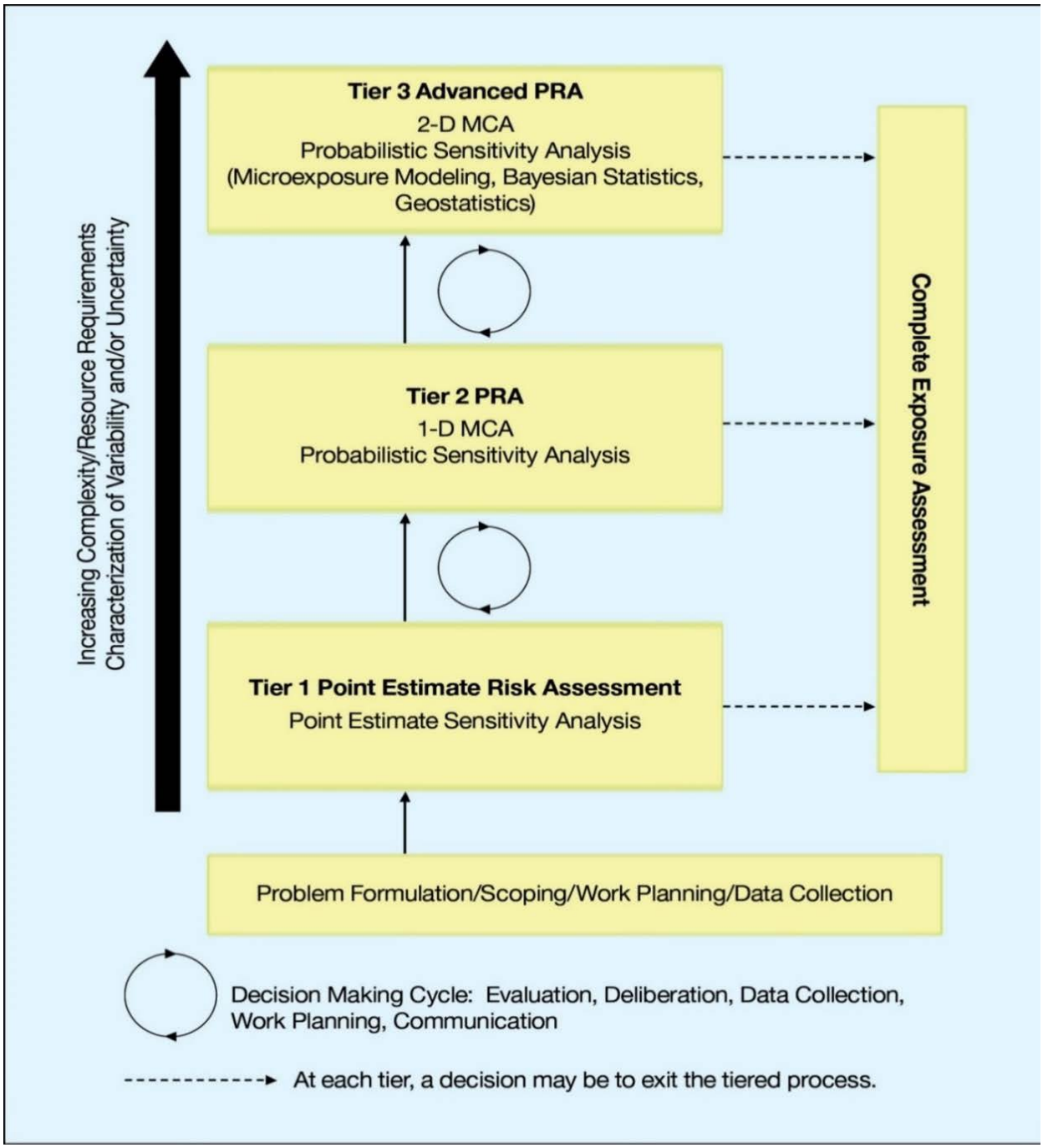
### 8.3.1. Selecting Input Parameters

For each input parameter of an exposure assessment (e.g., chemical concentration, exposure duration), a range of potential values exists. As the data uncertainty and variability evaluation becomes more sophisticated, an assessor will revisit and, as necessary, refine the input parameters. The decision uncertainty and the results of the exposure assessment are influenced not just by the people (e.g., stakeholders, assessor) selecting the input parameters but also the input parameters themselves.

At the beginning of an exposure assessment, an assessor often uses a screening-level approach (see Section 8.3.2) to gain an overall understanding of potential exposures. At the screening level, an assessor typically selects a single data point estimate to represent a central tendency, maximum or other exposure level. The goal of this approach is to achieve a conservative (i.e., health-protective) estimate of exposure. This step also is the first step of a data uncertainty and variability evaluation.

If, after completing the screening-level evaluation, an assessor determines that additional refinement of the input parameters is necessary, the assessor might advance to the next step in the process and conduct a sensitivity analysis (see Section 8.3.3). The sensitivity analysis determines the relative importance of various parameters (i.e., which parameters will benefit the assessment by refinement or additional data).

**Figure 8-1. Schematic Diagram of Tiered Approach to Data Uncertainty**



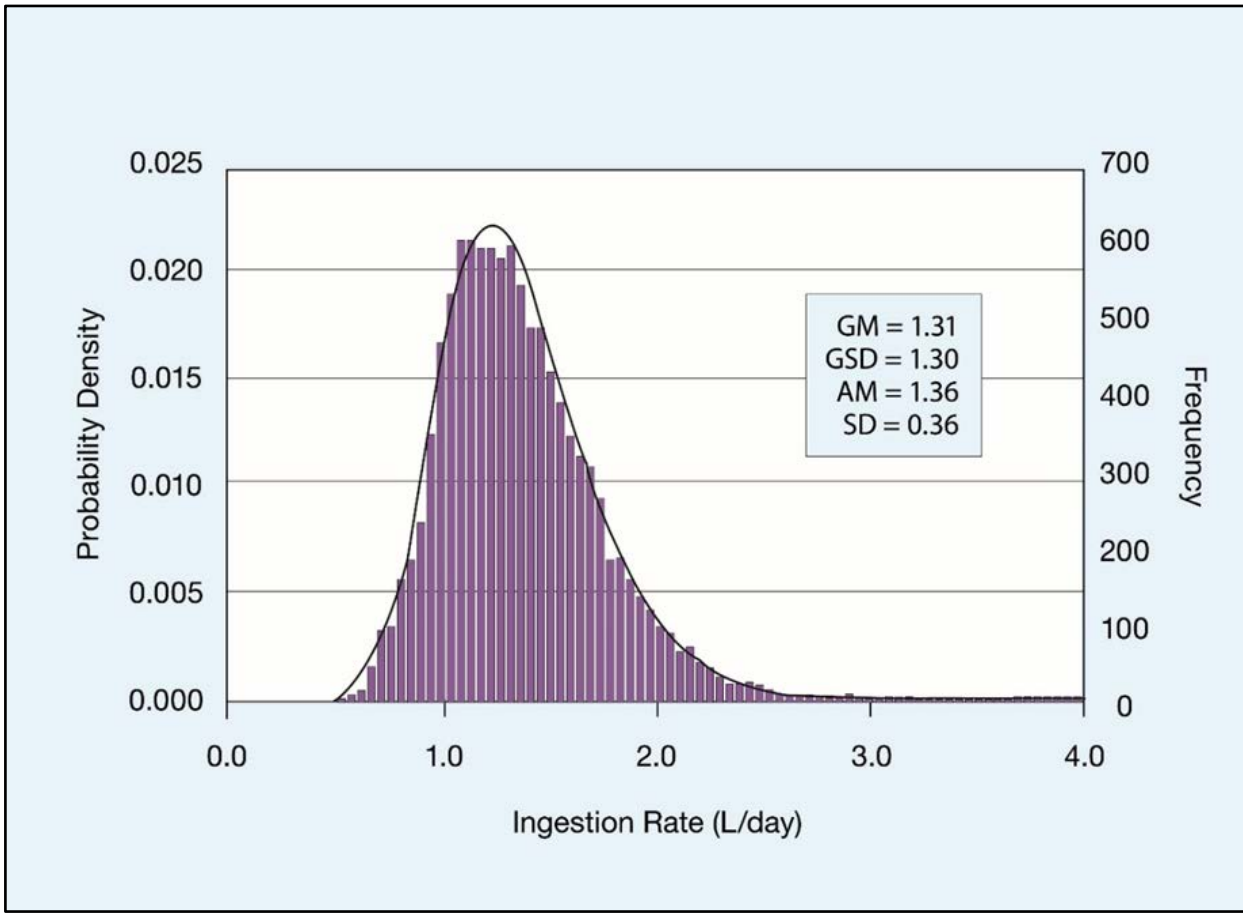

Note: MCA = Monte Carlo analysis; PRA = probabilistic risk assessment; 1-D and 2-D refer to 1-dimensional and 2-dimensional
Adapted from U.S. EPA (2001h)

Based on the sensitivity analysis, an assessor might select the maximum and minimum values as input parameters for the variables that most influence the assessment. The assessor uses these values to estimate the upper and lower bounds of exposure (referred to as an interval or range). Using professional judgment and experience, an assessor might assume a uniform or skewed distribution across this interval. These assumptions, however, introduce additional data

uncertainty in an exposure assessment (WHO 2008). In addition to selecting a minimum and maximum value, an assessor can develop an interval estimate by graphing the available data or conducting statistical analyses. As part of this process, an assessor distinguishes between the data that do and do not represent the receptor. For example, an analysis of fish consumption that focuses on individuals who consume fish can exclude data for those who fish but do not consume the fish they catch.

As an assessor moves through the tiers of the uncertainty and variability evaluation, the assessor can use a probabilistic risk assessment approach to refine the input parameters. In this case, the input parameters represent a probability distribution, defined as a mathematical representation of the probability associated with specified intervals of a value (U.S. EPA 2001h). For example, a probability distribution for drinking water intake would represent the range of possible intake rates and the spread of values within the range (Figure 8-2).

**Figure 8-2. Hypothetical Example of an Input Distribution for Drinking Water Intake Rates**




Note: GM = geometric mean; GSD = geometric standard deviation; AM = arithmetic mean; SD = standard deviation

An assessor can use various approaches to develop a probability distribution for one or more parameters in an exposure assessment. Specifying probability distributions for all parameters, however, generally is unnecessary. An assessor can use the results from earlier sensitivity analyses to select the critical parameters for the focus of the probability distribution. Alternatively, an assessor can consider analyses conducted to refine the exposure assessment.

The accuracy of the probability distribution also depends on the quality of the input data (see Section 5.3.2). For some parameters, location- or situation-specific data will be available. For others, such as exposure duration, water intake and body weight, an assessor more likely will need to develop distributions from published datasets and data summaries [e.g., *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011d)]. Once an appropriate dataset is identified, the assessor conducts statistical analyses to develop the probability distributions (U.S. EPA 2001h; U.S. EPA 2004c). Appendix B of EPA's *Risk Assessment Guidance for Superfund. Volume III: Part A, Process for Conducting Probabilistic Risk Assessment* (U.S. EPA 2001h) provides detailed guidance on selecting probability distributions. Assessors are encouraged to consult with their programs to identify preferred tools and guidance for selecting probability distributions.

Beyond a probabilistic risk assessment, advanced modeling tools are available to characterize uncertainty and variability further. Section 6.3.4 provided more information on these tools.

## 8.3.2. Screening-Level Analyses

Screening-level analyses serve as the first tier of a data uncertainty and variability evaluation. Relying on conservative values for important exposure parameters, an assessor can use these analyses to screen out exposure scenarios or pathways expected to pose little risk. If a scenario poses only a slight increase in the potential for an adverse effect to occur, even assuming the greatest potential exposure, an assessor might choose to eliminate this scenario from additional and more complex evaluations (U.S. EPA 2004c). The assessor needs to communicate the decision to exclude an exposure scenario from an assessment to the risk manager/decision maker and stakeholder(s) clearly. The decision maker/risk manager considers how stakeholders are involved in choosing the screening analysis and the type of screening analysis because this decision could influence the exposure assessment and contribute to decision uncertainty.

The use of screening-level analyses typically occurs during the initial phase of an evaluation. Usually at this stage in an assessment, little location- or scenario-specific information is available. Therefore, an assessor commonly relies on default values, which are point estimates for input parameters that are inherently broad in scope. An assessor often chooses conservative default values to examine exposures that would fall on or beyond the high end of the expected exposure distribution. The assumption is that if risks are not anticipated in a worst-case scenario, assessors, risk managers/decision makers and stakeholders can be confident that the exposure needs no further evaluation (U.S. EPA 2004c).

Screening-level analyses most commonly use a deterministic approach. This approach entails developing a point estimate of exposure and using point estimates of toxicity to calculate a hazard quotient (non-carcinogenic effects) or risk level (carcinogenic effects). This process includes:

- Selecting point estimates for input parameters. An assessor likely will base these estimates on default values, but can use location- or scenario-specific data, if available.
- Estimating potential exposures based on the scenarios identified.
- Comparing the estimated exposure to toxicology-based screening values. Screening values include health-based values expressed as a dose (e.g., reference doses) and chemical concentrations in a specific medium (e.g., soil concentrations). When using

chemical concentrations as screening values, an assessor usually can compare an exposure point concentration to the value directly. In this case, estimating the exposure quantitatively would be unnecessary.

- Determining which exposure pathways, if any, require additional evaluation. Typically, an assessor will carry forward exposures that exceed screening values. In some cases, an assessor might carry forward a scenario for further evaluation or eliminate a scenario based on community concerns, stakeholder input or other factors.

An assessor also can use probabilistic risk assessment approaches during the screening-level analysis. Probabilistic approaches are used more often when refining an exposure assessment (see Section 8.3.4). EPA programs also might implement specific procedures that vary from this basic process. Assessors need to consult with their programs and follow their standard operating procedures and guidance.

### 8.3.3. Conducting a Sensitivity Analysis to Better Characterize Uncertainty

For exposure assessment, EPA defines sensitivity analysis as "any systematic, common sense technique used to understand how risk estimates and, in particular, risk-based decisions, are dependent on variability and uncertainty in the factors contributing to risk" (U.S. EPA 2001h). Sensitivity analysis conducted as part of a data uncertainty evaluation is the process of determining which parameter(s) in an exposure assessment drives the results. This analysis places all relevant data into the context of the decision so that iterations that change data estimates and values can inform risk managers/decision makers about how data uncertainty might affect the evaluation of decision options.

For decision uncertainty, sensitivity analysis includes understanding the influence of compounded uncertainties on the exposure assessment result, including whether an assessor should have considered different data or models or could have made different judgments about how to use the data. In this context, sensitivity analysis is a process of placing all relevant data in the decision context so iterations that change data estimates and values (reflecting data uncertainty) can inform the risk managers/decision makers about how data uncertainty might affect the evaluation of decision options. The sensitivity analyses for data uncertainty and decision uncertainty can occur simultaneously so that an assessor can use the results to avoid additional data analysis or more time-consuming probabilistic analyses.

Identifying the parameter(s) driving data uncertainty and variability and understanding decision uncertainty on the results of an exposure assessment enable an assessor to:

- Use the evaluation of decision uncertainty to prioritize sources of data uncertainty, variability and other uncertainties pertaining to problem formulation, data choices, etc.
- Inform risk managers/decision makers and stakeholders about the potential impacts of exposure assessment on the risk management decisions
- Determine whether to support a cost-benefit analysis that weighs the cost of additional analyses or data collection efforts versus conducting a more refined exposure assessment
- Examine the merits of additional analyses or data collection efforts
- Evaluate the merits of additional model development and refinement that highlight key input parameters identified in the exposure assessment.

Sensitivity analyses can range from simple "back-of-the-envelope" calculations to more complex analyses, including modeling and regression analysis. The type of analysis needed depends on the complexity of the exposure assessment question (U.S. EPA 2001h). The essence of the analysis, however, remains the same: evaluating how changes in the input parameters change the output. Appendix A of EPA's *Risk Assessment Guidance for Superfund. Volume III: Part A, Process for Conducting Probabilistic Risk Assessment* (U.S. EPA 2001h) and the World Health Organization's *Uncertainty and Data Quality in Exposure Assessment* (WHO 2008) provide detailed guidance on conducting a sensitivity analysis. Because specific EPA programs might have their own procedures for conducting sensitivity analyses, assessors need to consult with their programs and follow their standard operating procedures.

In some cases, sensitivity analysis is a low-cost procedure that uses basic calculations to evaluate the relative contribution of the various exposure parameters. Other cases will require a more intensive and complicated sensitivity analysis. This complexity usually arises when multiple sources of uncertainty and variability, including correlation among the exposure parameters, influence an exposure assessment outcome. These sources could be linked such that changes to one source might affect another source (U.S. EPA 2001h).

Sensitivity analysis to determine whether further evaluation of uncertainty and variability is necessary has two potential outcomes, regardless of the method:

- Uncertainty and variability have been defined such that an exposure assessment is sufficient to support decisions (and hence, decision uncertainty is low), or
- Uncertainty and variability influence the outcome of an exposure assessment to the degree that the assessment is insufficient to support decisions (and hence, decision uncertainty is too high).

If the former is true, an assessor has completed the uncertainty and variability evaluation. The evaluation has reached the highest tier necessary to support decisions. If the latter is true, an assessor needs to move forward within the tiered approach to refine the exposure assessment (U.S. EPA 2001h).

### 8.3.4. Using Uncertainty and Variability Analyses to Refine an Exposure Assessment

If a sensitivity analysis indicates the uncertainty and variability in an exposure assessment could change decisions, an assessor needs to consider refining the assessment by reducing the uncertainty or better defining variability. At this stage, an assessor might decide to conduct a more sophisticated uncertainty and variability evaluation. At the screening level, an assessor might decide to analyze the data statistically (e.g., calculate standard deviations, confidence levels) to characterize the datasets more fully and inform the selection of input parameters (i.e., address data uncertainty). As the data uncertainty and variability evaluations become more sophisticated, an assessor might move to a one-dimensional Monte Carlo analysis, a multidimensional probabilistic risk assessment approach or an advanced modeling approach. These approaches, however, cannot address inherent uncertainty. Moreover, even though they can help improve an assessor's *understanding* of exposure variability, they cannot reduce it.

Refining an exposure assessment can require considerable time and effort, but refinement is a necessary step to inform decision making, particularly when the consequences of the decision impact public health and public health resources. Therefore, using decision uncertainty to determine the extent to which changes to multiple data uncertainties or other factors influence the assessment results can be instructive for stakeholders when deciding whether to invest additional time and effort (e.g., collecting additional data might be necessary; see Section 5.4.2). As discussed in Section 8.2.2, an assessor should balance the effort involved in conducting increasingly complex analyses with the benefits of reducing data uncertainty or better defining variability. The selected approach will depend on the type of data uncertainty (scenario, sampling or modeling) and the availability of techniques for reducing that uncertainty. An assessor likely will use deterministic approaches, as discussed in the description of the screening-level analyses (see Section 8.3.2), during the lower tiers of an evaluation. During upper-tier or more complex evaluations, an assessor will rely more commonly on a probabilistic risk assessment or advanced modeling approaches.

**Role of Probabilistic Risk Assessment in Data Uncertainty Analyses**

Probabilistic risk assessment is a statistical method that yields a probability distribution for risk, generally by using a probability distribution to represent data uncertainty or variability in one or more parameters of an exposure assessment. This approach is applicable when detailed statistical analysis is necessary to support sensitive decisions and to help risk managers/decision makers distinguish among possible alternatives. Probabilistic approaches also can help identify data gaps where additional data collection might be necessary to reduce uncertainty and address variability. An assessor can address identified data gaps by collecting more data (see Chapter 5) or conducting additional statistical analyses, such as meta-analyses of existing data or probabilistic approaches using multivariate analysis (Volstad et al. 2003; Weigel 2003). Box 8-2 lists resources for conducting a probabilistic risk assessment.

**Box 8-2. Guidance Documents and Resources Supporting Probabilistic Risk Assessment**

- Finkel (1990) *Confronting Uncertainty in Risk Management: A Guide for Decision Makers*.
- Morgan et al. (1990) *Uncertainty: A Guide to Dealing with Uncertainty in Quantitative Risk and Policy Analysis.*
- Finley and Paustenbach (1994) *The Benefits of Probabilistic Exposure Assessment: Three Case Studies Involving Contaminated Air, Water, and Soil.*
- U.S. EPA (1996e) *Summary Report for the Workshop on Monte Carlo Analysis.* EPA/630/R-96/010.
- U.S. EPA (1997b) *Guiding Principles for Monte Carlo Analysis*. EPA/630/R-97/001.
- Hansen (1997a) *Policy for Use of Probabilistic Analysis in Risk Assessment at the U.S. Environmental Protection Agency*.
- Hansen (1997b) *Use of Probabilistic Techniques (Including Monte Carlo Analysis) in Risk Assessment, and Guiding Principles for Monte Carlo Analysis*.
- U.S. EPA (1999b) *Report of the Workshop on Selecting Input Distributions for Probabilistic Assessments*. EPA/630/R-98/004.
- U.S. EPA (2001h) *Risk Assessment Guidance for Superfund. Volume III: Part A, Process for Conducting Probabilistic Risk Assessment.* EPA/540/R-02/002.
- U.S. EPA (2001h) *Risk Assessment Forum White Paper: Probabilistic Risk Assessment Methods and Case Studies*. EPA/100/R-14/004.

Probabilistic risk assessment methods of varying sophistication are available, depending on the exposure assessment objectives. Monte Carlo analysis is a widely used probabilistic method that relies on computer simulations to combine multiple probability distributions in a quantitative exposure assessment. During the simulation, exposure is estimated quantitatively using randomly selected variables, a process repeated many (e.g., 10,000) times. The output is a series of exposure estimates amenable to summarization with statistical analysis (e.g., mean, quartiles). Most commonly, the input parameters are assumed independent (i.e., the value of one parameter is not linked to the value of another). In simulations that are more complex, an analyst can link parameters using conditional distributions or correlation coefficients. A one-dimensional Monte Carlo analysis characterizes either uncertainty or variability, whereas a two-dimensional Monte Carlo analysis simulates both and is considered an advanced modeling method (U.S. EPA 2001h).

**Role of Expert Elicitation**

Expert elicitation can support probabilistic approaches when data are scarce or lacking. Expert elicitation is the process by which experts in multiple fields characterize data uncertainty and fill data gaps in an exposure assessment when traditional scientific research is infeasible or data are not available (U.S. EPA 2007e). The resulting information can inform decisions associated with the assessment. Each expert characterizes relationships, quantities, events or parameters of interest based on professional judgment and expertise, with the characterizations typically expressed as probabilities. Expert elicitation can be sought individually (each expert acts alone) or as a group (experts meet and provide a collective response). An individual approach typically applies when an assessor needs uncertainty characterization. A group approach is appropriate when an assessor needs a consensus or best estimate of uncertainty (Edlmann et al. 2016; Gregory et al. 2012; McKellar et al. 2017; U.S. EPA 2009a; U.S. EPA 2009c; Wallsten et al. 1997; Werner et al. 2017).

## 8.4. Communicating the Results of the Uncertainty and Variability Evaluation

Even when addressing only data uncertainty and variability, effectively communicating these concepts on an exposure assessment can be challenging. Risk managers/decision makers and stakeholders should evaluate and understand any preconceptions and biases that could influence their interpretations of the evaluation. Ultimately, an assessor seeks to communicate the information to ensure informed decisions about risks to health, safety and the environment (WHO 2008) and, more recently, the Intergovernmental Panel on Climate Change (Mastrandrea et al. 2010). Section 3.2.2 and Chapter 9 of this document provide details about how to communicate the overall exposure assessment process effectively. Communication about decision uncertainty is a critically important emerging area and the need for facilitation approaches remains great. Decision makers can communicate with stakeholders more effectively when they have introduced them to the issues early in the process (see Section 3.1.3).

WHO (2008) presents a list of questions for an assessor to consider and address when discussing the results of an uncertainty and variability evaluation with the public:

- How sure are you about the results?
- What evidence is available to support the methods used?

- What does your method mean for me (and my family)? What do your results mean for me (and my family)?
- What would the result be if you used your sophisticated model for me?
- Why do you use national reference data for us? Aren't we different?
- Your data are old. Hasn't the situation (or product) changed?

An assessor also might need to address questions about the tools used to evaluate different exposure scenarios. Because EPA encourages a tiered approach, an uncertainty and variability evaluation might discuss results from screening-level analyses for some scenarios and from analyses that are more complex for others. These analyses will differ markedly in the level of sophistication, quality of data and amenability to quantitative expressions of uncertainty (both data and decision). An assessor should outline the rationale for applying a specific method in a specific situation to facilitate communication with the risk manager/decision maker and stakeholders. An assessor will benefit from citing the sources, references and materials used to support the overall evaluation. These include resources describing when and how to use a specific tool and those defining parameter defaults.

Anticipating these types of questions and concerns will help an assessor, manager, community involvement coordinator and others prepare effective communication materials. In responding to these questions, an assessor also needs to recognize that, although resources (i.e., time and cost constraints) can influence decisions about data collection and additional analyses, stakeholders usually are less concerned about such constraints. In fact, their confidence might diminish in decisions that appear driven by resource considerations rather than by exposure assessment analyses. An assessor needs to focus on clearly communicating models, methods, assumptions, distributions and parameters applied during an exposure assessment and uncertainty analysis. Openness and transparency about the analyses builds trust and confidence between the risk manager/decision maker and stakeholder (WHO 2008). Using sensitivity analyses and evaluating decision uncertainty in exposure assessments can help decision makers better determine which uncertainties have greater influence on the assessment result, allowing them to focus on communicating those uncertainties.

Chapter 6 of EPA's *Risk Assessment Guidance for Superfund. Volume III: Part A, Process for Conducting Probabilistic Risk Assessment* (U.S. EPA 2001h) and Chapter 6 of the World Health Organization's *Uncertainty and Data Quality in Exposure Assessment* (WHO 2008) provide detailed information about communicating exposure assessment results, including the impacts of uncertainty and variability. In addition to providing general guidance about effective communication, both documents provide examples and suggestions for clearly communicating information about data and data uncertainty and variability pertaining to point estimates, probability distributions, sensitivity analysis, probabilistic risk assessment and additional concepts in uncertainty and variability. [For more information on decision uncertainty, see (Dalkmann et al. 2004; Davies et al. 1987; Illing 1999; Jamieson 1996a; Jamieson 1996b; Sarewitz 2004; Stahl and Cimorelli 2005.)] Chapter 9 in this document provides additional information about communication considerations for exposure assessments.

## 8.5. Summary

- Decision uncertainty is the compounded effect of the total uncertainty (and variability) on the decisions arrived at in an exposure assessment. It involves both the uncertainties of the scientific problem and the uncertainties involved when risk managers/decision makers choose how to formulate and execute the exposure assessment. It also includes uncertainties associated with data and models, whether the problem is scoped accurately and the most important factors are included and the degree to which experts and other stakeholders concur about how to consider those factors in the assessment.
    - EPA defines **data uncertainty** as "a lack of precise knowledge as to what the truth is, whether qualitative or quantitative."
    - **Decision uncertainty** includes uncertainty associated with the scientific problem and with the choices of risk managers/decision makers and stakeholders in formulating and executing the exposure assessment.
    - EPA defines **variability** as the "inherent heterogeneity across space, in time, or among individuals. Variability cannot be reduced with additional investigation, only better understood or characterized." Data uncertainty includes data variability.
- **Evaluating uncertainty and variability** helps in understanding the accuracy and effectiveness of the whole exposure assessment, as well as its individual components. Although an uncertainty evaluation will not eliminate all uncertainty, it can help address questions regarding exposure assessment results, including its influence on risk management decisions, and can help with communication of the assessment.
    - An assessor considers how to characterize uncertainty and variability for the assessment during the **planning and scoping** phase of an exposure assessment.
    - Understanding whether data uncertainty or data variability contributes more to the exposure assessment can be instructive for assessors. Statistical or other means, such as **gathering more data**, can help reduce data uncertainties and improve the understanding of variability and could help quantify it.
    - Transparency in the **communication** of information about an exposure assessment increases the common understanding of exposure assessment results and limitations.
- EPA emphasizes the use of a tiered approach to conducting data uncertainty and variability evaluations.
    - **Screening-level analyses** are the first tier of a data uncertainty and variability evaluation. These analyses often help screen out exposure scenarios or pathways expected to pose little or no risk. Screening includes selecting point estimates for input parameters, estimating potential exposures based on the scenarios identified, comparing the estimated exposure to screening values and determining which exposure pathways require additional evaluation.
    - **Sensitivity analysis** is "any systematic, common sense technique used to understand how risk estimates and, in particular, risk-based decisions, are dependent on variability and uncertainty in the factors contributing to risk." For data uncertainty, sensitivity analysis is the process of determining which parameter(s) in an exposure assessment drives the results. The essence of the analysis is to evaluate how changes in the input parameters change the output.
- If uncertainty and variability in an exposure assessment could change decisions, an assessor needs to consider refining the assessment by reducing the uncertainty or better

defining variability. **Refining an exposure assessment** is a necessary step to inform decision making, particularly when the consequences of the decision impact public health and public health resources. Using decision uncertainty to determine the extent to which changes to multiple data uncertainties or other factors influence the exposure assessment result can be instructive for risk managers/decision makers and stakeholders when deciding on the merits of investing additional time and effort.

- When stakeholders understand the effect of the compounded uncertainties on the exposure assessment result, **communicating** the importance of the results is easier. Effectively communicating the concepts, evaluation tools and their impacts on an exposure assessment nevertheless can be challenging.

# CHAPTER 9. DEVELOPING A COMMUNICATION PLAN AND PRESENTING RESULTS FOR EXPOSURE ASSESSMENTS

The purpose of an exposure assessment shapes the manner in which assessors communicate the exposure assessment results. This chapter highlights considerations when communicating the results of an exposure assessment. It presents:

- An overview of communication in an exposure assessment (Section 9.1)
- Development of a communication plan (Section 9.2)
- Characterization of the results of an exposure assessment (Section 9.3)
- Communication products (Section 9.4)

Section 9.5 summarizes this chapter.

## 9.1. Overview of Communication in Exposure Assessment

For this document, EPA defines "communication" as the exchange of information and viewpoints between the Agency and stakeholders to achieve a goal or objective, such as fostering greater understanding of science and assessment methods, or gaining greater insight into diverse public views and concerns about the scenarios affecting the potential for exposure of individuals or a community to a defined agent [adapted from NAS (2017)].

This chapter presents recommended approaches for planning, initiating, maintaining and delivering content associated with an exposure assessment. To be effective, communication begins at the outset of the assessment process and remains ongoing throughout. Section 3.1.3 emphasized the need for early engagement with stakeholders. This chapter expands on that content and addresses key points of ongoing communication between the assessor, community and other stakeholders. The approach to communication varies with the degree of community engagement, and the level of outreach and community engagement varies by program. Agency activities that directly involve engagement with communities and a wider array of stakeholders require more extensive planning (U.S. EPA 2016e). Box 9-1 lists EPA guidance and resources on public involvement.

Effective communication begins during the early phases of the assessment process (i.e., during planning and scoping and problem formulation) (NRC 2009). Section 3.1.3 presented guidance on engaging with stakeholders during the early phases of an exposure assessment. EPA's Office of Public Affairs and the communication staff within each program are available to facilitate the initial contact and maintain a relationship with stakeholders throughout the process. Ongoing coordination with the Office of Public Affairs is important to ensure effective communication.

EPA adopted the *Seven Cardinal Rules of Risk Communication* as a policy guidance document in 1988 (Covello and Allen 1988). These principles uphold the importance of dialogue with the community and other interested stakeholders (Covello and Sandman 2001).

**Box 9-1. EPA Guidance and Resources on Public Involvement**

*Guidance*

- *Public Involvement Policy of the U.S. Environmental Protection Agency*, EPA 233-B-03-002 (U.S. EPA 2003g)

  The purposes of this policy are to:

  - Improve the acceptability, efficiency, feasibility and durability of the Agency's decisions
  - Reaffirm EPA's commitment to early and meaningful public involvement
  - Ensure EPA considers the interests and concerns of affected people and entities when making decisions
  - Promote use of a wide variety of techniques to create early and, when appropriate, continuing opportunities for public involvement in Agency decisions
  - Establish clear and effective guidance for conducting public involvement activities

- *Framework for Implementing EPA's Public Involvement Policy*, EPA 233-F-03-001 (U.S. EPA 2003e)
- *Introducing EPA's Public Involvement Policy*

*EPA Resources*

- *About the Office of Public Affairs* website
- *Public Participation Guide: Introduction to Public Participation* website
- *Development and Review of EPA Communication Products* website
- *Stakeholder Involvement and Public Participation at the U.S. EPA. Lessons Learned, Barriers & Innovative Approaches*, EPA 100-R-00-040

## 9.2. Development of a Communication Plan

A communication plan identifies the stakeholders, establishes a working relationship among stakeholders and provides the approach for interactions. A communication plan needs to outline the objectives/goals of the activity and present the most appropriate method for communication throughout the exposure assessment. The plan also should consider how the information will be presented to various stakeholders.

EPA's Communication Strategies document states that a communication plan needs to consider:

- Why – identify why communication is necessary and define the objective(s).
- Who – define the audience(s) and how to reach them.
- What – meet with the assessment team to discuss the communication plan; coordinate communication plan content such as goals and objectives; focus on two or three key messages and rank them by importance, timeliness or other factors.
- How – identify key messages and determine approach(es) for delivering them. Delivery methods can include briefings, exhibits, fact sheets, the internet, mailings, presentations, public notices, responsiveness summaries, telephone, translation of documents into languages other than English, videos and social media.
- When – determine timing of meetings, outreach to stakeholders, budget considerations and feedback to the assessment team to evaluate the strengths and weaknesses of outreach and how it can be improved and revised to ensure continued effectiveness.

The document also includes worksheets.

Other resources include the *EPA Guidelines for Research Project Communication Plans* website.

## 9.3. Results of an Exposure Assessment: Exposure Characterization and Risk Characterization

Exposure characterization is the narrative that provides the discussion, analysis and conclusions to synthesize the exposure assessment results. It presents a balanced representation of the available data and their relevance to the health effects of concern and identifies key assumptions and major areas of uncertainty. Section 9.3.1 details the key elements of an exposure characterization. Section 9.3.2 presents information on developing the exposure characterization as part of the overall risk assessment. Section 9.3.3 discusses various formats for presenting exposure characterization results, and Section 9.3.4 describes ways for conveying uncertainties in the results. Section 9.3.5 presents considerations for communicating with stakeholders.

### 9.3.1. Elements of an Exposure Characterization

An exposure characterization:

- Provides the purpose, objective(s), scope, level of detail and approach used, including key assumptions
- Presents the estimates of exposure and dose by pathway and route for individuals, lifestages, groups or populations of concern
- Provides an evaluation of the overall quality of the assessment and the degree of confidence the assessors have in the estimates of exposure and dose and in the conclusions drawn
- Presents an interpretation of the data and results
- Presents information on uncertainty and variability
- Communicates the results within the context of the risk characterization.

The presentation of the exposure and dose estimates identifies and quantifies important source(s), significant pathway(s) and route(s) of exposure from the source to the individual, lifestage, group or population of concern as laid out in the conceptual model (see Section 3.2.2). The presentation also discusses reasons for excluding any individual, lifestage, group or population of concern from the assessment. If the exposure distribution is known, a variety of exposure descriptors and, where possible, the full population distribution is presented. An assessor provides risk managers/decision makers an estimate of how exposure is distributed across the population and how variability in population activities influences this distribution by including summary statistics, the average or central tendency exposure, high-end exposures, other program-specific outputs (e.g., the maximally exposed individual) or other descriptors as appropriate to regulatory needs (see Section 5.3). If the distribution is unknown, an assessor presents context for and characterizes, to the extent possible, the exposure estimates. Ideally, an exposure characterization links the purpose of the assessment with specific risk descriptors, which in turn facilitate construction of a risk characterization.

Where appropriate, a description of additional research and data needed to improve an exposure assessment can be helpful to risk managers/decision makers in making decisions. For this reason, an exposure characterization identifies key data gaps that can help focus further efforts to reduce uncertainty if additional information would inform key issues or provide greater certainty to the decision. Finally, most risk management decisions take into account a variety of factors in

addition to science: economic factors, technological factors, laws, socioeconomic considerations, political factors and public values (U.S. EPA 2000g).

## 9.3.2. Development and Use of an Exposure Characterization in Characterizing Risk

EPA's Information Quality Guidelines (U.S. EPA 2002f) lays out criteria for assessments made available to the public:

> "(i) each population addressed by any estimate of applicable human health risk or each risk assessment endpoint, including populations if applicable, addressed by any estimate of applicable ecological risk;
> (ii) the expected risk or central estimate of human health risk for the specific populations affected or the ecological assessment endpoints, including populations if applicable;
> (iii) each appropriate upper-bound or lower-bound estimate of risk;
> (iv) each significant uncertainty identified in the process of the assessment of risk and studies that would assist in resolving the uncertainty; and
> (v) peer-reviewed studies known to the Administrator that support, are directly relevant to, or fail to support any estimate of risk and the methodology used to reconcile inconsistencies in the scientific data."

In practice, an assessor writes characterizations for each component of the risk assessment (hazard assessment, dose-response assessment, exposure assessment) to carry forward the findings, assumptions, limitations and uncertainties in the three components. This set of characterizations provides the informational basis for writing the integrated risk characterization. The risk characterization conveys the risk assessor's judgment about the nature and presence or absence of risks, information about how the risk was assessed, the assumptions used and consideration of data uncertainty, and insights about where policy choices will need to be made.

Often these assessments lead to a regulatory decision (i.e., policy decision). The quality of the exposure characterization determines the ability to integrate the exposure assessment with the hazard identification and dose-response assessment into the risk assessment and incorporate it into a regulatory decision. The overall risk characterization informs the risk manager/decision maker and others about the rationale for EPA's approach to conducting the risk assessment (i.e., why EPA took that approach to assess the risk). The risk characterization restates the scope of the assessment, expresses results clearly, articulates major assumptions and uncertainty, identifies reasonable alternative interpretations and distinguishes scientific conclusions from policy decisions (U.S. EPA 2000g).

EPA's risk characterization policy calls for conducting risk characterizations in a manner consistent with the principles listed below (U.S. EPA 2000g). These principles apply to each component of the risk assessment:

- **Transparency.** The characterization needs to disclose—fully and explicitly—the methods, default assumptions, logic, rationale, extrapolations and uncertainty (distinguishing, when possible, between data and decision uncertainty) and the overall strength of each step in the assessment.

- **Clarity.** Readers within and external to the assessment process need to understand the products from the assessment. Documents need to be concise and free of jargon and include understandable tables, graphs and equations.
- **Consistency.** The conduct and presentation of the assessment need to be consistent with EPA policy and guidance.
- **Reasonableness.** Sound judgment needs to be the foundation of the assessment, with methods and assumptions consistent with the current state-of-the-science and conveyed in a manner that is complete, balanced and informative.

These four principles—transparency, clarity, consistency and reasonableness—are referred to collectively as TCCR. To achieve TCCR in an exposure characterization, an assessor needs to apply these principles in all steps of the process (U.S. EPA 2000g).

### 9.3.3. Formats for Exposure Characterization

EPA does not require a set format for exposure characterization reports, but some individual programs within the Agency do have specific format requirements. EPA's Office of Land and Emergency Management (formerly Office of Solid Waste and Emergency Response), for example, has developed standardized methods for presenting exposure information, described in the *Risk Assessment Guidance for Superfund Part D* (U.S. EPA 2001g). The tables in that guidance present an approach for summarizing and presenting information. They help organize information on the exposure point concentration, including statistics used, exposure variables for specific lifestages (e.g., children, adolescents, adults), toxicity values, calculated cancer risks and estimates of non-cancer health hazards.

EPA's *Risk Characterization Handbook* (2000g), Appendices B through E, presents several examples of exposure characterizations that are part of risk characterization case studies. EPA's Office of Research and Development provides templates for presentations at conferences, public meetings and other venues. Other EPA programs might have specific formats for communicating results (e.g., oral, written). Assessors need to consult with their programs and follow their standard operating procedures.

### 9.3.4. Communicating Uncertainty

One of the most challenging aspects of communication is the presentation of uncertainty (NRC 2009). Addressing uncertainties in assessments is an essential but often challenging task—particularly when communicating with stakeholders with a wide range of technical expertise (Spiegelhalter et al. 2011; Stirling 2010; Visschers et al. 2009). The most appropriate method for addressing uncertainty depends on the nature of the assessment and the audience (IOM 2013; U.S. EPA 2001h; U.S. EPA 2014h; U.S. EPA 2014i; WHO 2008).

In general, numerical, graphical or narrative formats can be used to present uncertainty, depending on the audience (IOM 2013). Regardless of the presentation type, it needs to be self-explanatory: capable of communicating the critical information without relying on the narrative to explain the main message. Numerous researchers provide additional information on presentation types [e.g., Helsel and Hirsch (1993), Lipkus (2007), Slovic (1986), Slovic et al. (1979) and Tufte (2001)].

When communicating results and their attendant uncertainties, the assessor needs to keep in mind that the use of numerical, narrative and graphical information is not mutually exclusive. Rather, these three presentation types used in concert can improve communication. Certainly, a table or graph can support a narrative in the presentation.

### 9.3.5. Stakeholders

Potential stakeholders (see Sections 3.1.3, 7.2.8 and 7.2.9) include residents of the community in which the assessment took place, community groups, advocacy groups, interested members of the public, medical organizations, university partnerships, industry groups, nonprofit organizations, nongovernment and government organizations, states, tribes and the media. Chapter 7 provided guidance on communicating results to study participants. Section 7.2.8 described ways to establish communication and dialogue with community members in the initial phases of an exposure assessment. This dialogue includes asking the community to define their questions of interest and the manner in which they wish to receive the assessment results. Payne-Sturges et al. (2004) noted that effective communication and translation of the exposure assessment approach enables the community to "credibly represent the study's implications to policy makers and other stakeholders, thereby closing the loop between science and the community."

The program with the most experience and activity with stakeholder involvement is EPA's Superfund. EPA's Office of Land and Emergency Management has developed the most extensive guidance for dealing with stakeholders; see the *Superfund Community Involvement Tools and Resources* website. This knowledgebase includes content on establishing, engaging and maintaining a working relationship with communities.

Covello and Sandman (2001) describe important obstacles to overcome in achieving effective risk communication to stakeholders: inconsistent, overly complex, confusing or incomplete risk messages; the lack of trust in information sources; selective reporting by the media; and psychological and social factors that affect how information is processed. Exposure assessors face significant challenges regarding how to interpret, report and act on results when the links between environmental chemicals and health are only partially understood, poorly known or complex (NRC 2006b). Examples include conveying both the risks and benefits of fish consumption and discussing the significance of elevated body burdens of chemicals that lack toxicological or epidemiological evidence regarding health effects. In this situation, the assessor needs to be candid with stakeholders about the availability of useful information.

Section 9.4 lists additional resources assessors can use for effective communication about exposures and risks.

## 9.4. Communication Products

The exposure characterization is consistent with the level of detail and complexity of the assessment conducted. The needs of the stakeholders, however, determine the depth and detail of subsequent products. When discussing assessment results with stakeholders, an approach would be to provide a short executive summary, clearly highlighting key issues and conclusions, with the technical information included in an appendix or as a reference to the exposure assessment

itself. Assessors need to consult with their programs and follow their standard operating procedures.

Communication products might include fact sheets, slide presentations, press releases, *Federal Register* notices, newsletters, site- or community-specific websites, social media, public meetings and hotlines. Release of all communication products related to the exposure assessment needs to follow appropriate Agency clearance procedures. Documents and other communication products need to be dated and replaced (e.g., on websites) as updates become available.

For assessments that involve the public, a communication plan often is essential. A communication plan includes the key messages for dissemination and the audiences, format, timing and frequency for distributing them. NRC (1989b) notes that developing risk messages is a collaborative effort between scientists and communications experts:

> "It is a mistake to simply consider risk communication to be an add-on activity for either scientific or public affairs staffs; both elements should be involved. There are clear dangers if risk messages are formulated *ad hoc* by public relations personnel in isolation from available technical expertise; neither can they be prepared by risk analysts as a casual extension of their analytic duties."

Increasingly, EPA is taking advantage of electronic media, such as Wikis, blogs, microblogs (e.g., Twitter) and social networking sites (e.g., Facebook), to communicate environmental and health information to the public (U.S. EPA 2011c). These tools can be an effective component of a communication plan for an exposure assessment.

The array of published literature on risk communication and public involvement is extensive and continues to evolve as the complexity of risk issues increases (Covello 1987; Deisler Jr. 1988; Fischhoff 1995; Fischhoff 1998; Fischhoff and Downs 1997; Holliman et al. 2008a; Holliman et al. 2008b; Hora 1992; Ibrekk and Morgan 1987; Johnson and Slovic 1995; Mastrandrea et al. 2010; Morgan and Martinez 1992; NAS 2017; North 1997; Thompson and Bloom 2000).

## 9.5. Summary

- Effective communication is a dialogue process between Agency staff and stakeholders that begins during the early phases of the assessment process: planning and scoping and problem formulation. EPA actively engages the public in many of its decision making processes.
- A **communication plan** developed and implemented early in an assessment should identify and establish a working relationship with the relevant and interested parties. The strategy introduces stakeholders to assessment vocabulary and processes. It should outline the goals and objectives, select the most appropriate method of communication and inform stakeholders about what to expect in the final report.
- **Exposure characterization**, an element of risk characterization, is the narrative that provides the discussion, analysis and conclusions to synthesize these results.
    - A characterization is written for each component of the risk assessment (hazard assessment, dose-response assessment, exposure assessment) and used to carry forward the findings, assumptions, limitations and uncertainties in the three

components. These characterizations collectively provide the information for writing the results of an integrated risk characterization analysis.
    - The **elements of an exposure characterization** are (1) the purpose, objectives, scope, level of detail and approach used; (2) exposure and dose estimates by pathway and route for individuals, lifestages, groups and populations of concern; (3) an evaluation of the overall quality of the assessment and the degree of confidence assessors have in the estimates and conclusions; (4) an interpretation of the data and results; and (5) communication of the results for integration with the other assessment elements to develop a risk characterization.
    - EPA has no set **format** for exposure characterization reports, but some individual programs within the Agency have specific format requirements. EPA's *Risk Characterization Handbook* presents examples of exposure characterizations.
    - One of the most challenging aspects of **communication** is the presentation of **uncertainty**. Using numerical, narrative and graphical information in concert can improve communication.
- The **stakeholders for an exposure assessment** can range widely: community groups, advocacy groups, the public, medical organizations, university partnerships, industry groups, nonprofit organizations, nongovernment and government organizations, states, tribes and the media. Upon completion of the exposure and risk characterizations, the focus turns to communicating the results to the **risk manager/decision maker**.
- Appropriate **communication products** are tailored to their intended audiences.

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