Guidelines for Human Exposure Assessment

Risk Assessment Forum
U.S. Environmental Protection Agency

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ABBREVIATIONS AND ACRONYMS

ADME	absorption, distribution, metabolism and elimination
AI	Atkinson index
APEX	Air Pollutants Exposure Model
AQS	Air Quality System
ATSDR	Agency for Toxic Substances and Disease Registry
ATUS	American Time Use Survey
BRFSS	Behavioral Risk Factor Surveillance System
CARES™	Cumulative and Aggregate Risk Evaluation System
CDC	Centers for Disease Control and Prevention
C-FERST	Community-Focused Exposure and Risk Screening Tool
CFR	Code of Federal Regulations
CHAD	Consolidated Human Activity Database
ChemSTEER	Chemical Screening Tool for Exposures and Environmental Releases
CMAQ	Community Multiscale Air Quality Model
CREM	Council for Regulatory Environmental Modeling
CTEPP	Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants Study
DB	database
DDD	dichlorodiphenyldichloroethane
DDE	dichlorodiphenyldichloroethylene
DDT	dichlorodiphenyltrichloroethane
DEARS	Detroit Exposure and Aerosol Research Study
DOJ	U.S. Department of Justice
DQO	data quality objective
EEO	Equal Employment Opportunity
E-FAST	Exposure and Fate Assessment Screening Tool
EHS	Environmental Health Sciences
EPA	U.S. Environmental Protection Agency
EPC	exposure point concentration
FOIA	Freedom of Information Act
GIS	geographic information system
HAPEM	Hazardous Air Pollutant Exposure Model
HEDS	Human Exposure Database System
HHE	health hazard evaluation
HHS	U.S. Department of Health and Human Services
HSRRO	Human Subjects Research Review Official
IPCS	International Programme on Chemical Safety
IRB	Institutional Review Board
ISES	International Society of Exposure Science (Formerly ISEA)
MCL	Maximum Contaminant Level
MEI	maximally exposed individual
NAS	National Academy of Sciences
NASQAN	National Stream Quality Accounting Network
NATA	National-Scale Air Toxics Assessment

NAWQA	National Water Quality Assessment Program
NCEA	National Center for Environmental Assessment
NCHS	National Center for Health Statistics
NEPA	National Environmental Policy Act
NHANES	National Health and Nutrition Examination Survey
NHEXAS	National Human Exposure Assessment Survey
NIOSH	National Institute for Occupational Safety and Health
NOES	National Occupational Exposure Survey
NRC	National Research Council
OMB	Office of Management and Budget
OPP	Office of Pesticide Programs
OPPT	Office of Pollution Prevention and Toxics
ORD	Office of Research and Development
OSHA	Occupational Safety and Health Administration
OSWER	Office of Solid Waste and Emergency Response
PBPK	physiologically based pharmacokinetic
PCB	polychlorinated biphenyl
PHED	Pesticide Handlers Exposure Database
PK	pharmacokinetic
PM	particulate matter
$PM_{2.5}$	particulate matter 2.5 micrometers in diameter and smaller
QA	quality assurance
QAPP	quality assurance project plan
QC	quality control
RDC	Research Data Center
REACH	Registration, Evaluation, Authorisation and Restriction on Chemicals
READ	Registry of EPA Applications and Databases
ReVA	Regional Vulnerability Assessment
RIOPA	Relationship Between Indoor, Outdoor and Personal Air Study
RME	reasonable maximum exposure
SEAOES	Scientific and Ethical Approaches for Observational Exposure Studies
SHEDS	Stochastic Human Exposure and Dose Simulation model
SHEDS-HT	Stochastic Human Exposure and Dose Simulation-High Throughput model
SOP	standard operating procedure
TCCR	transparency, clarity, consistency and reasonableness
TEAM	Total Exposure Assessment Methodology Study
T-FERST	Tribal-Focused Environmental Risk and Sustainability Tool
USGS	U.S. Geological Survey
WHO	World Health Organization
WQP	Water Quality Data Portal

PREFACE

This document updates and expands 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 update 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 update the *Guidelines for Exposure Assessment* was announced and developments in the field since 1992 were reviewed. In 2006, the Agency consulted with the EPA Science Advisory Board, describing its approach to the update and summarizing comments received from Agency scientists, the scientific community and the public. This update, the *Guidelines for Human Exposure Assessment*, benefits from many additional years of experience with exposure and risk 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.

As with the *Guidelines for Exposure Assessment*, this *Guidelines for Human Exposure Assessment* is designed to aid exposure scientists in developing exposure and risk assessments, status and trends analyses, mitigation strategies, regulatory decisions and epidemiological studies. This update focuses on human exposure to chemical agents (stressors) 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 detailed information on emerging topics such as high-throughput exposure assessment, the implications of *in vitro* based risk assessments on the field of exposure assessment, or the ongoing ExpoCast program. As emerging topics mature, EPA may update or supplement this document. The *Guidelines for Human Exposure Assessment* is principally intended for exposure and risk assessors in the Agency and consultants, contractors or others who perform this type of work under Agency contract or sponsorship, as well as academic, industrial and others who perform this type of work in accordance with EPA policies and procedures. Risk managers/decision makers in the Agency also might benefit from this document because it describes approaches, defines terminology and summarizes methods exposure and risk assessors use.

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.

EXECUTIVE SUMMARY

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, estimates and predicts exposures and provides information for developing exposure and risk assessments, as well as effective strategies for reducing exposure and risk. The Agency needs to understand whether an agent might cause a health effect and how exposure to the agent could be reduced. The increasing number and complexity of risk assessments the Agency conducts, and the corresponding risk management decisions, present new challenges.

The *Guidelines for Human Exposure Assessment* provides an updated resource on assessing human exposure for exposure and risk assessors in the Agency, consultants, contractors or others who perform this type of work under Agency contract or sponsorship, as well as academic, industrial and others who perform this type of work in accordance with EPA policies and procedures. This document builds on and supersedes the 1992 *Guidelines for Exposure Assessment* (U.S. EPA 1992c), incorporates advances in the field that have occurred since then, reflects current scientific practice across Agency programs and includes pertinent topics identified during public meetings and from a survey of the literature, 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 that can be used to conduct an exposure assessment and provides references for more detailed information. It does not, however, 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, the focus of the work is on exposure assessment as currently practiced in EPA programs. This document does not include detailed information on high-throughput exposure assessment, the implications of *in vitro* risk assessments on the field of exposure assessment or the ongoing ExpoCast program. As these emerging topics mature, the Risk Assessment Forum will update this document. Finally, this guideline provides links to exposure assessment tools and technical documents that address particular exposure assessment needs.

The focus of the *Guidelines for Human Exposure Assessment* is on human exposure to chemical agents (stressors) in the nonoccupational environment. The exposed populations (e.g., 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 the *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, that can be considered 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 guidance regarding the synthesis of exposure information also is presented.

Chapter 3 describes a process for planning and scoping and problem formulation for an exposure assessment that 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 2002f) and *Framework for Human Health Risk Assessment to Inform Decision Making* (U.S. EPA 2014b). 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 how lifestages, vulnerable groups and populations of concern could be at increased risk for adverse health effects from environmental contaminants due to disproportionate exposure or varied responses to exposure, or both. Consistent with the Agency's *Framework for Cumulative Risk Assessment* guidance (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, 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.

Data, the primary input to an exposure assessment, can include environmental, biological and exposure factors such as human activity patterns. Chapter 5 discusses data used for exposure assessments, including determining what data are needed; whether data are currently available and the quality of the available data; and when data are not available, whether data need to be developed. Understanding data availability, applicability, characteristics, quality issues and limitations is critical to conducting a scientifically sound exposure assessment. Guidance on the assessment of data uncertainty and variability is discussed in this chapter. The chapter 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 also includes information on modeling inventories and clearinghouses and resources that support the use of models of various levels of complexity.

Chapter 7 provides details on planning an observational human exposure measurement study. These studies are used in parts of the Agency to quantify people's exposures to chemicals in their everyday environments during their normal daily activities. They involve measurements of chemical, biological or physical agents in environmental media; collection of information about

the study participants and their homes, work environments and activities; and collection of personal exposure and biological samples. This chapter discusses the aspects surrounding planning an observational human exposure measurement study, including budget and logistical planning, establishing a study design, planning and executing both a pilot study and 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. The *Scientific and Ethical Approaches for Observational Exposure Studies* (U.S. EPA 2008a) 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 these types of studies.

EPA recognizes the importance of considering variability and uncertainty in data and decision making for exposure and risk assessments. The Agency's policies and guidance on these issues, released after the *Guidelines for Exposure Assessment* were finalized, provide recommendations for applying a tiered approach in determining the appropriate techniques to include in an analysis. Chapter 8 considers uncertainty and variability in exposure assessments, incorporating them into planning and scoping and problem formulation (Chapter 3) and data (Chapter 5). This chapter highlights how these concepts are used in the application of models in an exposure assessment. It also provides information that exposure assessors can consider in developing communication strategies for presenting the results of uncertainty and variability analyses to interested individuals, including participants, stakeholders and the public.

Throughout this *Guidelines for Human Exposure Assessment*, the importance of communication is discussed. Chapter 9 brings these concepts together into a final communication strategy with more specific information. This chapter emphasizes the importance of identifying the intended audience, the types of communication products, communication strategies that might be appropriate for different exposure assessments and related ethical considerations.

Chapter 10 provides references for all cited documents.

As appropriate, the Risk Assessment Forum will evaluate the need to update this document and make appropriate adjustments as the field of exposure science continues to evolve.

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 both space and time. It provides information to develop exposure and risk assessments and the most effective strategies to reduce human health risk through mitigating exposure. The Agency needs to understand whether the agent can cause an adverse health effect and how exposure to the agent could be reduced. The increasing number and complexity of risk assessments the Agency conducts, and the corresponding risk management decisions, present new challenges. Furthermore, advances in the field of exposure science require the Agency to consider the best available science for conducting exposure and risk assessments.

1.2. Purpose and Scope of the Guidelines

This document updates 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 the 1992 document was published, including:

- *Policy on Evaluating Risk to Children* (1995b) and the 2013 reaffirmation of the policy (2013b),
- *Policy for Use of Probabilistic Analysis in Risk Assessment* (Hansen 1997a) and *Guiding Principles for Monte Carlo Analysis* (1997b),
- *Cumulative Risk Planning and Scoping Guidance* (1997a),
- *Exploration of Perinatal Pharmacokinetic Issues* (2001d),
- *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),
- *Peer Review Handbook Fourth Edition* (2015),
- *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* (2008a),
- *Exposure Factors Handbook: 2011 Edition* (2011f) and *Highlights of the Exposure Factors Handbook* (2011g),
- *Recommended Use of Body Weight 3/4 as the Default Method in Derivation of the Oral Reference Dose* (2011j),
- *Benchmark Dose Technical Guidance* (2012c),

- *Microbial Risk Assessment Guideline: Pathogenic Microorganisms with Focus on Food and Water* (2012g), and
- *Framework for Human Health Risk Assessment to Inform Decision Making* (2014b).

This guideline describes the principles of exposure science and exposure assessment; offers guidance to the reader on various approaches that can be used to conduct an exposure assessment; and provides references for more detailed information, including exposure assessment tools and technical documents that address particular exposure assessment needs.

The *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. In addition, the focus of the work is on current practices in EPA programs. This document does not include detailed information on emerging topics such as high-throughput exposure assessment, the implications of *in vitro* based risk assessments on the field of exposure assessment, or the ongoing ExpoCast program. As emerging topics mature, EPA will consider updating this document. Agency exposure and risk assessors are encouraged to consult with their programs to obtain specific procedures and guidelines.

The principal focus of the *Guidelines for Human Exposure Assessment* is on human exposure to chemicals under nonoccupational scenarios; much of this discussion, however, can apply to exposure to biological and physical agents (e.g., noise, radiation, microbial hazards, nanomaterials) or other stressors.[1] Exposure assessments for physical and biological agents are beyond the scope of this document because of their unique characteristics. The impacts of social stressors on exposure also are not addressed in this document.

This guidance focuses primarily on the data and information used in exposure and risk 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 are used to 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 *Guidelines for Human Exposure Assessment*, and this document references sources with proven principles and approaches EPA uses.

[1] The term "agent" is used 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 is the exception to this statement because it incorporates National Research Council documents where the term "stressor" is used.

1.3. Organization of *Guidelines for Human Exposure Assessment*

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

- Chapter 2 provides an overview of the basic concepts and principles of exposure science.
- Chapter 3 addresses planning and scoping and problem formulation for exposure assessments.
- Chapter 4 describes lifestages, vulnerable groups and populations of concern in exposure assessments.
- Chapter 5 discusses collection and use of data for exposure assessment.
- Chapter 6 addresses modeling for exposure assessment.
- Chapter 7 discusses planning for an observational human exposure measurement study.
- Chapter 8 presents information on evaluating uncertainty and variability in exposure assessment.
- Chapter 9 addresses the presentation and communication of results of exposure assessments.
- Chapter 10 contains full references for all cited documents.

CHAPTER 2. PRINCIPLES OF EXPOSURE SCIENCE/EXPOSURE ASSESSMENT

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

- Key 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), and
- Development of exposure science and exposure assessment (Section 2.5).

Chapter 2 introduces key concepts that are 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.

2.1. Exposure Science

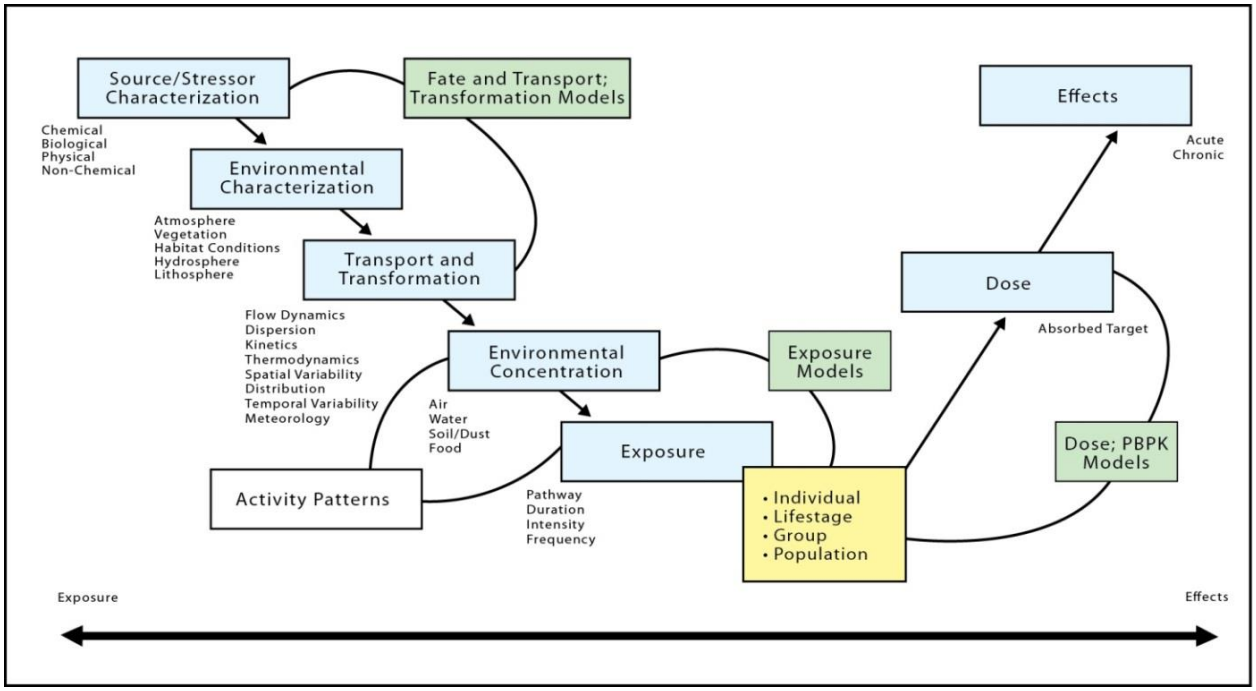
Human exposure science is the study of the contact of humans with chemical, physical or biological agents occurring in their environments. It is intended to advance the knowledge of the mechanisms and dynamics of events that result in adverse health outcomes, either to understand their cause(s) or to 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 contact and uptake of agents by humans. Exposure science uses this information to describe conditions in the real world that will 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 2012; Sheldon and Cohen Hubal 2009; U.S. EPA 2009a).

In 2012, the National Research Council (NRC) published the report, *Exposure Science in the 21st Century: A Vision and a Strategy*. The 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 2012). Consistent with this definition, the 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."

The processes and information that are important for exposure science can be visualized using a source-to-outcome framework, as illustrated in Figure 2-1. The text under each box in Figure 2-1

shows the information that is used to characterize the various processes and conditions represented in the boxes. The arrows between the boxes represent the models that are used to link the processes. The processes important for exposure science begin with a contaminant entering the environment and end with dose characterization. Starting in the upper left-hand corner, agents are released into the environment from a source. Many contaminants can be transformed by chemical reactions and physical and biological degradation. 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 the 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 can then be distributed throughout the body in either its native or metabolized form or both. The endpoint for exposure science is the dose received by the target internal tissue or organ: 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

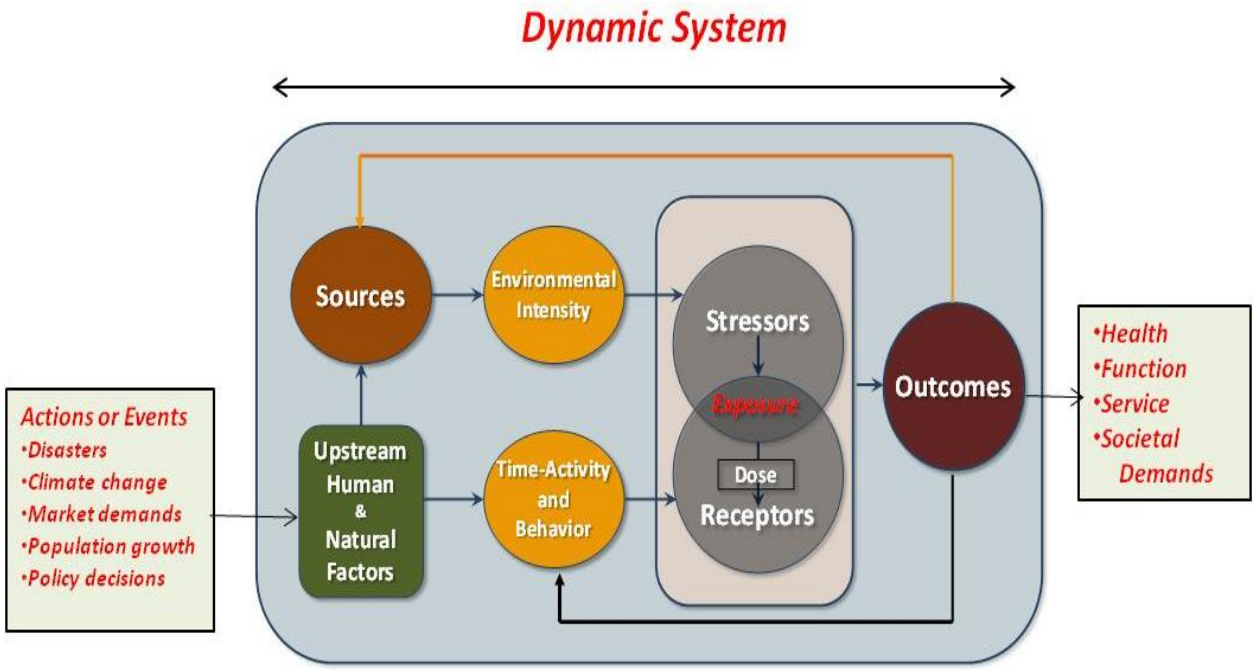


Note: PBPK = physiologically based pharmacokinetic.
Adapted from NRC (1983; 1997)

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, has 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 both human and natural factors, or that 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 along with risk.

Figure 2-2. Conceptual Framework for Exposure Science Developed by NRC (2012)



The NRC committee also recognized that exposure is 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 illustrated in Figure 2-1 and Figure 2-2. Multiple stressors can enter the environment at the same time from multiple sources. Stressors can remain unchanged or be transformed by physical, chemical or biological processes. Stressors in their native forms or their transformation products can take many different pathways to reach human receptors. Exposure is often characterized for a single stressor, in a single medium or as a single pathway. Real-world scenarios involve multistressor, multimedia and multipathway exposures. Exposure science is developing methods to characterize both aggregate exposure, which is the sum of exposures to a single stressor from all sources, and cumulative exposures, which address exposures to multiple chemicals by multiple routes over multiple periods.

The primary focus for human exposure science is the receptor rather than the sources of the stressor, taking into consideration potential contact based on locations and behaviors of the human receptor. 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 to which exposure actually occurs.

Receptors can be individuals, populations or lifestages within a 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, particularly for infants and toddlers. Lifestage, health status, sex and genetic differences can also 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) that are described by population distributions based on observational data.

The adverse impact of exposure depends not only on the characteristics of the exposures but also on the vulnerability of the receptor. Vulnerability refers to characteristics of individuals or populations that place them at increased risk of an adverse effect (U.S. EPA 2005c). It includes the biological, economic, demographic, social, psychological and physical states of the receptor or population that influence patterns of exposures to environmental contaminants, as well as those states that alter the relationship between the exposure or dose, or both, of the environmental agent and its health effect on the receptor (Gee and Payne-Sturges 2004). Vulnerability encompasses both inherent biological susceptibility (e.g., age, sex, genetic predisposition, preexisting health conditions) and differential exposure. It can also 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. The concepts of differential exposure and susceptibility are crucial given EPA's mandate to protect human health and the environment. Vulnerability is addressed in detail in Section 4.2.

Exposure science describes an open system (the environment with sources, stressors and human receptors). As with all open systems, developing research strategies for which conditions are carefully controlled and varied systematically to develop a complete understanding of the important processes is not possible. Instead, conditions and variables are measured or observed and analyzed to elucidate the relationship between multiple variables at a time. An important constraint associated with working in an open system is that hypotheses about exposure can be confirmed but not proven. Observational methods provide important information for developing the science. All important parameters for describing human exposure cannot 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 to be made and interpreted. Methods for human exposure science provide many challenges, especially for personal exposure monitoring. Devices for personal monitoring need to be extremely sensitive, accurate, selective, light in weight, easy to wear and self-powered. *Observational human exposure measurement studies* (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 (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. Models are used in research to develop exposure hypotheses, synthesize data collected on the state of the system, provide explanations of factors influencing exposure and identify gaps in our knowledge for which additional data are needed. Models are used in decision making to assess exposure/dose to stressors, assess the contributions of different sources, project future conditions or trends, extrapolate to situations where observations are not available and evaluate the impacts of different policies or future scenarios. Models are also used 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 standard vocabulary and consistent set of definitions for all concepts and technical terms. Exposure science overlaps with several other disciplines, many of which use different terms for the same concepts. The definitions used throughout this document are intended to reflect the field of exposure science. Definitions of exposure, dose and related concepts are presented in Zartarian et al. (1997; 2007). In addition, a glossary intended to harmonize the terms used in chemical hazard and risk assessment, developed and published by the International Programme on Chemical Safety (IPCS), has been adopted as the official glossary of the International Society of Exposure Science (ISES) (Zartarian et al. 2005). Table 2-1 summarizes general exposure-related terms directly cited from the IPCS/ISES glossary. The concepts associated with these terms are explained 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 known as the exposure period. Exposure can be described in terms of the magnitude (amount), frequency and duration 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 can have an important impact on 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 2-1. General Exposure-Related Terms

Term	Definition
Agent	A chemical, biological or physical entity that contacts a receptor.
Exposure	The contact between an agent and the external boundary (exposure surface) of a receptor for a specific duration. Types of exposure include: *Aggregate exposure:* The combined exposure of a receptor to a specific agent or stressor from all sources across all routes and pathways. *Cumulative exposure:* The total exposure to multiple agents or stressors that causes a common toxic effect(s) to 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 number and characteristics of the population exposed.
Exposure duration	The length of time of contact with an agent.
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.
Exposure point	The location at which the receptor comes in contact with the agent.
Exposure point concentration	Provides 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: Outer exposure surfaces (e.g., the exterior of an eyeball, the skin surface, a conceptual surface over the nose and open mouth). 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.

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

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, this metric is referred to by the terms "administered," "external" or "potential" dose. Terms in Table 2-2 are defined as they are used in exposure science. Within this document, the exposure science definition of "dose"—the amount of an agent that enters a receptor after crossing an exposure surface—is used.

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. Biological markers of exposure refer to cellular, biochemical, analytical or molecular measures that are obtained from biological media such as tissues, cells or fluids and are indicative of exposure to an agent.
Dose	Types of doses include: *Applied:* amount of agent at an absorption barrier. *Biologically effective*: amount of agent that reaches the target internal organ, tissue or toxicity pathway where the adverse effect occurs. *Dose (absorbed/internal dose):* amount of agent that enters a receptor by crossing an exposure surface that acts as an absorption barrier. *Potential dose:* amount of an 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.

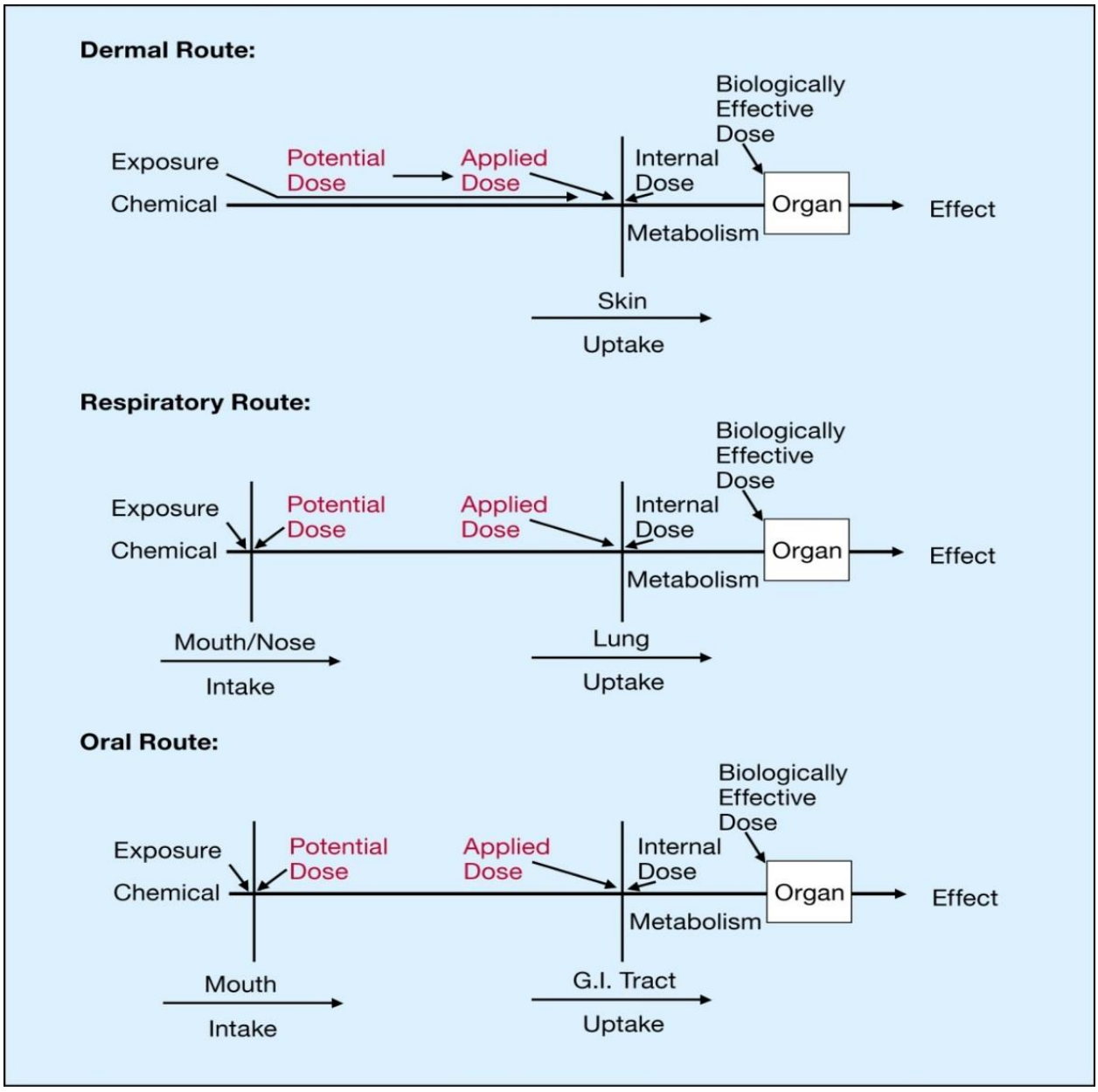
WHO (2004; 2012); Zartarian et al. (2005; 2007)

The exposure-to-dose portion of the source-to-outcome framework is expanded in Figure 2-3. 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 referred to as the chemical's bioavailability. Bioavailability can be affected by 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. 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. 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 2007l). The delivered dose is the amount of agent that is transported to the location where the adverse effect occurs. It is affected by internal processes such as transport, metabolism and excretion. The biologically effective dose is the amount of agent that reaches the target internal organ, tissue or toxicity pathway where the adverse effect occurs (Sobus et al. 2010; U.S. EPA 1992c).

Figure 2-3. Schematic of Exposure/Dose Terms



Note: Terms unique to toxicology are shown in red; G.I. = gastrointestinal.
U.S. EPA (1992c)

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 toxicity tests using blood concentration as the dose measure are used in the risk assessment, the exposure assessment also 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, biological and physical 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 needs to be taken 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 and generally is 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.
- **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* (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 and 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 are used to answer three primary questions:

1. **What are the characteristics of exposure (e.g., intensity, 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 the exposure be reduced?** Exposure assessment provides information on who is exposed and identifies the sources, routes and pathways for exposure. This information can be used to determine the most effective ways to reduce exposure and, hence, 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 can be used to monitor status and trends in exposure over time. The emphasis for these assessments is on what the exposure is at a particular time and how it changes over time. This type of assessment is used to evaluate 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 (Section 2.3.2) of the risk assessment, the risk management objectives and, in some cases, the regulatory or statutory requirements. For example, an exposure assessment can be developed to inform risk screening, priority setting, standard setting, permitting, enforcement, remediation decisions or program and policy evaluation.

Many choices can be made when selecting the approach for conducting an exposure assessment. A summary of the approaches and options for methods is given in Table 2-3. Within an exposure assessment, the choices are not mutually exclusive and several approaches can be selected. A brief description of the options in the table is provided below.

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 are used to 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. Factors that lead to chemical uptake can be used to estimate dose. 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 2012d) can be used with biomarker data (CDC 2012b) 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. Estimating exposure from biomonitoring data (Section 6.2.3) may be enhanced by modeling tools such as pharmacokinetic models and the data necessary to run these models such as physiological parameters, the biomarker measurement and information on the time between exposure and when the measurements were taken. 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. Identifying sources for exposure when multiple sources of routes exist may be difficult.

Table 2-3. Approaches for Exposure Assessments

Approach Considerations	Description	Options
Design	Determines the fundamental design of the exposure assessment	Direct Indirect Biomonitoring
Tiered approach	Considers the resources and the level of uncertainty that is acceptable	Range 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 Population based
Estimation approach	Determines how the assessment is conducted	Deterministic Probabilistic
Stressor evaluation	Determines how stressors are considered	Exposure to single stressor, single source, single pathway Aggregate exposure Cumulative exposure

Complexity—Tiered Assessments. Given the numbers of chemicals, other potential stressors or scenarios that are 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 used is based on the purpose of the assessment and on 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 be used to

evaluate large numbers of agents. Complex risk assessments, in contrast, can be used to address the most demanding problems in risk assessment. The goal is to design the exposure and risk assessment to fit the needs of the risk managers/decision makers, balancing the complexity of the assessment against time and resource constraints. Each level needs to be informed by exposure, hazard and risk management information.

- Screening-level exposure assessments are conducted to determine whether further work is needed to aid the risk management decision. These assessments are based primarily on readily available data, conservative assumptions and simple models. For example, a screening-level assessment might be used to evaluate a contaminated site to determine if additional data are needed or whether input parameters need refinement. Point estimates (i.e., single exposure values) often are used in screening-level assessments. Depending on the needs of the assessment, screening-level exposure estimates can be generated for multiple exposure scenarios.
- Exposure assessments increase in complexity, as more accuracy and precision are needed to limit uncertainty. Complex exposure assessments use sophisticated models or observational human exposure measurement studies, or both, to collect the data and exposure factors, and usually require more data. Probabilistic distributions often are used for one, some or all of the parameters in complex exposure assessments. Depending on the needs of the assessment, complex exposure estimates can be generated for actual environmental conditions or prospective or retrospective scenarios.

Population Selection—Scenario versus Population Based. Within an exposure assessment, populations can be described using either a scenario-based or a population-based approach. For the scenario-based approach, a specific receptor group of interest is defined based primarily on a distinguishable set of behaviors or locations that lead to exposure. 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. Care is taken to select exposure factors that do not result in 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 uses weighting of exposure input data and assessments are conducted for the population of interest. Input data are selected to 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 using a time-series approach may 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 as inputs to exposure equations or models. This approach most often is screening level. It can be used with conservative input variables to gain a quick estimate of potential exposures and possible concerns. Depending on the purpose, exposure estimates can be made using exposure factors that represent the high end (90th percentile), median (50th percentile) or low end (25th percentile).

Probabilistic exposure assessments use statistical distributions for input variables, parameterizing these distributions and characterizing the conditions or probabilities associated with the use of

particular distributions. Probabilistic approaches can be used to better depict the uncertainty and variability in influential input variables. The degree of complexity that is captured using a probabilistic approach can be far-ranging, depending on the number of variables that use statistical distributions, whether correlation among multiple variables (e.g., body mass, fat-free body mass, overall fitness) is maintained, and the degree to which the number and groups of receptors used in the exposure assessment are expanded. Ultimately, 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 yielded point estimates of exposure. Aggregate or cumulative assessments help describe real-world situations that consider multiple pathways and agents (aggregate and cumulative assessments) 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 ground water, inhaling volatilized chemicals while showering); and environmental sources (e.g., air, surface water, ground water, soil, sediment, fish) (ILSI 1999; U.S. EPA 1991a). Often, physiologically based pharmacokinetic or other dose models are used to combine estimated exposures from multiple sources, pathways and routes to provide a projected single dose or biologically effective dose metric. Alternatively, biomonitoring can be used to aggregate chemical stressors.

Within the Agency, multiple definitions exist for cumulative exposure and risk. The Food Quality Protection Act[2] mandates that EPA consider cumulative risk from exposure to all pesticides with common toxicity mechanisms (U.S. EPA 1996c; U.S. EPA 2002g). EPA's *Framework for Cumulative Risk Assessment* provides a more general definition that recognizes the consideration of combined risks from aggregate exposures to multiple agents or stressors, which could be chemical, biological or physical 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. 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.

2.3.4. Uncertainty and Variability in Exposure Assessments

Exposure predictions generated by models 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 factors that influence the exposure estimates are the ability to capture

[2] Food Quality Protection Act of 1996, Pub. L. No. 104–170, 110 Stat. 1489 (1996).

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 but can be accomplished with probabilistic methods such as Monte Carlo or Bayesian modeling tools. 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. In contrast to 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, uncertainty is classified in terms of three broad categories: (1) scenario uncertainty (itself consisting of several parts), (2) parameter uncertainty and (3) model uncertainty. Accounting for and describing these uncertainties are 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.

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 population. As described previously, both mass and time need to be defined and used to characterize exposure.

This section presents the route-specific equations (discrete form) and input variables that are used to estimate exposure via the inhalation, ingestion and dermal routes—the three most common exposure routes. General equations are presented here, but more detail is found in the *Draft Protocol for Measuring Children's Non-Occupational Exposure to Pesticides by All Relevant Pathways* (U.S. EPA 2001b), including equations on 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 the lungs, potentially affecting other systems of the body (target organ effect). Inhalation exposure is assumed equal to 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 take into account ADME parameters of the stressor. Larger particles can be inhaled but are less likely to reach the lowest parts of the lung (alveoli). Such particles sometimes are removed by upward movement of cilia in the lungs and swallowed. 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 1994; U.S. EPA 2009e).

In the simplest case, 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 1992c):

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

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)

For situations that are more complex such as exposure to particulate matter, deposition in the lung and exhalation also need to be considered.

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 at various locations throughout the entire gut. A chemical can directly target the tissue in the gut or be absorbed from various locations throughout 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 1992c):

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

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)

If multiple media are being considered 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. Dermal exposure primarily is caused by exposure to an aerosol, liquid, solid or contaminated surface. Liquid or solid aerosols can result in measureable exposure, but gases generally produce very low dermal exposures. 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 within which the contaminant is carried to the skin is important for estimating absorption—for example, whether the medium 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 dermal exposure is shown in the equation below:

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

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) and available measurement methods and data collected for the amount of 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. Different variations of this equation are used in the Agency (U.S. EPA 1997c; U.S. EPA 2007h; U.S. EPA 2007i).

Various programs at EPA evaluate dermal exposures using approaches specific to the needs of their program. 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 can be calculated by multiplying exposure (mass/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* (U.S. EPA 2004c) 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. It provided inputs to three fields with even earlier origins: epidemiology (Nieuwenhuijsen 2003; 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, new analytical methods were developed that would enable scientists to measure low-level, general population exposures for many chemicals. Thus, new data sources were 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 the 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), and 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 the *Guidelines for Exposure Assessment* (U.S. EPA 1992c), which describes steps to construct exposure scenarios or to collect data in field studies to estimate exposure. These guidelines make use of 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 (for example, 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 (OPPT) 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, respectively (U.S. EPA 2004a; U.S. EPA 2007e).
- Human health evaluation documents comprising the *Risk Assessment Guidance for Superfund* (U.S. EPA 1989; U.S. EPA 1991a; U.S. EPA 1991b; U.S. EPA 2001f; U.S. EPA 2001g; U.S. EPA 2004c; U.S. EPA 2007i; U.S. EPA 2009e) 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 Development's (ORD) National Center for Environmental Assessment (NCEA) has developed guidance materials for dermal exposure assessment (U.S. EPA 2000d), as has the Superfund division of the Office of Solid Waste and Emergency Response (OSWER) (U.S. EPA 2004c).
- The Office of Pesticide Programs (OPP) has updated the residential standard operating procedures (SOPs) that describe standardized scenarios for evaluating consumer product usage and other standardized behaviors for exposure analysis (U.S. EPA 2012i).

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:

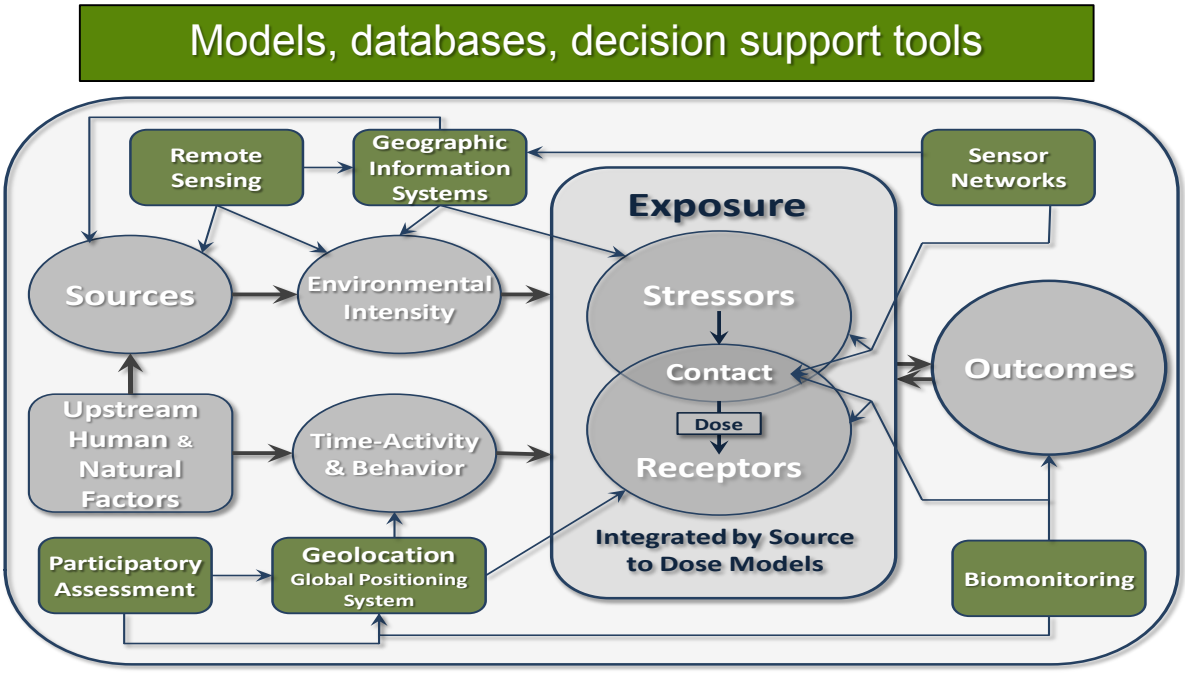
- Many more sources of exposure concentration data and information are available, ranging from national surveys and registries to small studies of individual chemicals. Some data sources are proprietary, and others are publicly available. Environmental and personal monitoring study data are available from peer-reviewed literature and are summarized in government compendia.
- The *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011f) provides information on exposure factors, activities and behaviors that might influence exposures. This handbook is updated as study data are published and made available in the peer-reviewed literature.
- 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. This was accomplished, in part, through studies such as the study of air pollution and mortality in six U.S. cities (Dockery et al. 1993); Total Exposure Assessment Methodology Study (TEAM; U.S. EPA 1987b); National Human Exposure Assessment Survey (NHEXAS; U.S. EPA 2009d); Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants Study (CTEPP; U.S. EPA 2007g); and Detroit Exposure and Aerosol Research Study (DEARS; U.S. EPA 2011a).
- Guidance specific to occupational exposure assessment is available from several sources. Ignacio and Bullock (2006) addressed the design and implementation of a strategy for occupational exposure assessment, including topics such as basic characterization, qualitative and quantitative risk assessment and priority setting, monitoring, interpretation and decision making, recommendations, reporting and evaluations. Mathematical models are used for worker exposure assessment and management (Keil et al. 2009). Guidance on applying risk assessment principles within the practice of industrial hygiene also can be used in occupational exposure assessment (Jayjock et al. 2000).
- 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, individuals' exposures to a variety of chemicals and other stressors as they perform their daily routines now can be measured and modeled. This, in turn, provides a means to identify the sources and routes of stressors of interest and the amount of exposure incurred because of personal characteristics, location and behavior. As a result, for some stressors, risk 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 (NHANES), the Centers for Disease Control and Prevention (CDC) continues to build a national database of biological levels to select chemicals (CDC 2012b). 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 Registration, Evaluation, Authorisation and Restriction on Chemicals (REACH; http://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment).

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* (2012), has created an opportunity for developing a "new" exposure science. Figure 2-4 from the NRC report 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 that can be used to better describe the multidimensional aspects of exposure;
- Expand the data landscape by developing, evaluating and applying methods for efficient monitoring;
- Advance modeling by strategically collecting data required 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; and
- Develop 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 (NRC 2012)



Looking to the future, an explosion of data is expected to characterize 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 linkage 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 potentially to reduce exposures as needed. 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. These new data, techniques and models will be incorporated into EPA's exposure and risk assessments as they are evaluated and reviewed, as appropriate, for use in Agency decisions.

CHAPTER 3. PLANNING AND SCOPING AND PROBLEM FORMULATION

Planning and scoping and problem formulation are the first steps in the risk assessment process. The purpose, scope, approach, participants, level of effort and resources for the risk assessment are established at this stage (U.S. EPA 2002f; U.S. EPA 2014b). Planning for the risk assessment needs to be designed around the decisions that the assessment is intended to inform. Multiple challenges and requirements could arise when conducting a risk assessment. For example, an assessment completed as part of a regulatory action could have various legal considerations, including the statute under which it is being conducted (e.g., Clean Air Act,[3] Clean Water Act[4]) and the regulatory program of which it is a part (e.g., Six-Year Review of Drinking Water Contaminants under the Safe Drinking Water Act,[5] Pesticide Registration Review, Risk and Technology Review program). Such legal considerations could influence specific aspects of the assessment.

As with EPA's *Human Health Risk Assessment Framework to Inform Decision Making* (http://www.epa.gov/raf/frameworkhhra.htm), the *Guidelines for Human Exposure Assessment* incorporates the "fit for purpose" concept to ensure that risk assessments are designed to maximize the utility of their intended purpose in Agency decision making. *The Human Health Risk Assessment Framework* elaborates on the concepts of planning and scoping, including consideration of stakeholder involvement, peer review and problem formulation.

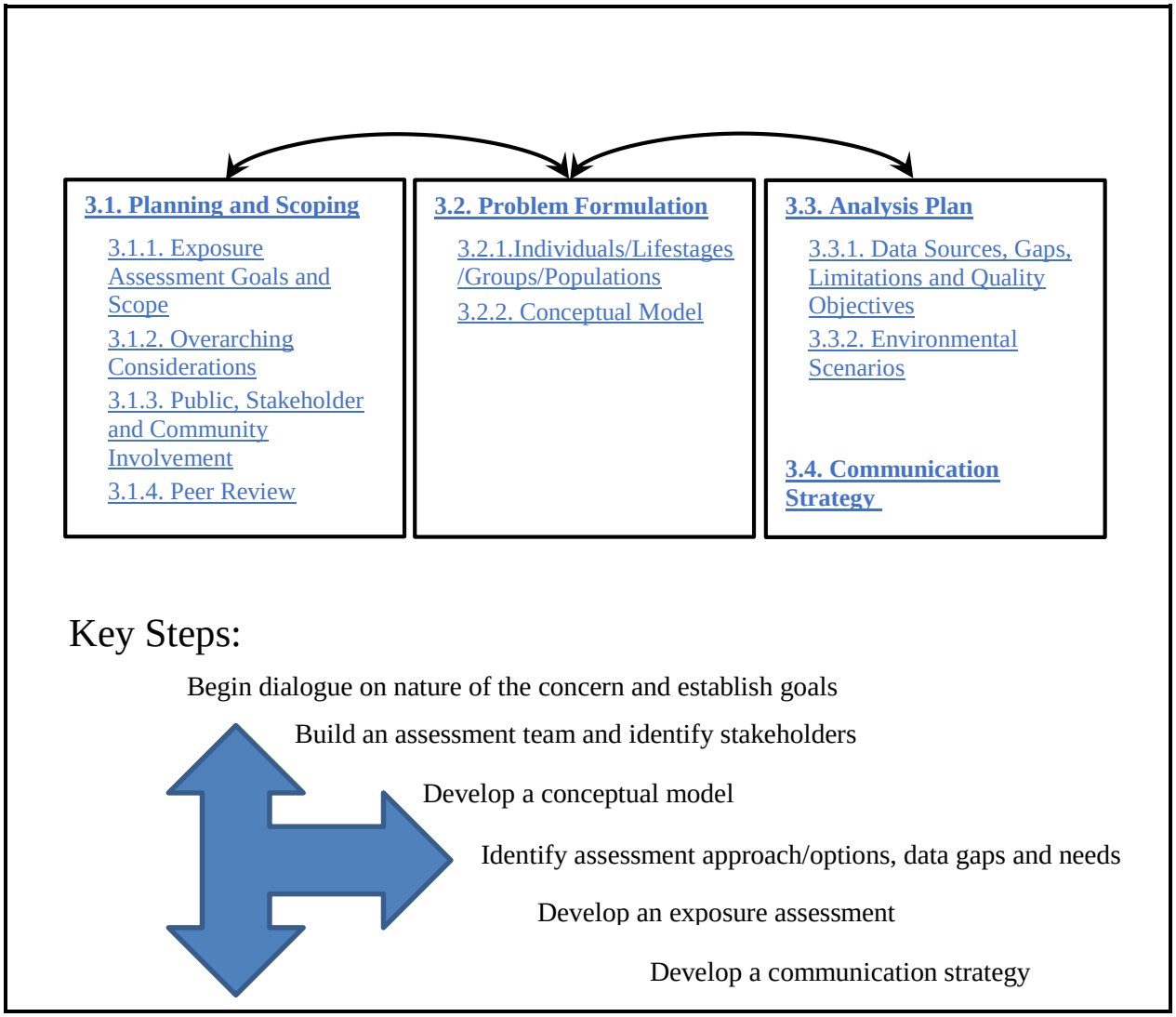
The level of complexity of the planning and scoping process is commensurate with the complexity of the risk assessment—from screening level to complex—being conducted. EPA programs might implement specific planning and scoping and problem formulation requirements to meet their programmatic needs. Risk assessors are encouraged to consult with their programs and follow the standard operating procedures (SOPs) regarding appropriate planning and scoping and problem formulation activities.

Planning and scoping and problem formulation related to exposure assessment within the risk assessment process involve a series of interrelated and iterative steps. These steps are presented in Figure 3-1, and this chapter presents guidance for each:

- Planning and scoping (Section 3.1);
- Problem formulation (Section 3.2);
- Develop an analysis plan (Section 3.3); and
- Begin defining a communication strategy (Section 3.4).

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

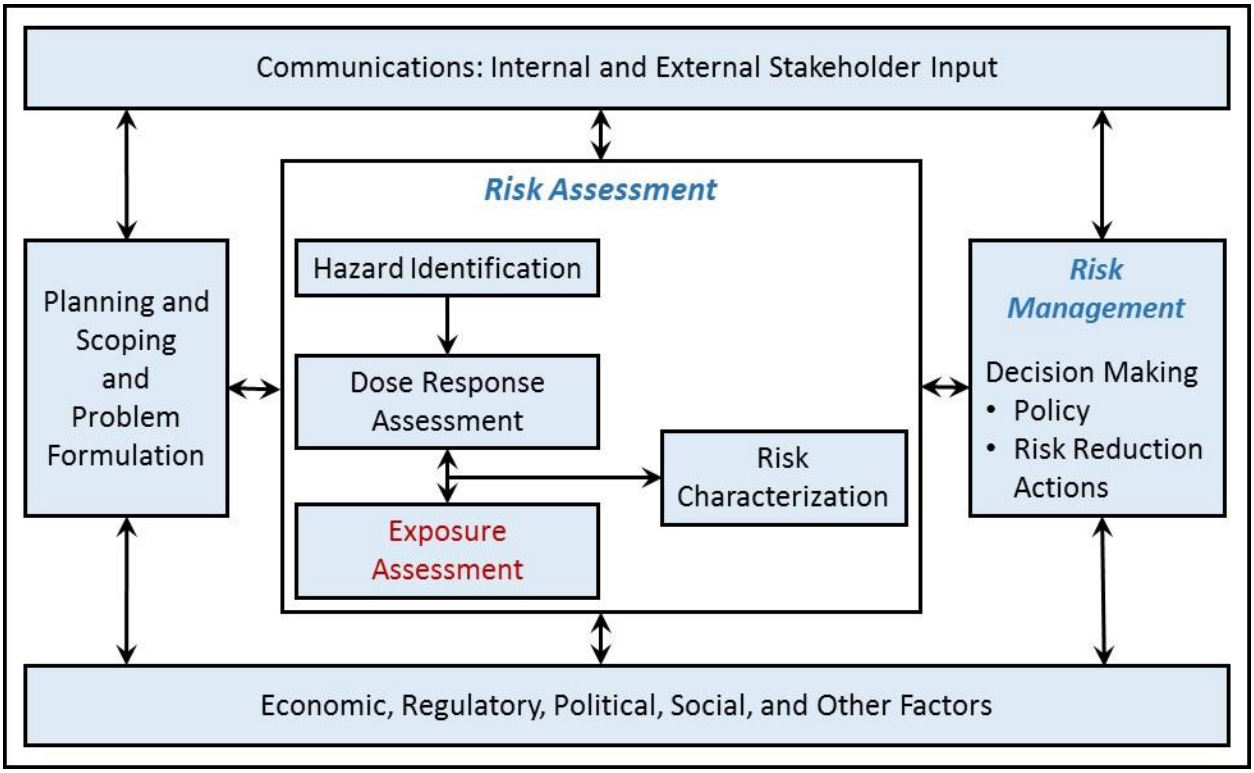
Figure 3-1. Planning and Scoping and Problem Formulation for Exposure Assessment



Adapted from U.S. EPA (2002f)

The nature and sequence of steps in the assessment will be driven by factors specific to a given exposure assessment, such as resources, regulatory drivers and public and stakeholder considerations. 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 and risk assessment, the planning and scoping and problem formulation process might need to be revised or updated (Figure 3-2).

Figure 3-2. The Overall Risk Assessment Process



Adapted from NRC (2009)

3.1. Planning and Scoping

Planning and scoping is an essential and integral part of an exposure assessment. A systematic and transparent planning and scoping process promotes:

- Efficient time and resource management;
- Agreement among the exposure assessor, risk assessor and risk manager/decision maker on the purpose of the exposure assessment;
- Communication within the risk assessment team and with stakeholders;
- Buy-in and realistic expectations on the part of stakeholders and other interested parties;
- Better-informed decisions that use high-quality data, and are based on established objectives and use scientifically established methods;
- Participation from multiple disciplines as a means of ensuring that the scope and degree of scientific complexity will adequately inform the exposure assessment question(s); and
- Documentation of what decisions were made and the rationale behind the decisions.

A team approach to planning exposure assessments can be beneficial (NRC 2009; U.S. EPA 2002f). For routine screening-level exposure assessments conducted in accordance with established SOPs, a project team might not be required; but for assessments that are more complex, 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, the risk assessor and the risk manager/decision maker. The composition of the team reflects the

specific expertise required during various parts of the exposure assessment and planning discussion. For example, the risk manager/decision maker might identify the regulatory needs of the risk assessment, timeframes and quantity of resources available for the analysis. The project team might focus on evaluation of the current and future concentrations of the contaminants in various media. An exposure assessor could help the team consider the nature of the contaminants, as well as understand potential sources, routes and pathways of contaminants, environmental fate, the extent of contamination and the availability of data at the national level or local level.

3.1.1. Exposure Assessment Goals and 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 that the exposure assessment seeks to address. The goal is to develop the dimensions and elements of the exposure assessment and clearly define the objectives. Information gathered during this goal-setting stage helps an exposure assessor answer questions such as the following: What questions need to be addressed by the exposure assessment? Why is an exposure assessment necessary? How will the assessment results be used? What resources and expertise will be needed? What is the timeframe? The goals of the exposure assessment determine its scope.

The most defensible assessments are those that are conducted with a clearly articulated goal and well-defined questions. Exposure assessments are conducted for many reasons, including use in risk assessment, status and trends measurements, mitigation, regulatory decisions, priority setting and epidemiological study support. More specific goals for an exposure assessment might include identifying exposed individuals/lifestages/groups/populations, including disparities in exposure; screening chemicals for potential exposure and identifying the source(s) of contamination; defining exposure pathways, fate and transport and routes of exposure; and assessing temporal considerations.

A thorough understanding of the purpose of the exposure assessment is necessary so that the information evaluated and derived is useful in meeting the established goals. The particular purpose for which an exposure assessment will be used (e.g., location-specific versus regional or national decision) and availability of data often have significant implications for the scope, level of detail and approach of an exposure assessment. 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 2014b)?

Care needs to be taken to reconcile the limitations of the scope with the questions to be answered. 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, a willingness to accept a higher level of uncertainty in the analysis through the application of default assumptions rather than

applying empirical data, or delaying the assessment pending the completion of studies to provide the data. Thus, defining the scope of an exposure assessment is a process that can include both analytical and deliberative aspects.

Reasons to limit 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 to be 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. Such judgments and approximations are presented in both the exposure assessment and risk characterization, along with their implications.

Given time and resource constraints on Agency products, a premium is placed on efficiency, cost-effectiveness and focus in the exposure assessment process. The complexity of the approach is based on the purpose of the exposure assessment and on 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 might require few resources and can be used to evaluate large numbers of agents. Complex risk assessments, in contrast, might be used to address the most challenging problems in risk 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.

Screening-level exposure analyses often are used during the initial phase of an exposure assessment. At this point, little location- or scenario-specific information typically is available, and an exposure assessor relies on default values that are selected so that analyses 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 bounding estimate scenario, assessors, risk managers/decision makers and stakeholders can be confident that the exposure evaluated is not a concern (U.S. EPA 2004b). 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; Section 8.3). These approaches, however, more often are used 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 approach of the exposure assessment. Aggregate exposure assessments (described in Section 2.3.3) are required under the Food Quality Protection

Act,[6] Safe Drinking Water Act,[7] Clean Air Act[8] and other regulatory programs. Various statutes require assessment of cumulative exposure (described in Section 2.3.3) to assess cumulative risk: The 1996 Food Quality Protection Act requires assessments based on multiple pesticides with a common mode of action, whereas the 1970 National Environmental Policy Act (NEPA)[9] requires broader based cumulative assessments that consider multiple chemical and nonchemical stressors.

More complex exposure assessments can 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 use observational human exposure measurement studies to collect data and exposure factors. Probabilistic distributions often are used for one, some or all of the parameters in complex exposure assessments.

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 define the resources and time that can be expended to obtain and analyze 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; 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 provide a systematic and transparent format and content for risk communication (U.S. EPA 2014b).

3.1.2. Overarching Considerations

Among the overarching themes that often are addressed in EPA's risk assessments are children's environmental health protection, cumulative risk assessment, environmental justice and sustainability. Although these overarching 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. That exposure assessors are cognizant of these overarching themes is essential so that they consider them during the planning and scoping process. Consideration of lifestage, susceptibility and environmental justice are addressed more fully in Chapter 4.

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

3.1.3. Public, Stakeholder and Community Involvement

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 2003f), a framework for implementing it (U.S. EPA 2003e) and other references are available at EPA's *Public Involvement Policy and Related Documents* website (U.S. EPA 2013a). Involving risk managers/decision makers, stakeholders and exposure assessors up front is critical to evaluating the exposure assessment question(s) fully and ensuring that the design of the exposure assessment supports the agreed-upon objectives. Communication and dialogue with community members need to be established in the initial phases of an exposure assessment. 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." The involvement of stakeholders (potentially interested or affected parties) helps ensure that the exposure assessment process is transparent and that risk-based decision making proceeds effectively, efficiently and credibly (NRC 2009).

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

Public Involvement refers to the full range of activities that EPA uses to engage the American people in the Agency's decision-making process (U.S. EPA 2011i).

Stakeholders are individuals or representatives from organizations or interest groups that have a strong interest in the Agency's work and policies (U.S. EPA 2011i).

- ***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 members (U.S. EPA 2011i).

The development of exposure assessments for regulatory decisions might be required to follow administrative procedures in which the process to engage stakeholders is clearly defined and described. Stakeholders can 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 nonregulatory). For routine or well-defined screening exposure assessments, input during planning and scoping might not be necessary, whereas for an exposure assessment that might be considered controversial, early stakeholder involvement is recommended. For community-based or location-specific exposure assessments, seeking and encouraging community involvement is important. In some cases, continuing dialogue with the community is encouraged throughout the process. Each project plan needs to 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 that the community could be aware of unique activities or practices that might result in higher or lower exposure assumptions than the default exposure assumptions used in an exposure assessment. Members of these groups who might be directly affected by the outcome of an exposure assessment can provide first-hand accounts of exposures and health concerns. Types of information that 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); and
- Highly exposed or susceptible population groups (e.g., subsistence activities, occupational exposure).

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 2005g).

Community involvement activities are essential to meeting data quality guidelines (U.S. EPA 2002e), improving transparency of the exposure assumptions and, ultimately, building trust and credibility with the community. Information and suggestions regarding community involvement in the Superfund process (U.S. EPA 2005g) can be helpful for other Agency exposure and risk assessments. Links to some relevant community involvement resources are provided in Box 3-2.

3.1.4. Peer Review

Peer review is a documented critical review of a specific Agency scientific or technical work product, conducted to ensure that activities are technically supportable, competently performed, properly documented and consistent with established quality criteria. It is conducted by qualified individuals or organizations that are independent of those who performed the work and are collectively equivalent in technical expertise to those who performed the original work (i.e., peers). 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. It is encouraged during the early stages of the project or as part of the culmination of the work product, as appropriate (U.S. EPA 2015).

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 (2000b) *Presenter's Manual for "Superfund Risk Assessment and How You Can Help." A 40*-Minute *Videotape*. EPA/540/R-99/013.
- U.S. EPA (2001h) *Stakeholder Involvement and Public Participation at the U.S. EPA: Lessons Learned, Barriers, and Innovative Approaches*. EPA/100/R-00/040.
- U.S. EPA (2005g) *Superfund Community Involvement Handbook*. EPA/540/K-05/003.
- *Citizen Involvement in Source Water Protection* website. U.S. EPA. Includes community resources on protecting drinking water and source water at the community level. http://water.epa.gov/infrastructure/drinkingwater/sourcewater/protection/citizeninvolvementinsourcewaterprotection.cfm.
- *Environmental Health Resources for Community Members* website. U.S. EPA. http://www.epa.gov/communityhealth/publicparticipation.html.
- *Community Involvement* website. U.S. EPA. Includes community resources, community involvement policies and guidance and Superfund community involvement publications. http://epa.gov/superfund/policy/remedy/sfremedy/cominvolve.htm.
- *Plain English Guide to the Clean Air Act* website. U.S. EPA. http://www.epa.gov/airquality/peg_caa/index.html.
- *Public Involvement Policy* website. U.S. EPA.
- *Public Participation Process for Registration Actions* website. U.S. EPA. http://www.epa.gov/pesticides/regulating/public-participation-process.html.

During the planning and scoping process, the risk manager/decision maker might need to determine whether any analyses or products of an exposure assessment require peer review independently or as part of the overall risk assessment peer review. Evaluating potential peer-review requirements early will help ensure that adequate resources are allocated. In addition, peer-review considerations are an integral part of setting exposure assessment milestones and schedules.

EPA's *Peer Review Handbook* (U.S. EPA 2015) 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 all influential scientific and technical work products used in decision making will be peer reviewed. The Office of Management and Budget (OMB) 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 controversial 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 controversial methodological or scoping issues would need to be peer reviewed. In general, conceptual models and exposure assessment plans are candidates for peer review (U.S. EPA 2015).

Exposure assessment products also could be the subject of public comment, as required under specific regulatory programs. Public commenters generally include a wide range of interested parties, both experts and nonexperts, but are not expected to provide the kind of independent, expert information and in-depth analyses obtained from the peer-review process

(U.S. EPA 2015). An exposure assessment also might benefit from other types of review such as peer input. The risk manager/decision maker needs to consider whether these types of reviews need to be included and factored 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. The problem formulation concept has been integrated into standard Agency practices 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 2012g) and *Framework for Human Health Risk Assessment to Inform Decision Making* (U.S. EPA 2014b). Problem formulation continues to be emphasized as an integral component of any exposure assessment planning activity (NRC 2009). Problem formulation represents a systematic planning step that identifies major factors to be considered 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.

As the assessment proceeds, the exposure assessor needs to keep the risk assessor and risk manager/decision maker apprised of the progress and periodically revisit the analysis plan to determine whether changes are needed.

Three components comprise problem formulation: identification of the population of concern around which the assessment is conducted (e.g., general population, infants or nursing mothers, the elderly); a conceptual model that presents the anticipated pathway of the agent from source to the population of concern; and an analysis plan that lays out the approach for conducting the assessment.

3.2.1. Individuals/Lifestages/Groups/Populations

An important aspect of an exposure or risk analysis is the approach to representing the receptor (Chapter 4). For a scenario-based 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/population to a potentially greater exposure concentration or dose. Scenario-based approaches commonly are used for several purposes, can be implemented for deterministic (point) estimates or might sometimes also involve probabilistic analyses for a set of exposure factors.

Population-based approaches commonly are used when information on the broader context of exposures is needed. In contrast to scenario-based approaches, a population-based approach frequently incorporates probabilistic methods with an objective to better estimate interindividual variability in exposures or dose.

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) into lifestages or discrete populations for an exposure assessment. Exposure

assessments need to identify and understand those conditions that lead to the highest concentrations and resulting exposures and those situations that lead to exposure for the most susceptible individual/lifestage/group/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.

Methodologies that can be used to select specific populations include traditional methods (Section 4.4.1), case studies (Section 4.4.2), neighborhood methods (Section 4.4.3), population-based methods (Section 4.4.4) and social process methods (Section 4.4.5). Exposure assessments of selected individuals/lifestages/groups/populations can be performed at the national and local levels (Section 4.4.6). When identifying potential differences in the general population due to socioeconomic status, exposure assessors might consult social scientists, geographers, demographers and social epidemiologists.

Individual risks frequently are calculated 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 1987b; U.S. EPA 2007g; U.S. EPA 2009d; U.S. EPA 2009e; 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. Guidance specific to assess differential exposure due to occupation is available from several sources (Ignacio and Bullock 2006; Jayjock et al. 2000; Keil et al. 2009).

3.2.2. Conceptual Model

The conceptual model is a planning tool that can be used for various types of exposure assessments, including site-, location- and national-scale problems/assessments. The conceptual model maps out a framework designed to demonstrate 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.

The conceptual model is developed at the start of a project and 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 will the exposure outputs be linked to the health endpoints?
6. **Timeframes of exposures:** What are the relevant timeframes—frequency, duration, intensity and overlap of exposure intervals—for a stressor or mixture of stressors?
7. **Exposure-to-dose considerations:** What is known about the toxicokinetics? How is this influenced by factors such as lifestage, race, sex and genetics?

Identifying health effect endpoints and exposure-to-dose considerations is part of the hazard identification step of a risk assessment, which precedes the exposure 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.

The conceptual model can take a variety of forms, such as a flow diagram or a pictorial depiction incorporating data, models and hypotheses. The graphical display can be accompanied by a detailed narrative explaining the rationale for the elements and their linkages, including the risk management options.

Sources

Among the first steps in developing a conceptual model is to identify possible sources of the agent(s). In some cases, the source might not be known. In addition, whether the source is a point source (e.g., discharge from a pipeline) or nonpoint source agent (e.g., runoff from a field) is important. Identifying the source can improve the ability to quantitatively estimate the releases and predict exposure better.

Pathways, Fate and Transport and Routes of Exposure

The conceptual model describes the relevant exposure pathways and routes of exposure, and the fate and transport of stressors 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., dichlorodiphenyltrichloroethane [DDT] degrades to dichlorodiphenyldichloroethylene [DDE] and dichlorodiphenyldichloroethane [DDD]). Photolysis; reactions with other chemicals in air, water or soil to form new chemicals; microbial degradation; or adsorption onto the medium also can occur. 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.

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. Analysis Plan

Exposure assessments can be conducted at various levels of technical detail. Sometimes more than one approach is used to estimate exposure. For example, the Total Exposure Assessment Methodology Study (TEAM) combined point-of-contact measurements, the microenvironment (scenario evaluation) approach and breath measurements for the reconstruction of dose approach (U.S. EPA 1987b). The intended use of an exposure assessment generally will favor one approach to quantifying exposure over others or suggest that two or more approaches be combined. The analysis plan specifies the technical aspects of conducting an exposure assessment. In developing the 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. Resources for technical study design for different types of data acquisition approaches are presented in Box 3-3.

Box 3-3. Resources for Technical Study Design

Data Acquisition

- **Database Design** (U.S. EPA 2011b).
- **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, an 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, additional documentation might be needed. This documentation includes describing the strategies for sampling (e.g., purpose, design, quality objectives/control measures), modeling (e.g., needs, goals, availability of input parameters, use of the model outputs in the exposure assessment) and communications (e.g., personnel involved, types of communication planned and scheduled) (Section 6.1).

3.3.1. Data Sources, Gaps, Limitations and Quality Objectives

The approach selected for an exposure assessment will determine what data and information are needed. As part of the 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, exposure areas, the extent of contamination and the availability and representativeness of data at the national, regional or local levels.

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

The analysis plan also specifies data quality objectives (DQOs) and quality assurance (QA) 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), DQOs are a set of performance and acceptance criteria that ensure that newly collected and existing data, respectively, are of sufficient quality and quantity to address the project's goals (Section 5.2).

Data Sources

A wide range of existing data can support an exposure assessment. When developing the 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.

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 • Local survey data • Site assessments	• Emission inventories • Product information	• Historical environmental sampling data (e.g., air, water, soil, biota) • Personal monitoring data	• Surveys of activity patterns used to establish exposure factors • Land use (current, planned) • Climatic or meteorological data • Hydrogeology data	• Toxicological data • Bioconcentration /bioaccumulation data • Physiologically based pharmacokinetic models	• Activity patterns • Physiological parameters

The topic of availability and quality of data is addressed in Chapter 5.

3.3.2. Environmental 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 scenarios are created to aid exposure assessors in estimating human exposure to chemicals in their environment. These might include the source, exposed population (e.g., young children), timeframe of exposure, routes and pathways of exposure, microenvironment(s) and activities. The term microenvironment refers to surroundings (e.g., home, office, automobile) that can be treated as homogeneous or well characterized in the concentrations of an agent. People can be exposed to a variety of potentially harmful chemicals in the air they breathe, food they eat and products they use and by skin contact with treated or contaminated surfaces. Examples of sources could be 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 potential future exposure scenarios because land use and associated activities can change over time.

3.4. Communication Strategy

Communication strategies routinely begin before an exposure assessment is conducted and commonly continue throughout the process (Superfund Community Involvement Handbook, U.S. EPA 2005g). When appropriate, early and continuous communication with the community provides the opportunity for an exposure assessor to learn about the community's concerns, identify potential sources of exposure data, establish a relationship with local and state environmental and health agencies and work with local and state elected officials. This initial coordination also provides insights into community preferences for communication (e.g., availability sessions, local newspapers, blogs).

As the output of the planning and scoping process, the exposure assessment analysis plan describes the technical details for conducting the exposure assessment. It needs to be reevaluated throughout the life of the exposure assessment to ensure appropriate risk management decisions. An exposure assessment plan need not be a lengthy or formal document, especially for assessments that are routine or well established. For complex exposure assessments, a written plan is useful. 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.

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 and populations. 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 can 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. Addressing one or more contributors of human vulnerability and susceptibility in exposure assessment presents a challenge. The public, however, expects EPA to make advancements in developing exposure (and risk) assessments that better reflect reality, which is consistent with recommendations from the EPA Science Advisory Board and the National Academy of Sciences (NAS) (NRC 2009; NRC 2012; SAB 2000). Tools and methods are available and continue to be developed to incorporate these vulnerability factors in exposure (and risk) assessment and are being applied, particularly by academic researchers and some state agencies. Programs might need to tailor their approaches to incorporate population-specific issues in exposure assessments to meet their regulatory, program or policy needs.

In assessments involving potentially vulnerable populations, economic, public health and other factors can be considered along with environmental conditions (Section 3.2.1). Identifying highly exposed groups or characterizing exposures of specific populations can help target interventions to reduce or eliminate exposures. Considering vulnerability and susceptibility when making risk management decisions is important to protect not only the general population but also those populations at greatest risk (U.S. EPA 1995b; U.S. EPA 2010a). As appropriate, exposure assessors identify and characterize those conditions that lead to the highest stressor intensities and resulting exposures and those situations that lead to exposure for the most susceptible receptors (U.S. EPA 2009a).

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); and
- Identifying sensitive populations for exposure assessment (Section 4.4).

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 and risk assessments (Box 4-1). Additional information related to consultation and policies related to working with Indian tribes is found at http://epa.gov/tribal/basicinfo/presidential-docs.html. Provisions in the Food Quality Protection Act of 1996, the Safe Drinking Water Act Amendments of 1996 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 and Agency Policies

- **Executive Order 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; and
  - Identify and address disproportionately high and adverse human health or environmental effects of its programs, policies and activities on minority and low-income populations.
- **Executive Order 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 (OMB) Office of Information and Regulatory Affairs for review:
  - An evaluation of the environmental health or safety effects of the planned regulation on children; and
  - An explanation of why the planned regulation is preferable to other potentially effective and reasonably feasible alternatives the Agency is considering.
- **Executive Order 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.

In addition, a growing body of literature (e.g., Agency guidance documents, government reports, scientific articles, reports by environmental health and justice advocates) highlights the importance of evaluating differences in exposures (especially aggregate exposures) among sociodemographic groups and taking into account the social, cultural, economic and political context in which these exposures occur (Box 4-2).

4.2. Vulnerability and Susceptibility in Exposure Assessment

Environmental exposures and health risks are not distributed randomly across the landscape, and in some cases, environmental exposures and health risks are concentrated among certain population groups and in potentially vulnerable communities. The population characteristics related to vulnerability and susceptibility are important because the combination of these factors in conjunction with the toxicity of environmental contaminants could translate into increased health risks. The planning and scoping phase of the exposure assessment is the optimal point for

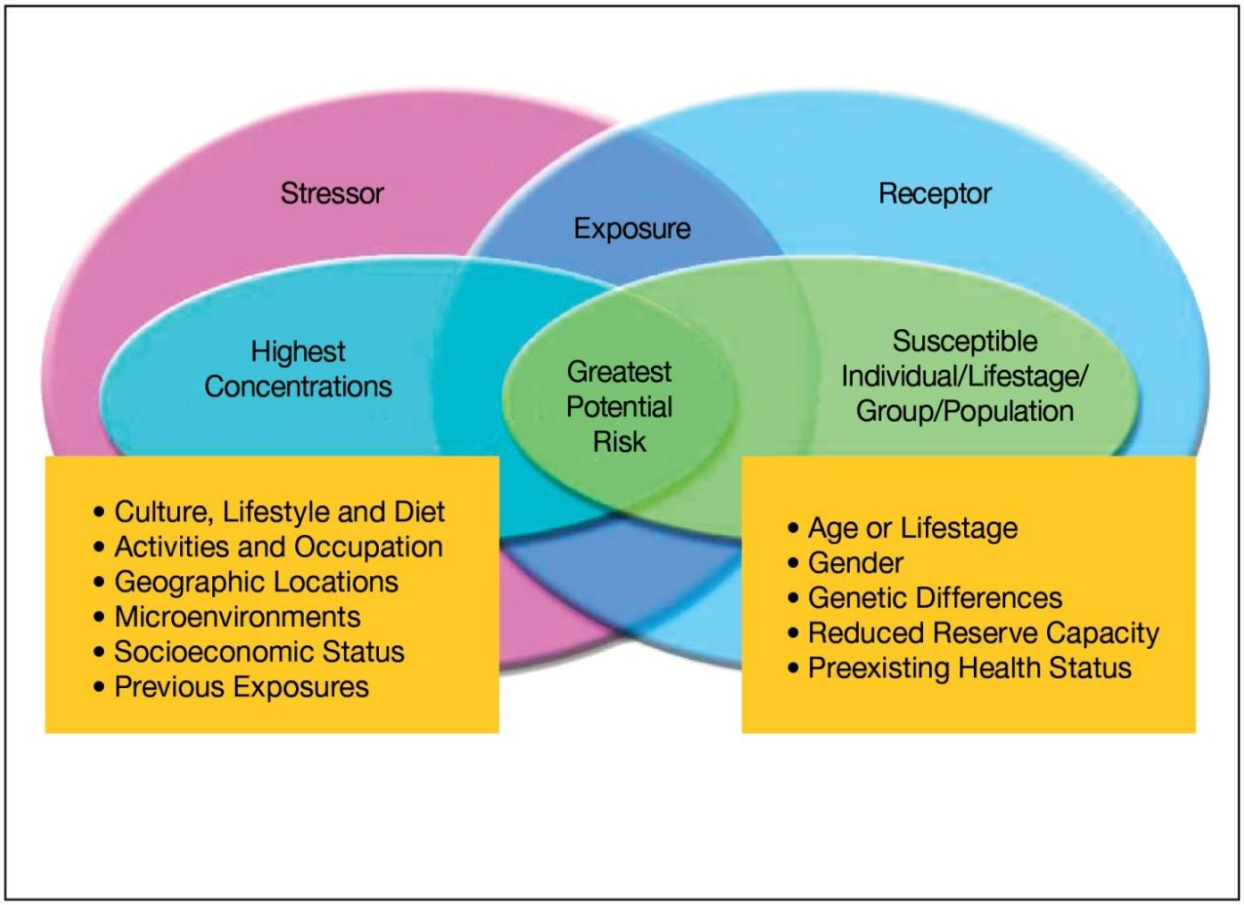
the exposure assessor to outline the approach that will be taken to identify and consider population vulnerability and conceptualize the linkages to health risk and risk assessment (Chapter 3). Figure 4-1 depicts vulnerability and susceptibility factors in exposure and risk assessment.

Box 4-2. Resources on Disparities in Exposure

- NRC (1993) *Pesticides in the Diets of Infants and Children.* Recommends policy changes to reflect children's health factors in evaluating environmental risks.
- U.S. EPA (1999b) *Sociodemographic Data Used for Identifying Potentially Highly Exposed Populations*. EPA/600/R-99/060. A companion document to the U.S. EPA (2011f) *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 and risk 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 (2011f) *Exposure Factors Handbook: 2011 Edition.* EPA/600/R-09/052F.
- U.S. EPA (2011h) *Plan EJ 2014*. A roadmap for integrating environmental justice into the Agency's programs, policies and activities.
- *Tribal Science Priorities* website*.* U.S. EPA. Presents environmental and health priorities identified by the National EPA-Tribal Science Council. http://www.epa.gov/osp/tribes/priorities.htm.
- *Environmental Justice* website. U.S. EPA. Presents information for environmental justice considerations for healthy environments and communities. http://www.epa.gov/environmentaljustice/.
- EPA-Expo-Box, an online toolkit to assist individuals in government, industry and academia and the public with assessing exposure. http://www.epa.gov/risk/expobox/index.htm.

Within the context of populations of concern, vulnerability refers to characteristics of individuals or populations that place them at increased risk of an adverse health effect. Vulnerability includes economic, demographic, social, psychological and physical states of the receptor that influence patterns of exposure to environmental contaminants or alter the relationship between the exposure/dose of environmental contaminants and the health effect of the exposed individual or population (ATSDR 1997; deFur et al. 2007; U.S. EPA 2003d). Susceptibility, a component of vulnerability, refers to the increased likelihood of an individual or population to be more affected by a stressor 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).

Figure 4-1. Vulnerability and Susceptibility Factors



Adapted from U.S. EPA (2009a)

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 a stressor. For example, an individual or population group might be more likely to show a response to a stressor 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, the elderly, pregnant women)).
- **Differential exposure:** Differences in exposure (e.g., magnitude, duration, frequency, pathway, route) from a variety of factors, including lifestage, socioeconomic status, occupation and cultural characteristics. For example:
  - Children might have a higher exposure and proportionately higher body burden of pesticides than adults because of their patterns of behavior 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 stressors.
- **Differential ability to recover:** Refers to resources and coping systems, such as income level, ability to move away from an affected area or access to health care, which can affect recovery from the effects of a stressor.

Environmental exposures and health risks are not distributed randomly across the landscape, and in some cases, have been concentrated among certain population groups and in potentially vulnerable communities (http://ajph.aphapublications.org/toc/ajph/101/S1). Considering vulnerability or susceptibility is important because the combination of these factors with the toxicity of environmental contaminants might translate into increased health risks. The planning and scoping phase of the exposure assessment is the optimal point for the exposure assessor to outline the approach that will be taken to identify and consider population vulnerability and conceptualize the linkages to health risk and risk assessment (Chapter 3).

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

Sections 4.3.1 to 4.3.7 present detailed discussions on exposure concerns for lifestages (particularly children), 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 population groups. Note that the concerns described under one section might overlap with another. For example, an exposure assessment might focus on children in a poor rural community or might need to consider both socioeconomic disadvantages and cultural differences related to tribal populations.

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 population 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 population group, the Agency has moved toward viewing childhood as a sequence of lifestages from conception through fetal development, infancy and adolescence.

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 October 2013, EPA reaffirmed its support of this important policy. Since fall 1996, the Agency has followed a seven-step *National Agenda to Protect Children's Health from Environmental Threats* (U.S. EPA 1996b).

The Agency has developed guidance on selecting age groups to consider when assessing childhood exposure to and potential doses of environmental contaminants (U.S. EPA 2005c). Diet and behavior change with lifestages, for example, young children have proportionately greater milk and fruit intake compared to adults. 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 include pregnancy, nursing and old age. For each of these lifestages, exposures typically differ from those of an adult. For example, during pregnancy, eating habits and nutritional needs change; during the third trimester, mobility often is impacted, 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 often become reduced. In addition, aging can affect the body's capacity to defend against toxic stressors. During the planning and scoping process (Section 3.1), an exposure assessor considers whether establishing dialogue with toxicologists/health scientists is needed to consider specific "windows of susceptibility" in an exposure or risk assessment. For example, a window of susceptibility in development during which an agent causes the greatest effect, a description of that period and an estimate of the exposure during that window are important in better informing the risk assessment. If data exist that support early life exposures leading to effects later in life, the exposure and risk assessor can discuss them during the planning stage.

4.3.2. Childhood

In 1993, the National Research Council (NRC) issued the report *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's report provided the impetus for Executive Order 13045 (Clinton 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, EPA is investigating ways to improve methods for conducting risk assessments for children.

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 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 of body weight than adults. Young children play close to the ground, come into contact with contaminated soil outdoors, come into contact with contaminated 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 2011f).

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 (e.g., Braun and Hauser 2011; Guan et al. 2010; Lin et al. 2011; Perera and Herbstman 2011; Perera et al. 2006; Rothenberg et al. 2011; Whyatt et al. 2009). Similarly, chemical concentrations in the mother's breast milk are important in determining exposure of nursing infants and young children (LaKind et al. 2009). 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 polychlorinated biphenyls (PCBs) 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 and risk 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. 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 Set of Childhood Age Groups for Monitoring and Assessing Childhood Exposures

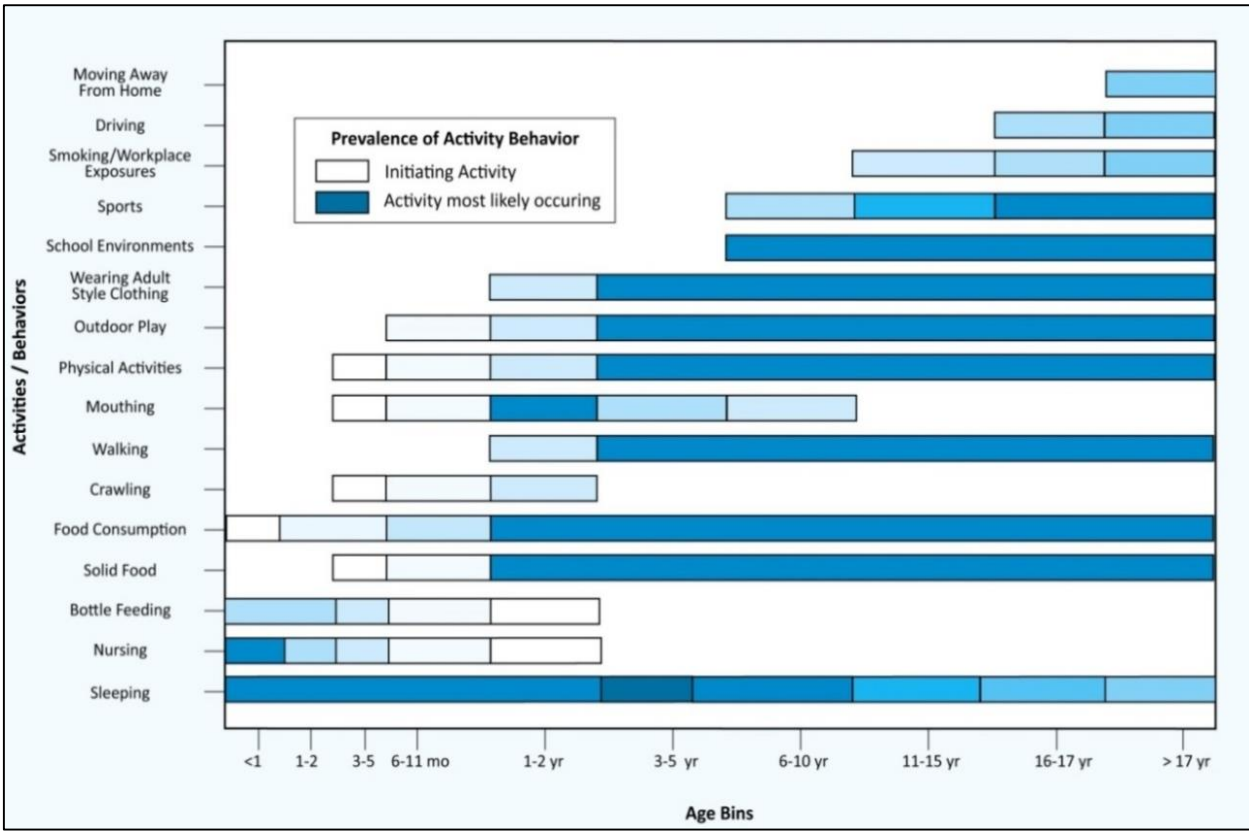
Age Groups <1 Year	Age Groups ≥1 Year
Birth to <1 month 1 to <3 months 3 to <6 months 6 to <12 months	1 to <2 years 2 to <3 years 3 to <6 years 6 to <11 years 11 to <16 years 16 to <21 years

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. Lifestages considered need to match the periods of greatest susceptibility.
- U.S. EPA (2011f) *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; and
  - Duration of lifetime.

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



Adapted from WHO (2006)

4.3.3. Other Lifestages

An exposure assessor considers the activities of the population of concern and ages of the participants engaged in those activities. Pesticide exposures from playing golf on treated turf are relatively age independent. Exposures to indoor air pollutants from spending time indoors might be greater at the extremes of age: the very young and very old.

Examples of available resources and ongoing research associated with other lifestages include:

- EPA provides information on its efforts to protect the environmental health of older persons on its *Aging Initiative* website, http://www.epa.gov/aging/.
- 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 2007k) summarizes the discussions held during the workshop, highlights several sources of existing data and provides recommendations for additional research. This panel agreed that aged individuals 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* (McCurdy 2010) 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.

4.3.4. 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 and appropriate (U.S. EPA 2005h). Historically, cancer risks have been assessed assuming 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 old (U.S. EPA 2005h). 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 fetal, childhood, adulthood and old age and averaging across the total exposure period.

Table 4-2 presents the exposure duration and potency adjustments for the recommended set of childhood age groups (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 (for example, the Office of Solid Waste and Emergency Response's [OSWER] *Handbook for Implementing the Supplemental Cancer Guidance at Waste and Cleanup Sites*, available at http://www.epa.gov/swerrims/riskassessment/sghandbook/index.htm).

Table 4-2. Integrating Childhood Age Groups Used for Assessing Exposure and Potency for 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)	Potency Adjustment (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×

4.3.5. Tribal Populations

The U.S. Government recognizes more than 500 tribal governments as sovereign entities (U.S. DOI 2013). The land base of American Indian and Alaska Native tribes in the United States is varied from no land base to more than 14 million acres. The total land base is about 71 million acres, which is about 4 percent of the land of the United States (U.S. 2010 Census and tabulated by U.S. EPA American Indian Environmental Office).

According to the 2010 U.S. Census, 5.2 million people in the United States are identified as American Indian and Alaska Native (Norris et al. 2012). The 5.2 million is assumed to include individuals who are not currently citizens or members of at least one of the federally recognized tribes. From this census, the total number of American Indians and Alaska Natives who live on or near the tribal areas of federally recognized tribes in 2010 was 1,969,167. Many tribal people, whether they live on or near their tribal areas, maintain their traditional cultural way of life occasionally visiting their tribal homeland and participating in cultural activities, including hunting, fishing, plant gathering and ceremonies (U.S. DOI 2014).

This section provides background, important considerations, examples and references for an assessor to consider when planning and conducting an exposure assessment in areas with affected tribal populations.

Unique Exposure Issues and Scenarios for Tribal Populations

Assessors need to be aware of issues unique to tribes and their traditional way of life (also referred to as traditional lifeways). For example, some tribes reside on a fixed land and resource base and in many cases have no option to move from their areas or homelands. This can result in

exposures that are more continuous and concentrated than those experienced by nontribal populations.

Each tribe follows unique traditional practices that are not included in "general population" risk assessments, including diets, religious practices and cultural practices (e.g., basket making, sweat lodge ceremonies). Some traditional practices create higher exposures to certain natural materials (e.g., soil, plants) that need to be considered when constructing exposure scenarios. Although traditional practices are unique to each tribe or group, exposure pattern information for similar activities often can be used in estimating exposures.

Some tribes follow a subsistence-based lifestyle, while others have diets that are more western or seasonally variable. The percentage subsistence and frequency need to be determined because they are not accounted for in the general population estimates of consumption based on a western diet. Subsistence diets often include much higher than average quantities of fish or other game (Box 4-4).

Box 4-4. Fish Consumption Among Native Americans

Several exposure assessments have examined the exposure of Native Americans to contaminants in fish. Using values in EPA's *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011f) fish ingestion rates were determined for recreational marine anglers (adults) from the northern Pacific region of 6.8 g/day at the 95th percentile and 2.0 g/day for the average angler. By comparison, the highest consumption rate for Native Americans (adults) was for the four Columbia River Nations of Oregon, at a rate for all responding adults of 170 g/day for the 95th percentile compared to 59 g/day for the average consumer (U.S. EPA 2011f).

Several tribes are working to restore their natural resources, revive traditional life patterns and return to the use of traditional food sources. Some have reduced their consumption of traditional foods because of advisories but want to increase traditional food use in the future. Exposure scenarios involving tribal populations need to account for sustainability and the future growth of traditional practices as data and methods become available.

Challenges in Conducting Exposure Assessments for Tribal Populations

Assessors sometimes face cultural and technical challenges in conducting exposure assessments for tribal populations, such as the following:

- Typically, EPA risk assessments are performed to address outcomes. The resulting risk management solutions sometimes recommend that populations move away from contamination by obeying fishing/hunting advisories. Tribes, however, are tied to fixed land and resource bases and cannot simply move away from the problem. They also might be unwilling to discontinue traditional practices that they consider essential to their existence.
- Any tribal data gathered potentially are sensitive. Tribes need to be made aware of the issues of informed consent so that they are informed on both the possible risks and the potential benefits of their involvement. Some, but not all, tribes have their own

Institutional Review Board (IRB). Section 7.2.10 presents additional information on human subject considerations.

- Any exposure assessment on tribal lands needs to incorporate tribal consultation to gain insights into historical observations regarding environmental impacts. This information needs to be gathered sensitively and correctly to be representative of the tribe's health and lifeways.
- Exposure assessment models require relevant and standardized data to estimate results. Some tribes, however, might want nonquantifiable impacts to be considered (e.g., loss of culture) in addition to western quantitative metrics. The need for standardized data needs to be balanced with the need for tribal input.
- If tribes participate in data gathering, quality assurance (QA) procedures need to be in place beforehand to ensure data will meet EPA criteria to be included in assessments.
- Sampling of soil, water, human tissue or other media, or the taking of photographs, might be contrary to the belief systems of some tribes.
- Self-reported rates of food consumption and traditional practices might not be reliable or standard within a community. Some tribal members might be reluctant to participate because of fear of prosecution, memory of past government abuses of information, desire to provide politically correct answers and distrust of western-style surveys.

Resources for Assessing Exposures of Tribal Populations

As EPA examines the aspects of exposure and risk assessment unique to tribal groups, the Agency has developed several resources to assist EPA and tribal representatives in risk assessment (Box 4-5).

EPA Tribal Network

EPA has established a network of staff members who can serve as resources for planning and conducting exposure assessments for tribal populations. This EPA tribal network includes:

- The American Indian Environmental Office (http://www.epa.gov/tribal/);
- Headquarters program tribal coordinators (http://www.epa.gov/tribal/contactinfo/index.htm); and
- Regional Indian coordinators (http://www.epa.gov/tribal/contactinfo/index.htm).

Regional staff members work directly with tribes in their region. They are invaluable for making the appropriate contacts and often are knowledgeable about protocols of individual tribes.

Annually, EPA mandates a *Working Effectively with Tribal Governments* training. Interested members of the public can access this free government-wide training program at http://www.golearn.gov/.

Models

An example of a pattern-specific model of tribal activity with adjustable inputs is Tribal Lifeline, produced by the Lifeline Group (Resek et al. 2008). The *Traditional Tribal Subsistence Exposure Scenario and Risk Assessment Guidance Manual* (Harper et al. 2007) presents exposure scenario and risk assessment guidance for traditional tribal subsistence exposures. A tool the Agency developed to assist in evaluating tribal exposures is the Tribal-Focused Exposure and Risk Screening Tool (Zartarian and Geller 2010).

Box 4-5. 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 (2006c) *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.* Presents ways that EPA can consider traditional lifeways in the Hazard Ranking System to determine eligibility for a site in 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.
- Harper et al. (2007) *Umatilla Exposure Scenarios.* Develops regional subsistence exposure scenarios, which include tribal cultural and lifestyle activities that might increase environmental exposures as compared to general suburban population exposure scenarios; reviews scenarios, exposure factors and major activities for broad categories of tribes; and develops and describes a system of ecoregions that provide common approaches for broad groups of indigenous peoples based on the land, food and cultural practices across geographic regions.
- U.S. EPA (2011f) *Exposure Factors Handbook: 2011 Edition.* EPA/600/R-09/052F. Provides links to many references for data to inform exposure assessments on tribal populations.
- *Research Program* website. Indian Health Service. Oversees all human participant research conducted in Indian Health Service facilities and is a source of information about tribal-specific human research issues. http://www.ihs.gov/Research/.
- *Tribal Programs* website. EPA Region 10. Compiles EPA's and other organizations' environmental resources available to tribes. http://yosemite.epa.gov/R10/tribal.NSF.
- EPA American Indian Environmental Office Tribal Portal. http://www.epa.gov/indian/.

Additional Resources

- The Agency for Toxic Substances and Disease Registry's Office of Tribal Affairs provides assistance with tribal-specific environmental health needs resulting from exposure to hazardous waste sites and pollution, http://www.atsdr.cdc.gov/tribal/.
- The U.S. Geological Survey's (USGS) Native American Tribal Liaison Team offers training on geographic information system (GIS) methods, water monitoring, wildlife health and other issues, http://www.usgs.gov/indian/training/.

Working Effectively with Tribal Governments

EPA adopted a formal Indian Policy in 1984 (U.S. EPA 1984), which provides guidance to EPA managers and staff for working with tribal governments and responding to environmental management issues on Indian reservations to protect public health and the environment. EPA recognizes the rights of tribes as sovereign governments to self-determination, acknowledges the federal government's trust responsibility to tribes and works with tribes on a government-to-government basis to protect air, land and water in Indian country.

Becoming familiar with tribal culture and traditions can improve communication and interaction between an assessor and tribal people. For example, the concept of assessing risk and determining an acceptable level of risk might be foreign to a traditional Native American approach of maintaining harmony with the environment. Tribal people, in general, do not specifically define "health" or "environment" separately. The very way that life is viewed

(i.e., the value system or set of principles) also plays a tremendous part when examining the meaning of "health" and "environment." In addition, tribes represent relatively small populations, unique in facing the possibility of cultural loss and extinction in the face of environmental hazards.

Assessors need to be aware that tribes sometimes are influenced by activities related to exposure assessments not only on their lands, but also on lands outside the boundaries of areas in which they have a legally recognized interest (e.g., treaty-rights area) or on nontribal lands where activities can affect the health of tribal populations. If an EPA activity impacts one or more tribes, the Agency's Indian policy emphasizes the need to work directly and consult with tribal governments (U.S. EPA 1984).

4.3.6. Other Racial and Ethnic Populations

"Race" refers to the socially constructed groups specified by the Office of Management and Budget (OMB).[10] "Ethnicity" refers to cultural groups, such as Hispanic or Latino. As noted by Directive 15[11] and numerous scholarly organizations, racial and ethnic groups are social categories and not biological taxa (i.e., no biological basis exists for assigning people to a given racial classification). 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 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 et al. 2002). Some examples of racial and ethnic disparities in exposures to environmental contaminants are presented in review articles such as Brulle and Pellow (2006) and Brown (1995). Other examples include racial, ethnic and income disparities in exposures to lead, mercury and other metals, PCBs and pesticides, as well as proximity to hazardous land uses. Morello-Frosch and Lopez (2006) and Morello-Frosch and Jesdale (2006) examined racial segregation in relation to environmental exposures and risks.

Cultural traditions and practices can influence exposures for many of the diverse populations found throughout the United States. Exposure assessors need to be aware of these cultural traditions and practices when conducting exposure and risk assessments with diverse populations. 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 bodyweight of 62 kg. Of significance to exposure assessors, however, is the significant variation in consumption rates between ethnic groups—for example, Vietnamese, Japanese and

[10] Revisions to the Standards for the Classification of Federal Data on Race and Ethnicity; Notice of Decision, 62 *Fed. Reg.* 58782 (October 30, 1997).
[11] 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.

Hmong (Sechena et al. 2003; U.S. EPA 2001a). In addition, the study reported fish fillets were eaten 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 (known to accumulate lipophilic chemicals such as 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 and are more likely to fish in contaminated waters.

4.3.7. Socioeconomically Disadvantaged Populations

In 1999, the Institute of Medicine in its report *Toward Environmental Justice* (IOM 1999) advised that "policy makers should be attentive to potential environmental hazards and adverse health outcomes of minority and low income populations" and urged policy makers "to exercise caution on behalf of affected communities, particularly those that have the least access to medical, political and economic resources, taking reasonable precaution to safeguard against or minimize adverse health outcomes." Since then, concern has remained that minority and economically disadvantaged populations might bear a disproportionate share of environmental exposures and related illnesses. Differences in exposures to environmental contaminants, combined with exposure to other stressors such as poverty, segregation and lack of resources, are thought to contribute to the persistent disparities in health by race, ethnicity and social class (deFur et al. 2007; Gee and Payne-Sturges 2004; NEJAC 2004; U.S. EPA 1999b). Although the specific mechanisms are not well understood regarding how social and physical environmental factors combine to produce health disparities between populations, recent research is providing evidence that exposures to social stressors such as material deprivation enhance toxicity with coexposure to environmental contaminants (Rauh et al. 2004; Weiss and Bellinger 2006). This finding suggests that if the social contexts in which environmental exposures occur are not considered, the associated health risks/impacts might be underestimated.

When examining exposure information, therefore, risk managers/decision makers also need to examine potential differences in the susceptibilities and vulnerabilities of members of the community to adverse health effects.

Socioeconomic Factors to Include in Exposure Assessment

Socioeconomic factors leading to disparities in environmental exposures can occur by one or all of the following mechanisms operating at both individual and community levels:
(1) socioeconomic disadvantages related to location or proximity to pollution sources or degraded environments; (2) sociocultural activities (e.g., subsistence fishing, diet, handcrafts) that create an opportunity for exposure to toxicants/environmental hazards; and (3) cumulative risks from workplace hazards, community stressors and social stressors (U.S. EPA 1999b). Several published papers discuss these mechanisms in detail (deFur et al. 2007; Gee and Payne-Sturges 2004; Hynes and Lopez 2007).

Socioeconomic Position and Class

In general, individuals with fewer economic resources are associated with an increased risk of almost every studied disease, increased exposure to the risk factors associated with environmentally mediated diseases and decreased ability to access the care to meet these health

needs (Diez Roux et al. 2001; Evans and Kantrowitz 2002; Hillemeier et al. 2003). Public health researchers commonly use the terms socioeconomic status or socioeconomic position. Socioeconomic position is the term some social epidemiologists use because it emphasizes the hierarchy of social class and its relationship to health. Socioeconomic position covers several domains: occupational class, income, poverty, wealth and education.

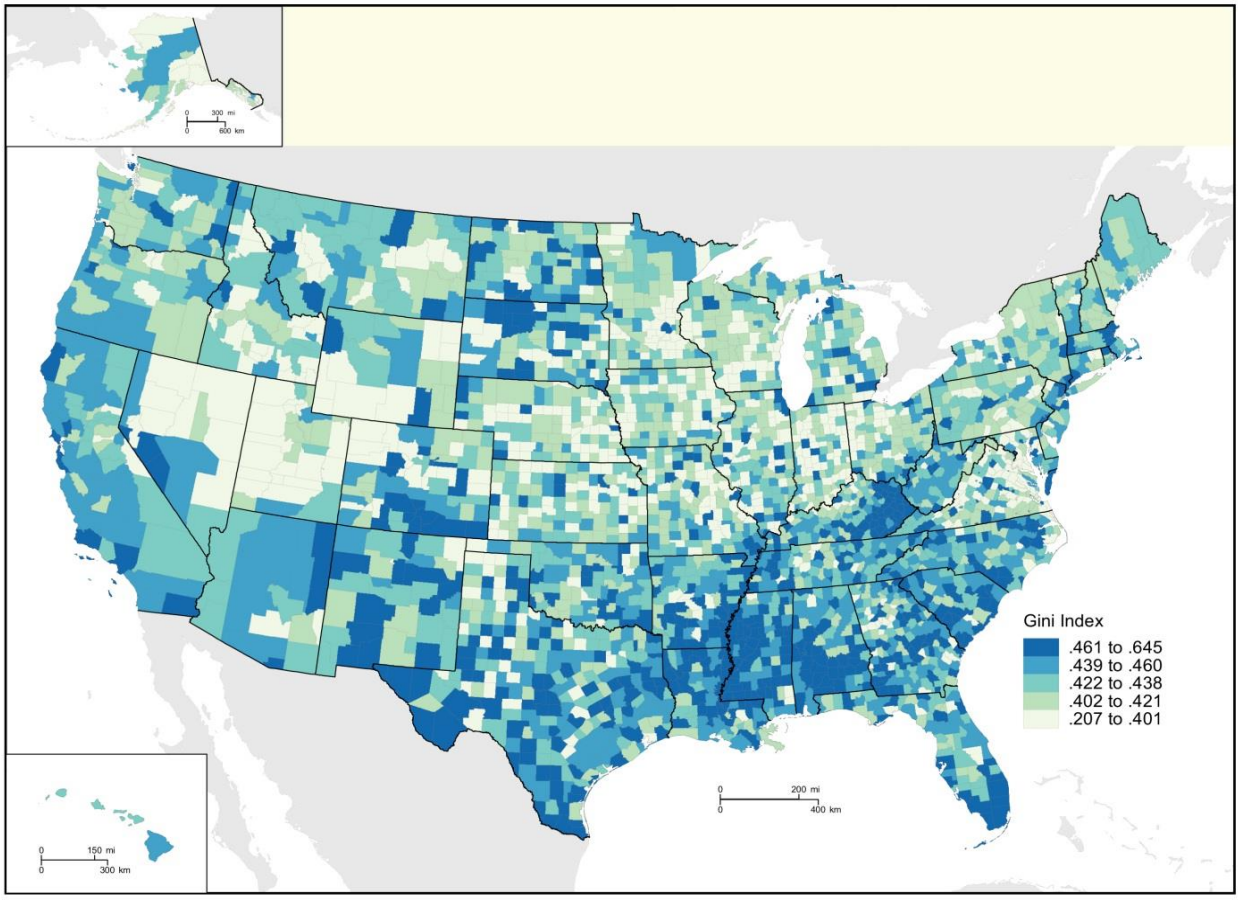
A variety of methods have been used to measure socioeconomic position at the individual level, including measures of income, occupational title, prestige, education, wealth and control over job demands in the workplace (decision latitude). Measures at the macroscopic level include neighborhood poverty, median household income, median housing value and measures based on a combination of factors. Although the rate of poverty is higher among certain population groups, remembering that race/ethnicity and income are different variables is essential.

Income inequality, the degree to which income and wealth are concentrated in relatively few households, is increasing in the United States (Levy 2007; Regev and Wilson 2007). The concept of income inequality builds on the "relative income" hypothesis—that is, health and other problems are not just a function of absolute poverty but are related to the distribution of wealth across a society. Environmental health researchers are increasingly recognizing social inequality as an important factor to consider and are including inequality metrics in their analyses to quantify the distribution of inequalities in exposures and health outcomes across social groups of concern. These inequity metrics are drawn from the methods used in the income inequality literature. Boyce et al. (1999) found that states with higher levels of income inequality are more likely to have reduced levels of environmental regulation. Income inequality also was found to be related to the overall level of air toxics in a metropolitan area (Lopez 2002). Levy et al. (2006) demonstrated in their pollution control examples how inequality indices can help a policy maker determine which control strategies are optimal from efficiency and equality standpoints, allowing for more informed pollution control policies.

Numerous inequality measures have been developed and applied to characterize inequality in health, income and, more recently, environmental conditions. The most commonly used income inequality measure is the Gini index. Named after the Italian economist Corrado Gini, it measures inequality across the entire society rather than by simply comparing groups. As inequality increases, the value of the Gini index increases from 0 to 1 (The World Bank's *GINI Index* website, http://data.worldbank.org/indicator/SI.POV.GINI). The most common values tend to be between 0.3 and 0.5 (Figure 4-3). The Gini index has been used to evaluate associations between income inequality and environmental outcomes (Wilkinson and Pickett 2006). The Gini and other similar inequality indices (e.g., Atkinson, Theil or Concentration indices) have been used to summarize social group differences associated with environmental exposures (Fann et al. 2011; Su et al. 2009). The Atkinson index has been used in several income and health inequality applications because it can decompose into between-group components and within-group components and it allows for varying sensitivity to inequalities in different parts of the distribution (Box 4-6 presents an example using the Atkinson index). The Atkinson index incorporates a sensitivity parameter (ε) that can range from 0 (meaning that the analyst is indifferent about the nature of the distribution) to infinity (where the analyst is concerned only with the position of the very lowest group). In practice, ε values of 0.5, 1, 1.5 or 2 are used; the higher the value, the more sensitive the Atkinson index becomes to inequalities at the bottom of

the distribution. This sensitivity parameter is appealing because it forces the analyst to make transparent any assumptions about how the different population groups have been weighted.

Figure 4-3. Quintiles of Gini Index by U.S. County: 2006–2010



Note: The Gini index is a measure of wealth or income equality. A Gini of 1 means that one person has all of the wealth and everyone else has nothing; a Gini of 0 means that everyone has the same wealth. This figure from the U.S. Census Bureau shows each U.S. county's level of income inequality as measured by the Gini index.

Bee (2012).

Other income inequality measures tend to be based on the percentage of total income earned by various segments of the population. These include the Robin Hood index, which compares the percent of total income earned by the top 50 percent of a population to that earned by the bottom 50 percent, and various income inequality measures such as the "90/10 ratio" (the ratio of total income earned by the highest 10 percent of households to the lowest 10 percent). In general, the Gini index can be used for examining the level of inequality across the entire population, including the effects of middle-income households. The ratio measures are best for measuring inequality at the extremes of the income distribution. See Coulter (1989) and Harper and Lynch (2005) for more information on the Gini and Robin Hood indices. See Levy et al. (2006) and Harper et al. (2013) for applications specific to analyses (exposure and risk assessments and cost-benefit analyses) that support environmental decision making. Because several inequality

indices are available to choose from, understanding the underlying principles of the inequality index is essential when choosing an index for an exposure assessment.

Box 4-6. Applying the Atkinson Index

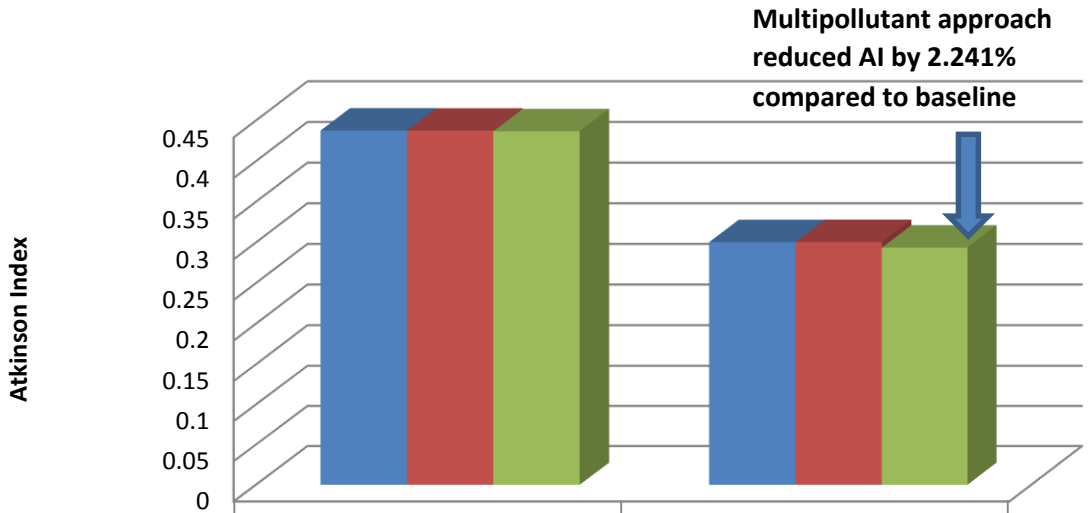
Fann et al. (2011) combined information on ambient $PM_{2.5}$ (particulate matter 2.5 µm in diameter and smaller) exposures, baseline health status, concentration-response functions for mortality and asthma risk, hospitalization risk because of $PM_{2.5}$ exposures and socioeconomic characteristics to assess how well different air pollution control strategies (status quo or multipollutant approach) reduced existing social disparities in health outcomes by applying the Atkinson index (AI) to quantify health risk inequality.

The Atkinson index is defined as follows:

$$\mathrm{AI} = 1 - \left[\frac{1}{n}\sum_{i=1}^{n}\left[\frac{x_i}{X}\right]^{1-\varepsilon}\right]^{\frac{1}{1-\varepsilon}}$$

where n is the number of individuals in the population, x_i is the risk for individual i, X is ___ and ε is a parameter representing the degree of weight applied to the lower end of the distribution (to indicate the degree of "aversion to disparity" assumed). The value of ε can range from zero to infinity, where zero represents no societal concern about inequality and higher values represent increasing concern about the low end of the distribution.

Fann et al. (2011) concluded that "For both asthma and mortality, the multi-pollutant approach does a better job than the status quo approach of reducing inequality in risk because of $PM_{2.5}$ in the study population as a whole."



	Mortality Risk	Asthma Hospitalization Risk
Baseline	0.437776	0.300454
Status Quo	0.437661	0.300614
Multipollutants	0.43694	0.293722

Fann et al. (2011)

Social Stressors

Psychological stressors, like environmental exposures, are not randomly distributed. They tend to concentrate in low-income communities and are more likely to impact people of color. Over time, psychological stress can lead to an increase in an individual's allostatic load, defined as an individual's overall biological stress level. The effects of this chronic stress can include an increased risk of poor health, cardiovascular disease and other problems (Evans and English 2002; Evans and Marcynyszyn 2004; McEwen 1998).The synergistic effects of stress and cumulative exposures to a wide variety of environmental agents are not well characterized. Some evidence exists, however, that exposure to stress, including exposure to violence, can increase susceptibility to asthma and other environmentally related diseases and also can potentiate (through an interaction or effect modification) the effects of exposure to the agent—for example, environmental tobacco smoke and lead (Evans and Marcynyszyn 2004; Rauh et al. 2004; Weiss et al. 2008). Again, this indicates that efforts to predict the health effects of a given environmental exposure might be inaccurate in communities with high levels of stress (Clougherty and Kubzansky 2009).

Geographic Location

Place matters for environmental health because environmental hazards and exposures can vary according to location. For instance, rural, urban and suburban populations each have unique characteristics that can influence their environmental exposures (e.g., proximity to polluting facilities, living close to major roads and highways, age and condition of housing, food sources). Human activities and the built environment contribute to geographic differences in environmental exposures (e.g., buildings placed on the land, farming practices, chemicals applied to the land, types of industries operating nearby). The social environment in a geographic area (e.g., levels of poverty, isolation, changing racial/ethnic demographics) also influences environmental exposures.

GIS applications have become integral tools for displaying place-based environmental information and for exploring factors associated with spatial disparities in exposure and related health outcomes. For example, EPA has developed the Environmental Justice View (EJView) Tool (http://epamap14.epa.gov/ejmap/entry.html) with features and technology, intended to be used at the start of an assessment. The tool provides information relevant to assessing health, environmental, aggregate or cumulative impacts; unique exposure pathways; vulnerable or susceptible populations; and lack of capacity to participate in risk management/decision making, among other conditions. The data from EJView have been incorporated into the EnviroMapper, a system that includes multimedia models and a geospatial display of uploaded monitoring data (http://www.epa.gov/emefdata/em4ef.home). Other EPA tools include that from the Regional Vulnerability Assessment (ReVA) program (http://www.epa.gov/reva/), EJScreen (http://www2.epa.gov/ejscreen) and the Community-Focused Exposure and Risk Screening Tool (C-FERST; http://www.epa.gov/heasd/c-ferst/). The ReVA program is designed to develop the methods needed to understand a region's environmental quality and the spatial pattern and impacts of human activities. C-FERST is a tool that can be used to identify pollution sources at the community level and prioritize exposures and risks for mitigation.

4.4. Identifying Lifestages, Vulnerable Groups and Populations of Concern for Exposure Assessment

Two approaches to identify vulnerable populations are consulting available scientific literature and seeking community input. Census and other government data are sources of information on the distribution and presence of vulnerable populations in a community. Differential exposure can be indicated by elevated body burdens of contaminants. Biological levels can be combined with other types of data, including activities, geospatial data relative to sources and consumption, to reconstruct exposure.

4.4.1. 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 (available at http://www.epa.gov/TRI/) and similar state databases of contaminants, pollution discharge permits and air monitoring data. The population surrounding these locations then is characterized 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 GIS methods). The population in these target areas then is compared to the overall state or U.S. population or to other areas that do not have the 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 have tended to find that race/ethnicity is a greater risk factor than income for exposure. In response to recommendations from an EPA symposium on environmental justice, the Agency commissioned a systematic review of proximity analysis and GIS methods (Maantay et al. 2010).

4.4.2. Case Studies

A case study describes a particular neighborhood's or group's experience with 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. They are particularly important when documentation of past exposures is lacking or when a particular exposure was proposed but ultimately did not happen.

4.4.3. Neighborhood Methods

Neighborhood methods begin with the identification of particular areas that have high proportions of disadvantaged people or other populations of concern. These areas include census blocks, census tracts, ZIP codes, counties, or specially or traditionally defined neighborhoods. Data on neighborhood demographic composition usually are obtained from U.S. census data or other government surveys. Next, the overall or specific level of contaminants or pollution sources is measured or estimated, using sources 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.

4.4.4. Population-Based Methods

In a population-based method, the overall or person-specific mean, percentile or distribution of exposure for a given population(s) of concern is compared 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, little is known about individual exposures. Instead, individuals are assigned exposure values 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.

4.4.5. Social Process Methods

Social process methods are used to assess the association between a social-level variable(s) and pollution 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 exposure metrics as dependent variables. The regression models often use other demographic, social or environmental independent variables as well. 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. Additional evidence, however, might be needed to assess causation.

4.4.6. 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 geographic scope that is most relevant.

National-Level Assessment

At the national level, screening for differential exposure can use the large, comprehensive databases developed by national organizations, such as EPA, the U.S. Bureau of the Census and the Centers for Disease Control and Prevention (CDC), on pollutant concentrations in environmental media (e.g., air, water) and the locations of pollution sources. 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; http://epa.gov/airtoxics/natamain/), an ongoing comprehensive evaluation of air toxics in the United States. EPA developed the NATA program in 2002 for screening. These assessments estimate the risk of cancer and noncancer health effects from inhaling air toxics, including estimates of exposures at the census-tract level. Assessments include estimates of cancer and noncancer 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 air toxic emissions levels remained unchanged.

In its 1999 NATA, EPA described the program's cumulative risk assessment approach, focusing on a single year (U.S. EPA 2006a). The assessment included four steps: (1) compiling an inventory of 1999 air toxics emissions from outdoor sources, (2) estimating annual average outdoor air toxics concentrations, (3) estimating exposure concentrations (what people are estimated to breathe) and (4) characterizing potential public health risks. The exposure assessment approach uses computer models to estimate ambient air toxics concentrations and population exposures nationwide.

Another example of a national-level assessment would be that associated with examining exposure of migrant agricultural workers to pesticides. This type of exposure is national in the sense that migrant workers are not only employed throughout the United States, but they also tend to move from one location to another during the year. According to CDC, doctors diagnose between 10,000 and 20,000 farm workers with pesticide poisonings each year. Workers can become exposed to toxic levels of pesticides during spills, direct spraying or pesticide drift. In addition, migrant farm workers might not be supplied the protective gear needed to protect their health or the equipment they do receive is defective. To help reduce risks to migrant farm workers associated with pesticide exposures, EPA has awarded grants to train migrant farm workers in southern New Jersey about steps they can take to protect their health on the job more effectively.

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 (http://www.epa.gov/ncer/cra/). Several reports, including workshops, case studies and modeling tools (e.g., C-FERST, Tribal-Focused Environmental Risk and Sustainability Tool [T-FERST], ReVA, 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).

CHAPTER 5. DATA FOR EXPOSURE ASSESSMENT

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, location-specific or population-based activity information and scientific research findings. 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 in which data can be processed 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.

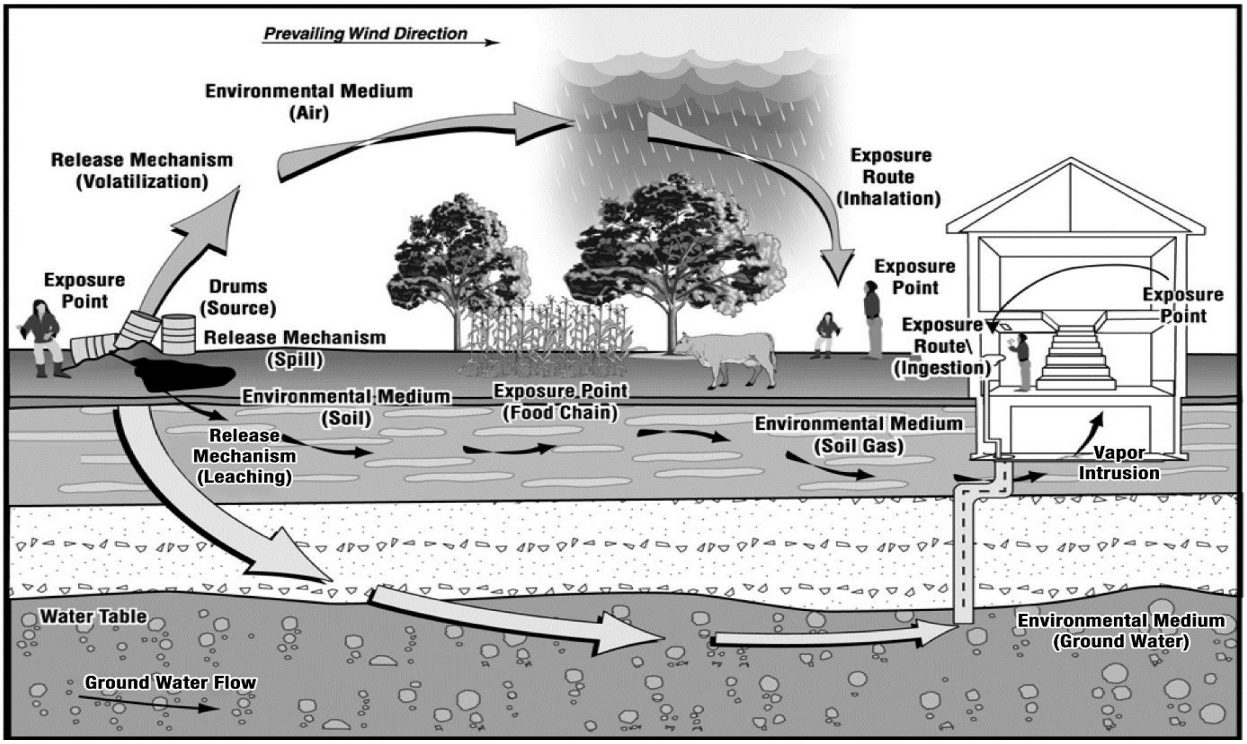
The process of identifying and addressing data needs is iterative, involving repeated reviews of data availability, quality and gaps. This chapter provides a framework for addressing data needs, including an overview of key data considerations and links to relevant data sources, resources and tools. Specifically, this chapter:

- Discusses considerations in identifying data gaps and data needs (Section 5.1);
- Describes quality assurance (QA)/quality control (QC) needs for an exposure assessment (Section 5.2);
- Identifies the types of data used in 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 uncertainty and variability (Section 5.5);
- Provides an overview of data management considerations (Section 5.6); and
- Describes communication considerations specific to data (Section 5.7).

5.1. Identifying Data Gaps and Data Needs

Identification of data gaps and data needs begins with understanding the conceptual model presented in Section 3.2.2. Figure 5-1 provides a graphical presentation of a conceptual model for potential exposures from the release of chemicals from drums. Table 5-1 describes exposure routes and potential receptors for a hypothetical exposure scenario resulting from the release of chemicals from a spilled drum. Potential sources of exposure include direct contact with soil, ground water, air and biota the chemical release affects (Table 5-1). Assessors need to consider both current and potential 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 and completed routes of exposures for individuals to the various media (e.g., soil, ground water, ambient air, indoor air) where sampling might be needed.

Figure 5-1. Conceptual Model of Exposure Pathways of a Leaking Chemical Drum



Adapted from ATSDR (2005)

Table 5-1. Hypothetical Exposure Scenario for a Leaking Chemical Drum

Release or Transport Medium	Exposure Point	Exposure Route	Exposed Population
Air	Ambient air Vapor intrusion	Inhalation	Residents (adult and child) Workers
Soil	Residential yards	Ingestion Inhalation Dermal	Residents (adult and child)
	On site	Ingestion Inhalation Dermal	Workers
Ground water	Private wells	Ingestion Inhalation Dermal	Residents (adult and child) Workers
	Public water supply	Ingestion Inhalation Dermal	Residents (adult and child) Workers
Biota	Locally grown food Naturally occurring food Contaminated fish and game	Ingestion	Residents (adult and child) Subsistence populations

For each variable, an exposure assessor considers how to obtain the data from existing sources, if available, or whether and how to gather new data. Before concluding that an exposure assessment can rely on existing data, an exposure assessor needs to identify whether existing data are available to meet the data needs, identify potential surrogate data sources and obtain and critically review the data quality of existing data to assess usability in an exposure assessment.

When evaluating any type of existing data for use in an exposure assessment, EPA's Office of Pollution Prevention and Toxics (OPPT) recommends that assessors consider the objective of the study or program that gathered the data, collection and analytical methods, QA/QC procedures employed and key study and data uncertainties (U.S. EPA 2012i). EPA's *Guidance for Data Usability in Risk Assessment* 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 office.

The review of available data can identify information gaps. The exposure assessor needs to consider what gaps in knowledge need to be filled through assumptions, estimates, default values or targeted data collection. 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 new data are acquired.
- Will the missing data make a real difference in the exposure assessment? In other words, what is the direct relevance of the data to the problem or risk management objectives?
- How do the missing data relate to anticipated or known specified stakeholder concerns about exposures and risks?

Before planning a sampling program, the project team needs to evaluate the cost versus the benefit of such a sampling program carefully (Whitmore et al. 2005). Sampling often is a resource-intensive endeavor (i.e., requiring substantial time and money). The following questions, modified from OPPT's *Considerations When Evaluating Exposure Assessments* (U.S. EPA 2012f), can be considered when assessing the cost-benefit 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? Have these methods been adopted or otherwise accepted by the scientific community? Does EPA have standard operating procedures (SOPs) for these methods?
- How many samples will be needed to meet the objectives of the study?
- What QA/QC procedures are required?
- What will the sampling program cost?
- Will the uncertainty substantially limit usability of the data in an 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 satisfactorily). 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 time, resources and institutional framework. The decisions to use existing data are captured in the exposure assessment/characterization, including appropriate discussion of any data limitations.

5.2. Data Quality

The quality of the exposure characterization, and ultimately the risk characterization, depends on the quality of data used to conduct an exposure assessment. EPA has published guidance documents and compiled resources on data quality for existing data and the collection of new data to meet this objective. Figure 5-2 provides an outline of the process and Box 5-1 lists some of the available guidance documents and resources most relevant to data used in exposure assessments.

EPA's *Assessment Factors* (U.S. EPA 2003a) also describes quality considerations that the Agency takes into account when evaluating scientific and technical information. These include the following five general assessment factors:

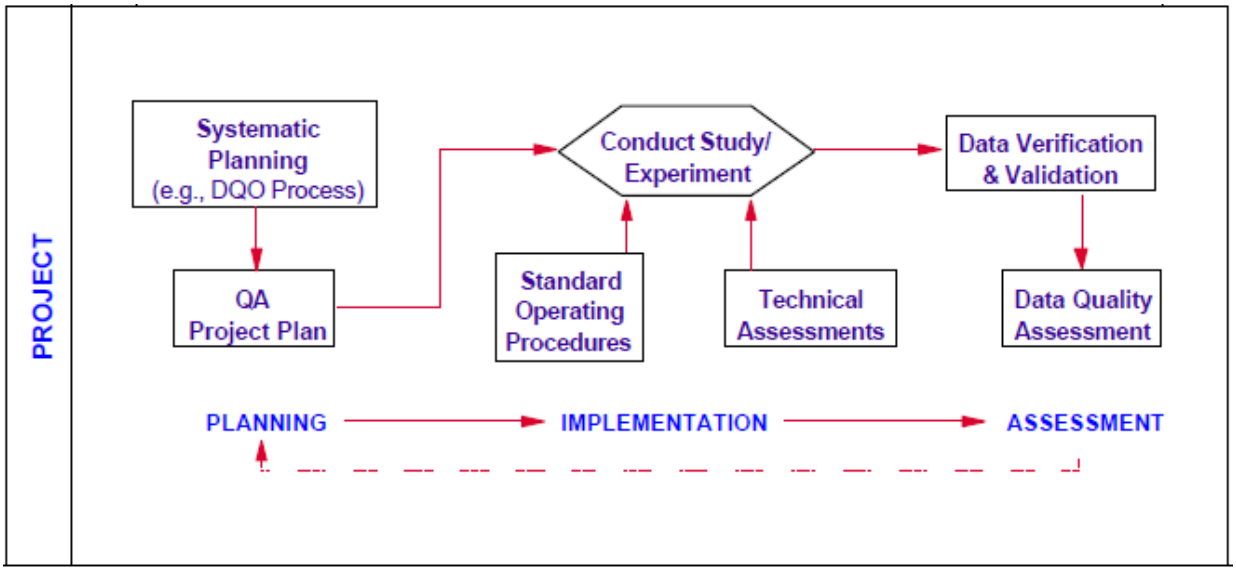
- **Soundness.** The extent to which the scientific and technical procedures, measures, methods or models employed to generate the information are reasonable for and consistent with the intended application.
- **Applicability and utility.** The extent to which the information is relevant for the intended use.
- **Clarity and completeness.** The degree of clarity and completeness with which the data, assumptions, methods, QA, sponsoring organizations and analyses employed to generate the information are documented.
- **Uncertainty and variability.** The extent to which the uncertainty and variability (quantitative and qualitative) in the information or in the procedures, measures, methods or models are evaluated and characterized.
- **Evaluation and review.** The extent of independent verification, validation and peer review of the information or of the procedures, measures, methods or models.

5.2.1. Data Usability and 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 analysis, 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 (Section 3.3.1). EPA programs also may implement specific procedures that vary from this basic process. Exposure assessors need to consult with their programs and follow their SOPs.

Figure 5-2. EPA Quality System Components and Tools



U.S. EPA (2002d)

The data needed for an exposure assessment depend on the assessment approach selected during planning and scoping and the assessment objectives (Section 3.3.1). 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 the data quality objectives (DQOs) for those data;
- For each data value needed, determine whether the data currently are available and if so, obtain the data and evaluate their quality and appropriateness;
- When appropriate data are not available, determine how crucial these data are to the assessment and whether they need to be obtained or estimated (e.g., collecting data, using models); and
- When new data are collected, establish a quality assurance project plan (QAPP) 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, however, can 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 needs. Upon receipt of data generated during a sampling program, an exposure assessor reviews the quality of those data. These new data need to meet the five general assessment factors outlined in EPA's *Assessment Factors* (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.

Box 5-1. EPA Quality Assurance (QA)/Quality Control (QC) Web Pages and Resources

EPA' 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 Web page www.epa.gov/quality includes the following information:

- *Frequent Questions*: Answers to common questions on EPA's Quality System, resources, quality management plans, QA project plans and more.
- *Quality Management Tools*: Links to guidance, training, frequent questions, examples and references by topic.
- *Information Specific to EPA Organizations*: Policies, procedures, organizational implementation, the graded approach, Agency oversight and more.
- *Information Specific to non-EPA Organizations*: Federal regulations, procedures for your agreement with EPA, the graded approach and more.
- *Guidance*: Downloadable copies of Agency-wide quality system guidance and policies.
- *Training and Conferences*: Information about upcoming training events and conferences, downloadable copies of training courses and technical papers from previous conferences.
- *EPA Contacts and Websites*: List of EPA quality personnel by EPA organization with quality-related program-specific websites.
- *Other Useful Websites*: List of other quality-related websites on statistical software, records management, professional organizations, other federal quality programs, the EPA Information Quality Guidelines and more.

The **EPA Quality Program Policy and Procedure** for Agency products and services was issued in October 2008 is available. EPA Quality Program Policy – CIO 2106.0 (PDF 11pp, 129K) and Procedure – CIO 2106-P-01.0 (PDF 17pp, 340K).

Common Starting Points:

- If you are developing a quality management plan: *Quality Management Tools – Quality Management Plans*.
- If you are writing a quality assurance project plan (QAPP): *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 QAPP.
- 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.

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 being measured in various media (e.g., soil, ground water, sediment) and analytical measurement approaches also can introduce uncertainty. DQOs describe the degree of uncertainty that the project team is willing to accept based on the needs of the risk manager/decision maker. Setting realistic DQOs is an important step 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 terms of time and resources. DQOs, which outline minimum performance and acceptance criteria, are established for an exposure assessment during planning and scoping (Section 3.2). 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 do provide sufficient information. For example, air pollution sampling might be conducted as part of a network to track pollution trends, but these data also can be used to represent exposure concentrations at a regional or local level, depending on the locations of the samples.

The use of low-quality data in an exposure assessment is possible if the limitations in the data can be demonstrated not to affect the results significantly. In these cases, an assessor needs to explain clearly in the exposure characterization why the limitations in the data do not invalidate conclusions. In some cases, inadequate or partially relevant data might be the only data available, and some information might be gained from their consideration. Discarding these data entirely might not be possible unless better data are available. If these data are used, the uncertainty and resulting limitations need to be stated clearly in the exposure characterization.

Establishing a Quality Assurance Project Plan

Developing a sound QAPP is critical to the success of any data collection effort. EPA defines a QAPP as a written document that describes the QA procedures, QC specifications and other technical activities that need to be implemented to ensure that the results of the project or task to be performed will meet project specifications. Primary data collection, secondary data usage and data processing (such as modeling) project activities funded by EPA are described and documented in QAPPs (U.S. EPA 2011c).

EPA has compiled guidance and information about preparing a QAPP on the *Quality Management Tools—QA Project Plans* website (http://www.epa.gov/QUALITY/qapps.html). This website includes links to guidance on preparing QAPPs for environmental data collection, modeling, secondary research data and other topics. The EPA *Requirements for Quality Assurance Project Plans* guidance document (U.S. EPA 2001c) outlines the specifications for QAPPs prepared for activities conducted or supported by EPA. In addition to discussing project management, assessment and oversight needs, this document details requirements for data generation, acquisition, validation and usability. Several examples of QAPPs also are provided on the website. Box 5-1 identifies data quality resources, such as guidance on preparing QAPPs 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 QAPP 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. As with the planning and scoping process, the QAPP documents the implementation activities needed to ensure that the results of the project or task meet project specifications.

Peer Input to Data Review

With few exceptions, data documentation (e.g., sampling and implementation plans, QAPPs, SOPs, data analysis plans) and data undergo some level of review, as described in EPA's quality process (www.epa.gov/quality). Many Agency work products are developed with the input of various scientific and technical experts inside and outside the Agency. EPA's *Peer Review Handbook* (U.S. EPA 2015), identifies the following categories of review that can be useful in the evaluation of data including:

- **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 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 might be sought for major exposure assessments such as those involving controversial methodological or scoping issues. Other exposure assessment products for which peer input might be warranted include observational human exposure measurement studies (Chapter 7), probabilistic exposure analyses (Section 8.2.2), community-based exposure assessments, aggregate and cumulative exposure assessments and variability and susceptibility evaluations within populations.

Peer input usually involves a one-time interaction or a limited number of interactions. It 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 will help ensure that adequate resources are allocated. In addition, peer input considerations are an integral part of setting assessment milestones and schedules.

Evaluating Data Quality

Upon receipt of data generated during sampling, an assessor reviews 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* (U.S. EPA 2003a) and described in Section 5.2. The evaluation includes a data verification and validation process that is 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 its completeness, correctness and consistency using the methods and criteria defined in the project documentation. Data validation follows 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.

Data Validation and Quality Review of the Sample Collection and Analysis Methods

Methods and Data

EPA has developed several validated sample collection and analysis protocols. 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 2002d). 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 placed in conclusions.

Data validation is the process of reviewing laboratory data to identify potential QA/QC issues. During data validation, data qualifiers might be assigned to values of individual chemicals (http://water.epa.gov/type/rsl/monitoring/132.cfm). Examples of qualifiers used under EPA's *Contract Laboratory Program for the Superfund Program* (U.S. EPA 2010b) to indicate QA/QC issues such as blank contamination and usability of data, 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; and
- 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 are opened in the field and used to determine if field sampling procedures resulted in sample contamination. Laboratory blanks are used to 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 produces 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 are used to demonstrate acceptable method precision by the laboratory 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.

5.2.2. Assessment – Using Data to Evaluate Exposures

Addressing Nondetect Values

All analytical methods have sensitivity limitations. These limitations are referred to as the detection limit, quantification limit, method detection limit, reporting limit or other similar terms. Analytical chemistry datasets often will include values that are lower than limits deemed reliable enough to report as numerical values (i.e., nondetects). 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. Although a variety of techniques have been described in the literature, no single procedure is appropriate for all exposure assessment circumstances; thus, an assessor will need to decide on the appropriate method for a given situation. Techniques for analyzing nondetect 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 nondetect 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 nondetect 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 nondetects, the overall distribution and standard deviation of the dataset might be severely biased and need to be evaluated by the exposure assessor.
- **Distributional methods** use the detected values in the dataset to extrapolate values for the nondetects. 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 nondetect values rather than the entire dataset. The nondetect 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 nondetect values. These methods involve somewhat more data manipulation than distributional methods.

EPA developed a statistical software package for the analysis of environmental datasets with and without nondetect observations: ProUCL. ProUCL is a comprehensive statistical software package with statistical methods and graphic tools to address many environmental sampling and statistical issues (http://www.epa.gov/osp/hstl/tsc/software.htm). Calculating upper statistical limits is a primary function of the software and the graphical analyses offered includes probability plots, histograms, box plots and line/trend plots. Results for statistical intervals are offered with several options and relevant cautions.

Other software packages, including R Software, provide several statistical analysis tools (e.g., linear and nonlinear modeling, classical statistical tests, time-series analysis, classification and clustering) and graphical techniques. The R Software is Open Source and can be used for developing spatial survey designs and subsequent statistical analyses of data from those designs.

The software is available at http://www.r-project.org. The "Aquatic Resources Monitoring" Web page provides an example of the use of this software at http://www.epa.gov/nheerl/arm/analysispages/r_guide.htm.

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 nondetect 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

Outlier data (i.e., data points that are numerically distant from the other data points in a dataset) need not be eliminated from the data analysis 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 can be used to determine the presence of outliers (Dean and Dixon 1951; Dixon 1950; Dixon 1953; Dixon 1960). The ProUCL software provides graphical techniques and programs to aid in the identification of outliers.

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) and 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. 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/population. Bounding estimates can be used to show that true exposures are not greater than estimated exposures. 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) (Section 2.4). 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 for a specific

frequency (e.g., days/year) and duration (e.g., years). Exposure assessors need to contact their specific programs for specific guidance on calculating an EPC consistent with their legislative mandate.

5.3. Types of Data Used in an Exposure Assessment

Data used in an exposure assessment represent a wide variety of information, from environmental concentrations of chemicals 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, biological, exposure factors and activity patterns. Sections 5.3.1 through 5.3.4 describe these types of data and the role they serve in an exposure assessment.

5.3.1. Environmental Data

EPA defines environmental data as "any measurements or information that describe environmental processes, location or conditions; ecological or health effects and consequences; or the performance of environmental technology." 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 2002d). In an exposure assessment, environmental data typically are used to characterize either:

- Chemical concentrations in a medium (e.g., solvents in ground water) or at an exposure point (e.g., volatile organic compounds in the breathing zone); or
- Physical characteristics of the medium in which the chemical is present (e.g., groundwater flow direction, depth to ground water, soil porosity, solubility).

Environmental data are used throughout an exposure assessment process. During the planning and scoping process, they 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. For example, data about chemical concentrations in soil at a playground might highlight incidental ingestion by children as a concern. 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 that estimate likely exposure concentrations. For example, the concentration of a solvent in a drinking water supply could directly represent an exposure concentration for the population served by the water supply. The concentration of a solvent detected in ground water that is upgradient of a drinking water well, on the other hand, could serve indirectly as an input value for 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 how the environmental data fit into the conceptual model.

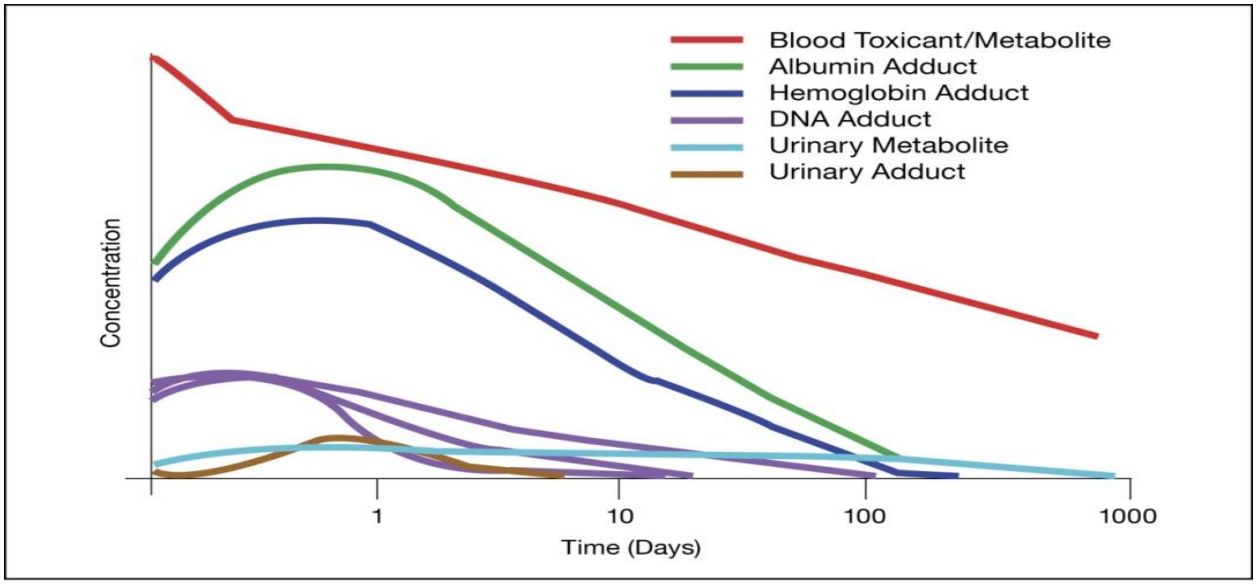
5.3.2. Biomonitoring Data

Biomonitoring is a method to assess human exposure to chemicals by measuring the chemicals or their metabolites in human tissues or specimens, such as cells and fluids. Biomarkers are cellular, biochemical, analytical or molecular measures that can indicate exposure to a chemical. Biomarkers of exposure record the concentration of the chemical or its metabolites in biological

media, whereas biomarkers of effect indicate cellular, biochemical or molecular change that occurs as a result of human exposure to the chemical (WHO 2004).

The ideal biomarker is sensitive, specific, biologically relevant, easy to collect, inexpensive to analyze, easily identified and persists in the body for long periods (Needham and Sexton 2000). Figure 5-3 illustrates how a hypothetical chemical or metabolite can persist in human tissue after a single exposure, although residence times might vary depending on the tissue and the type of chemical (Needham and Sexton 2000; Sohn et al. 2004). In addition, as described in Section 6.2.3, human dose models can be developed to estimate a dose based on biomonitoring data. This section describes forward dosimetry modeling that relies on environmental measurements and exposure factor data to estimate an internal dose. Reverse dosimetry is also described as a method to estimate external exposure to a chemical based on biomonitoring data.

Figure 5-3. Representative Profiles of Possible Biomarkers Following a Single Exposure to a Persistent Chemical



Adapted from Needham and Sexton (2000)

Biomonitoring studies are used to address data gaps associated with possible exposures, baseline conditions and internal chemical or metabolite concentrations. Biomarkers of exposure can link a chemical in the environment with a health outcome. Biomonitoring data can be used 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 intensity of exposure, impacts of removing chemicals from the environment where changes in blood or urine concentrations during specific lifestages or over time can be evaluated. Reference ranges describe general population exposures to chemicals for segments of the population (http://www.cdc.gov/exposurereport/; http://www.cdc.gov/nchs/nhanes.htm). Biomonitoring data complement environmental and modeling data in estimating exposure (e.g., temporal, scale, media, biodegradation). Biomonitoring data provide a useful tool for assessors to identify chemicals found in the environment and human tissues and to monitor changes in exposure (NRC 2006b). Biomonitoring data also help establish baseline and reference levels for environmental

chemicals, determine the prevalence of individuals with levels of chemicals above established toxicity benchmarks, determine whether exposure levels are higher among certain individuals/lifestages/groups/populations, identify chemicals for which appropriate toxicological and environmental data are lacking, refine future biomonitoring efforts and identify future research needs. In general, biomonitoring data demonstrate that human exposure to and absorption of a chemical actually have occurred.

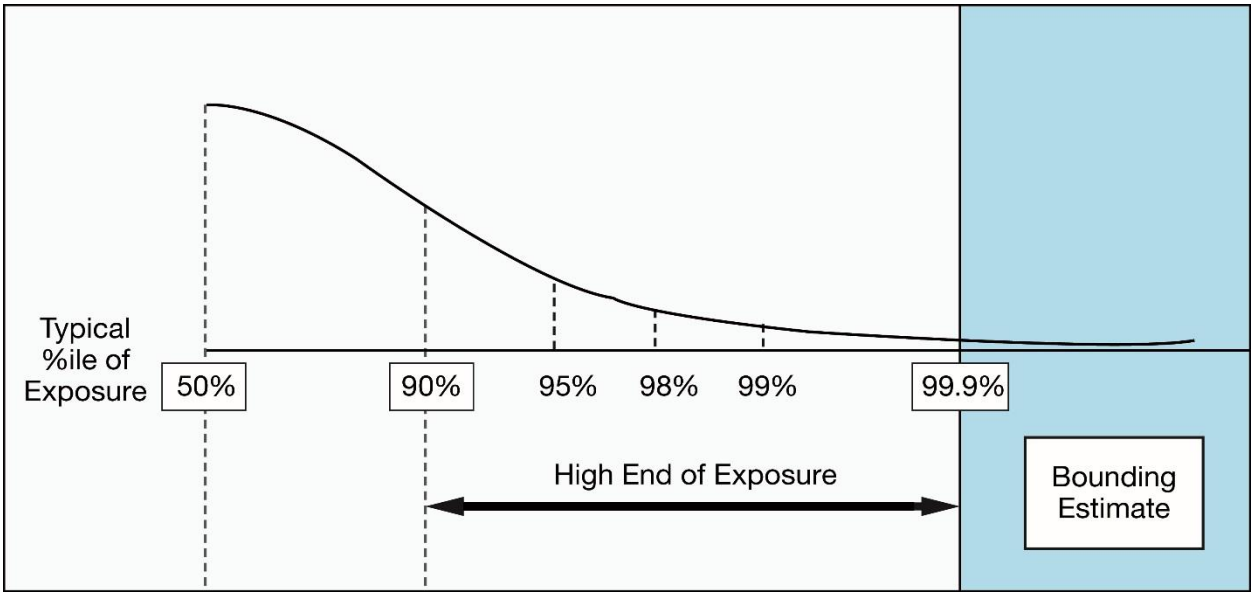
Biomonitoring data have several limitations. For example, analytical methods are unavailable for some chemicals, and results can be difficult to interpret because of background levels, confounding coexposures, metabolic processes with uncertain transformation times and limited information correlating exposures to chemical measurements or metabolites. Also, biomonitoring data may not identify the relative contribution from different sources of exposure. 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 to the biomarkers used.

The science behind biomonitoring and biomarkers is advancing rapidly, and biomonitoring in human populations is becoming more common. New research is expanding our knowledge of biomonitoring, biomarkers and the links to environmental exposures. The Centers for Disease Control and Prevention (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 its National Health and Nutrition Examination Survey (NHANES). 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 2012b). The CDC's *NHANES* website (http://www.cdc.gov/nchs/nhanes.htm) provides detailed information about the methods, datasets, data analyses and documentation associated with NHANES. Comprehensive reports are periodically released and are available at http://www.cdc.gov/exposurereport/. When using biomonitoring data in an exposure assessment, an assessor needs to be mindful of confidentiality and privacy considerations. Confidentiality concerns associated with using data from individuals are discussed in Sections 5.4.3 and 5.4.4. Chapter 7 specifically discusses the confidentiality and privacy issues associated with conducting observational human exposure measurement studies.

5.3.3. Exposure Factors

As described in Section 3.2.1, individuals within a population fall within a distribution of exposures and risks based on several factors, including personal characteristics, individuals' activities and behaviors and exposure media. Because uncertainty and variability are present in exposure assessments, EPA might incorporate a "high-end" exposure level to ensure adequate protection of potentially exposed individuals/lifestages/groups/populations. EPA's high-end levels are around the 90th percentile and above as shown in Figure 5-4. Even with a high-end value, the potential exists for individuals to be exposed at higher or lower exposures. EPA's programs estimate central tendency values and often provide a range of exposures that encompass the actual distribution (U.S. EPA 2004b).

Figure 5-4. Schematic of the Distribution of Exposures for Individual Receptors within a Population



U.S. EPA (1992c)

Exposure descriptors are used to 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 2005b). Exposure descriptors are also useful when characterizing exposure and can aid communication between exposure assessors and risk managers/decision makers. Box 5-2 provides a summary of common exposure descriptor terms used to describe exposure distributions for various individuals. The terms include definitions based on the distributions, types of exposures and types of exposed individuals.

In estimating exposure using percentiles, the exposure assessor needs to understand that the effect that using a particular percentile value has in the ultimate exposure calculation depends on more than just its position in the percentile rankings. It also depends on the variability of the data within the distribution for the input factors, the shape of the input distributions and the number of data points (U.S. EPA 2004b).

Exposure factors are used to estimate contact rates for different media (e.g., the amount of air inhaled in a breath, breathing rates). Data on people's physical characteristics (e.g., average body weight, age) also are considered exposure factors.

Box 5-2. 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 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 can be used to show that true exposures are not greater than estimated exposures. Bounding estimates often are used during screening-level assessments to eliminate exposure pathways of minor importance from further consideration or to determine whether more data and information are needed to evaluate other exposure pathways.
- **Central tendency exposures:** an estimate of exposures 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 (RME):** defined as the highest exposure that is reasonably expected to occur at a site, and is intended to estimate a conservative exposure case (i.e., well above the average case) that is still within the range of possible exposures. Used in the Superfund Program.
- **Worst-case exposure:** historically, used for the maximum possible exposure that occurs 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):** generally describes the uppermost portion of the high-end exposure range, although actual usage has varied.
- **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.

Exposure factors, along with activity pattern information and other data inputs, are used in developing an exposure scenario and a conceptual model to estimate exposures. EPA's *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011f) 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 the activity and where and when the activity occurs. Activity pattern information can be collected by using time-activity diaries (e.g., paper diaries), electronic devices (e.g., global positioning system, other hand-held devices), questionnaires or surveys.

EPA developed the EXPOsure toolBOX (EPA-Expo-Box; http://www.epa.gov/risk/expobox) to help individuals assess exposure. EPA-Expo-Box is a compendium of exposure assessment tools

that links to guidance documents, databases, models, reference materials and other related resources. Exposure assessment resources are organized into the following six Tool Sets, each containing a series of modules, which are described below.

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

Exposure assessors need to be aware of their programs' specific exposure parameters for the assessment.

5.3.4. 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, biological or physical agents or other stressors 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 2008a; U.S. EPA 2009a; Zartarian et al. 2005). Section 7.2.13 provides considerations the exposure assessor needs to consider regarding the evaluation of data from observational human exposure measurement studies in line with the study DQOs.

Observational human exposure measurement studies are used to identify the agents to which people are exposed; exposure concentrations; important sources, routes and pathways of exposure; and the factors that have the greatest impact on exposure. In addition, results from such studies are used to determine whether mitigation measures have been successful and whether regulatory standards have been exceeded. Data generated in an observational human exposure measurement study also can be used as inputs to exposure and dose models (for examples, Hore et al. 2006; Xue et al. 2006; Xue et al. 2004; Zartarian et al. 2000; Zartarian et al. 2006; Zartarian et al. 2003).

5.4. Acquiring and Evaluating Data for an Exposure Assessment

When developing the analysis plan for an exposure assessment, an exposure assessor determines what data are needed (Section 3.3.1). 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 only some of the many resources and concerns that an exposure assessor might encounter.

Each data type discussed in Section 5.3 has unique characteristics that need to be evaluated to determine their appropriateness for an exposure assessment. Also discussed in these sections are the types of activities needed to gather these data for an exposure assessment: environmental sampling; biomonitoring; compiling exposure factor information; and conducting questionnaires, surveys and observations. Resources to consult when planning and implementing a sampling program, and conducting questionnaires, surveys and observational studies are included in these sections. In addition, an exposure assessor needs to review program-specific protocols and consult with experts when planning a sampling program.

During planning and scoping (Chapter 3), an assessor determines what data are needed for an exposure assessment. For each data need, an assessor considers how to obtain the data from existing sources, if available, or whether and how to gather new data. This section provides information about existing data sources and methods for collecting new data. It also highlights some of the questions an assessor needs to answer when evaluating the data for use in an exposure assessment. The information sources and the questions provided in the following paragraphs represent only some of the many resources and questions that an assessor might encounter.

Sometimes the data needed to support an exposure assessment are available from existing resources. Additional data, however, are gathered for many reasons that might or might not align with the goals of an exposure assessment. An exposure assessor normally would consider the following issues prior to using existing data:

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

Numerous resources 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).

Table 5-6 (at the end of this section) highlights some of the more common data sources for exposure assessments EPA and other federal agencies have developed.

EPA's *Guidance for Data Usability in Risk Assessment* 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). Many of the concepts outlined in that document apply to risk assessments serving functions beyond Superfund. EPA's OPPT recommends that assessors consider the questions listed in Table 5-2 when evaluating any type of existing data for use in an exposure assessment (U.S. EPA 2012i).

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? Have these methods been adopted by an authoritative body, and do they meet project data quality objectives (DQOs) (e.g., the National Institute for Occupational Safety and Health [NIOSH]) or are they otherwise accepted by the scientific community?	Are appropriate data collection and analytical methods available? Have these methods been adopted or otherwise accepted by the scientific community? Does EPA have standard operating procedures (SOPs) for these methods? How many samples will be needed to meet the objectives of the study?
What quality assurance (QA)/quality control (QC) procedures, if any, were employed?	What QA/QC procedures are required?
What are the key uncertainties of the study or program data?	Will the uncertainty substantially limit the usability of the data in an exposure assessment?
	What will the sampling program cost?

In addition, each data type—environmental, biomonitoring and exposure factor—also has unique characteristics that need to be evaluated to determine their appropriateness for an exposure assessment. Sections 5.4.1 through 5.4.3 describe data sources, present examples of typical data and discuss special evaluation considerations for each data type.

The data needed for an exposure assessment, as outlined during the planning and scoping process (Chapter 3), are not always available in 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., requires substantial time and money) requiring 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* (U.S. EPA 2012f), can be considered when assessing the cost-benefit implications of implementing a sampling program to provide data for an exposure assessment.

Depending on the answers to these 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 that would be sufficient to fill 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 exposure assessment objectives require time, expertise or financial resources beyond the capacity of the organization; or

- 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 5.4.6 discuss the unique aspects of conducting activities to gather data for an exposure assessment: characteristics of environmental data; environmental sampling; biomonitoring; compilation of exposure factor information; conduct of questionnaires, surveys and observations; and modeling. These discussions focus only on sampling programs and methods that are 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.

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; and
- Peer-reviewed scientific literature.

Environmental data are collected 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. 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 ▪ Identify changes in existing conditions	▪ Air ▪ Ground water ▪ Surface water ▪ Soil ▪ Sediment	▪ National Stream Quality Accounting Network ▪ Water quality network ▪ Air Quality System (EPA)
Short-term media monitoring	▪ Characterize conditions at a location for a relatively short period of time	▪ Air ▪ Ground water ▪ Surface water ▪ Soil ▪ Sediment	▪ Remedial investigation sampling under the Comprehensive Environmental Response, Compensation, and Liability Act ▪ Resource Conservation and Recovery Act ▪ Special studies of environmental media ▪ Indoor air monitoring
Source monitoring	▪ Track chemical release rates to the environment from sources ▪ Characterize the relationships between release amounts and various source operating parameters ▪ Ensure regulatory compliance ▪ Identify disposal options for waste streams	▪ Air ▪ Ground water ▪ Surface water ▪ Waste streams	▪ National Emissions Inventory (EPA) ▪ Toxics Release Inventory (EPA) ▪ Stack sampling ▪ Effluent sampling ▪ Leachate sampling from landfills ▪ Incinerator ash sampling ▪ Fugitive emissions sampling ▪ Pollution control device sampling
Consumer product sampling	▪ Characterize chemical concentrations for exposure assessment ▪ Assess the quality of the food supply ▪ Ensure regulatory compliance	▪ Drinking water ▪ Food ▪ Consumer products	▪ Tap water sampling ▪ Water supply sampling ▪ Prepared food diet sampling ▪ Shelf surveys ▪ Fish sampling from contaminated water bodies ▪ Crops and livestock
Microenvironmental sampling	▪ Evaluate ambient conditions in a defined area ▪ Identify exposure concentrations	▪ Air ▪ Dust ▪ Contaminated surfaces	▪ Special studies of residences ▪ Radon measurements ▪ Office building monitoring
Personal monitoring (e.g., breathing zone samples, skin patch samples)	▪ Assess exposure to airborne chemicals ▪ Characterize dermal exposure	▪ Ambient air ▪ Indoor air ▪ Skin	▪ Observational human exposure measurement study results published in the peer-reviewed literature ▪ Industrial hygiene studies ▪ Pesticide applicator surveys

- **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 to the east, but local topography (e.g., streams, hills) might alter the direction of the flow.
- **How might the chemical concentrations vary over space and time?**
  Chemical concentrations can vary considerably from place to place, seasonally and over time because of changing use patterns, degradation and migration. Changes are of particular concern when the measured data will be used 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 concentration might exist from naturally occurring or anthropogenic sources (U.S. EPA 2002d). Naturally occurring chemicals are 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 2002a). The degree to which background needs to be considered in the sampling design can depend on the program-specific guidance. The exposure assessor needs to contact the appropriate organization for further guidance.
- **If data were collected from a microenvironmental study, do these data represent an exposure assessment population?**
  Microenvironmental measurement approaches define specific zones that are thought to be relatively homogeneous and then characterize conditions in that zone. For example, typical microenvironments include the entire home or parts of the home, office or other indoor settings and the automobile. Microenvironments also can be divided into time segments (e.g., kitchen-day, kitchen-night). This approach can produce measurements that are closely linked with the point of contact in both location and time. Because these 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.

5.4.2. Environmental Sampling

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., groundwater flow rates) further.

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; and
  - 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 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 that 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 2002c). More information on sampling and study designs is found in Section 7.2.

5.4.3. 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 of the common biomonitoring measurements, including typical measurement objectives, media sampled and key sources for this type of data. Evaluation questions specific to this type of data include:

- **Are suitable biomarker and analytical methods available to evaluate exposures?**
  Currently, biomarkers are available to assess several hundred chemical exposures and this area is the subject of ongoing research. 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 can be used in the exposure assessment.
- **Do confidentiality concerns restrict the access to or use of biomonitoring data?**
  Sometimes biomonitoring data exist but assessors cannot access them or release them publicly because of concerns or requirements about maintaining the confidentiality of personal data. For example, assessors can access NHANES "public-use" datasets but often cannot access other datasets because of confidentiality restrictions. Section 7.2.10 provides further considerations regarding confidentiality of data. The National Center for Health Statistics (NCHS) has established Research Data Centers (RDCs) to allow researchers access to restricted data. The RDC hosts restricted data from a variety of groups within the U.S. Department of Health and Human Services (HHS). Release of the

data follows strict protocols to protect the confidentiality of the participants. Further information regarding RDC is available at http://www.cdc.gov/rdc/index.htm.

- **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 that exposure to a chemical has occurred and quantify the concentration of the chemical or its metabolite in the sampled matrix. However, biomonitoring may 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 associations between biomonitoring data and exposures (Section 6.2.3) (e.g., Morgan et al. 2008; Tulve et al. 2011).

Table 5-4. Common Biomonitoring Measurements

Typical Measurement Objectives	Typical Target Media	Examples of Sources of Existing Data
▪ Confirm exposure to a chemical without without establishing an exposure source ▪ Contribute to exposure assessments by measuring the internal concentration of a chemical ▪ Assess the relationship between biomarker concentrations and body burden	▪ Adipose tissue ▪ Blood ▪ Breath ▪ Hair ▪ Nails ▪ Urine	▪ NHANES ▪ Blood lead sampling in children ▪ ATSDR National Exposure Registry ▪ National Human Adipose Tissue Survey

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

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 to 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. Sampling programs that include gathering data from individuals need to address confidentiality needs, ethical issues and protocol reviews and approvals as required by EPA policy and detailed in Section 7.2.10.

Biomonitoring studies can address data gaps associated with:

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

Evaluating Biomonitoring Data

Although these data may 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. 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 also are similar for environmental and biomonitoring studies. The objectives of an exposure assessment and tolerable level of uncertainty drive the selection of study methods and design.
- **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 needs, ethical issues and protocol reviews. Chapter 7 provides a detailed discussion of the implications associated with conducting observational human exposure measurement studies (Section 7.2.10).

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

- CDC (2012a) 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. http://www.aphl.org/aphlprograms/lss/pages/default.aspx.
- "Publications and Products" Web page. *Division of Laboratory Sciences* website. CDC. http://www.cdc.gov/nceh/dls/publications_products.html.
- "Publications and Products" Web page. *National Biomonitoring Program* website. CDC. http://www.cdc.gov/biomonitoring/publications_products.html.
- *National Center for Environmental Health* website. CDC. http://www.cdc.gov/nceh/.

5.4.4. Exposure Factor Information

Key sources of exposure factor information include:

- EPA Exposure Factors
  - EPA's *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011f);

  - EPA program, office or region default values [e.g., *Superfund Standard Default Exposure Factors* (U.S. EPA 2014c)];
- Datasets compiled by EPA:
  - Consolidated Human Activity Database (CHAD; http://www.epa.gov/heasd/chad.html);
- Datasets compiled by other federal agencies:
  - American Time Use Survey (ATUS; http://www.bls.gov/tus/),
  - Food Commodity Intake Database (http://www.ars.usda.gov/services/docs.htm?docid=14514),
  - National Health and Nutrition Examination Survey (NHANES; http://www.cdc.gov/nchs/nhanes.htm), and
  - *Continuing Survey of Food Intakes by Individuals* (http://www.ars.usda.gov/Services/docs.htm?docid=14392); and
- Peer-reviewed scientific literature.

EPA's *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011f) is the most widely known source of exposure factor data. The summary data and mean values cited in these documents are based on published studies that provide general population data (e.g., food survey findings) or data collected from sample populations from a specific group or region (e.g., fish consumption by Native Americans, outdoor activity in the Northeast). EPA also presents confidence ratings for summary data or mean values 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. These defaults are used in the absence of location- or scenario-specific information. For example, default drinking water intakes can be used when deriving Maximum Contaminant Levels. The use of defaults in risk assessment raises concerns, however, and EPA's policies about using defaults have been the subject of scrutiny. This issue was raised by public commenters and addressed in the 2004 Office of the Science Advisor staff paper *An Examination of EPA Risk Assessment Principles and Practices* (U.S. EPA 2004b). 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 can provide an assessor 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.

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

- **If default values are selected because of a lack of location- or scenario-specific information, what is the basis for these values?**
  The use of defaults needs to be considered carefully and thoughtfully 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).

- **Are the exposure factor data representative of the exposures being assessed?** Exposure factor data are derived 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. For example, a study of activities in the general population might not represent activities in a specific population group.

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 ▪ Surveys ▪ Questionnaires	▪ Body weight ▪ Height ▪ Skin surface area
Activity frequency and duration	▪ Identify how long and how frequently individuals engage in a particular activity ▪ Determine how often individuals engage in activities that could reduce potential exposures	▪ Questionnaires ▪ Surveys	▪ Time spent indoors/outdoors ▪ Frequency of hand washing ▪ Duration of showering ▪ Occupational tenure
Intake rates	▪ Determine the amount of a substance that individuals could take into their bodies from exposure	▪ Population surveys ▪ Questionnaires	▪ Drinking water ingestion ▪ Fish consumption ▪ Incidental soil ingestion ▪ Inhalation rates

U.S. EPA (2011f)

5.4.5. Questionnaires, Surveys and Observations

Data gaps in exposure factor information can be addressed by administering questionnaires and surveys or by conducting observational measurement studies. Because exposure factor data contribute to the development of a conceptual model and exposure scenarios and the quantitative assessment of exposure, findings can alter assumptions about exposure route, duration and frequency.

Data collected in an observational measurement study of human exposure need to be of sufficient quality and quantity to support the study objectives/hypotheses/scientific questions. The most efficient way to ensure both high-quality and high-quantity data is to establish the data quality criteria before the study begins and then develop a data collection design based on 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 2002b). Detailed guidance on the DQO process and other related information are available in EPA's report *Guidance for Quality Assurance Project Plans* (U.S. EPA 2002b) and at the *EPA Quality System* website (http://www.epa.gov/quality/). 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 2003g).

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. 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 simply 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. These data are less precise and likely to be somewhat less accurate than a study using a carefully conducted diary approach.
- **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 2012i).
- **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. Diary forms are designed to have respondents report all of their activities and locations for the specified period. Carefully designed forms are especially important for diary studies to ensure that the data reported by each individual are comparable. The resulting time budget can be used to 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. They can be completed by the person(s) under evaluation or by an observer. These studies sometimes employ behavioral monitoring devices (e.g., accelerometers, geographic information system [GIS] 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 that each federal agency obtain approval from the Office of Management and Budget (OMB) before collecting information from 10 or more people. 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. Because questionnaires and surveys can be components of observational human exposure measurement studies, Section 7.2 provides a detailed discussion of considerations associated with gathering data from people.

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 (2003g) *Survey Management Handbook*. EPA/260/B-03/003.
- OMB (2006) *Questions and Answers When Designing Surveys for Information Collections*.
- U.S. EPA (2007f) *Guide for Measuring Compliance Assistance Outcomes*. EPA/300/B-07/002.

5.4.6. 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" (U.S. EPA 2009c). Chapter 6 provides detailed information regarding the selection of models and their use in exposure assessments.

In exposure assessment, models can be used to address data gaps associated with:

- Chemical release rates from sources;
- Chemical fate and transport;
- EPCs;
- Exposure factors;
- Internal chemical or metabolite concentrations; or
- 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 ground water. The estimates generated by models also might comprise the conclusions of an exposure assessment (e.g., exposure models that estimate the cumulative impacts of exposures to multiple chemicals).

Box 5-5 presents useful 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. In addition, the following questions set forth in the *Guidance on the Development, Evaluation, and Application of Environmental Models* (U.S. EPA 2009c) for consideration when using a model for regulatory or research purposes provide a useful list for assessors to consider when evaluating 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 model fit with the conceptual model for the project?
- Has the model been peer reviewed?
- Has the model been evaluated with data?

The Agency has a community of practice that addresses environmental modeling. Modeling content including database and training, can be found at http://www2.epa.gov/modeling.

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 (2009c) *Guidance on the Development, Evaluation, and Application of Environmental Models.* EPA/100/K-09/003.
- EPA Modeling website. http://www2.epa.gov/modeling
- *Exposure Assessment Tools and Models* website. U.S. EPA. http://www.epa.gov/opptintr/exposure/.
- "Models Knowledge Base" Web page. *Council for Regulatory Environmental Modeling* website. U.S. EPA. http://www.epa.gov/crem/knowbase/search.htm.
- "Publications, Technical Documents, and Guidance" Web page. *Radiation Protection* website. U.S. EPA. http://www.epa.gov/radiation/cleanup/pubs.html.

5.5. Data 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 uncertainty and variability. A

detailed discussion of data uncertainty and variability, including processes and methodologies to evaluate and potentially reduce data uncertainty and variability, is presented in Sections 8.1.1 through 8.1.3. That chapter 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 used in an assessment. 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?**
  Many concepts are encompassed by the term "data uncertainty." Sampling uncertainty, also referred to 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 have been developed, ranging from classical statistical analyses to probabilistic uncertainty analyses (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, if not, can be estimated by an assessor. For example, EPA provides confidence ratings for data presented in the *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011f). A higher confidence rating typically is associated with data having fewer uncertainties. An assessor can conduct statistical analyses, such as standard deviations 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?**
  Variability—the natural differences that occur in a sampling medium or population—is introduced into an exposure assessment by all datasets. 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 (Section 2.3.4).
- **How does decision uncertainty affect exposure assessment decisions?**
  Decision uncertainty includes data uncertainty and pertains to whether the analyses have been designed adequately so that they 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 (e.g., Is there a need to further evaluate the data statistically to close data gaps? Can it be determined if the data are adequate for the decision being made? Will uncertainty in the data or in how the data 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.[12] This website houses data standards that have been 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, as well as accessibility to the project team. 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. Spreadsheets and databases are two standard technologies. Spreadsheet and database programs now are standard desktop applications. GIS 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, as well as 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. Typically, only one user can work in a spreadsheet at a time, which might present difficulties if multiple users need to access the data concurrently.
  - **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 multiple tables within a database can be linked to establish relationships between datasets. For example, a table containing activity data for individuals can be linked to another data table housing biomonitoring results. Statistical analyses also are possible using databases. Databases can be shared among users, who can access the data simultaneously.
  - **GIS** applications are sophisticated tools used to depict spatial relationships in data. Although historically they were considered to be mapping tools, current programs also 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

[12] http://iaspub.epa.gov/sor_internet/registry/datastds/home/overview/home.do.

data management system used, the data need to be appropriately annotated with supporting information so that future users can assess its quality and utility.

- **What are the implications of the Freedom of Information Act (FOIA) on data management?**
  Under the 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, http://www.epa.gov/foia/index.html.
- **What are the restrictions on releasing data publicly?**
  Some types of data, such as data exempted under FOIA, are considered confidential, and assessors need to take precautions to avoid releasing these data inadvertently. For example, the formulation of pesticides under review for registration would be considered a trade secret or confidential business information. More information about FOIA exemptions is provided at the U.S. Department of Justice's *DOJ Guide to the Freedom of Information Act* website (http://www.justice.gov/oip/foia_guide09.htm). The 1996 FOIA update[13] identifies specific provisions for the protection of 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?**
  Data management QA/QC 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 are part of records management and are a requirement of all government employees (http://www.epa.gov/records1/index.htm).

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 in more detail. Several data-related topics are essential to communicate effectively with risk managers/decision makers and stakeholders about existing data reviews or data collection efforts (Table 5-6 for data sources):

- **Data representation.** Often, quantitative data are reported as a single point (e.g., average concentration of a chemical in soil) or represent only a moment in time (e.g., concentrations in emissions from an incinerator). Rarely, however, 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

[13] Freedom of Information Act, Pub. L. No. 104-231, 110 Stat. 3048 (1996).

capacity or varying waste stream composition. Therefore, discussions about data indicate what the data do and do not represent. Presentation of data in graphical formats might be helpful in showing locations of concentrations, outliers and other parameters.

- **Data limitations.** Data can be used to 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 samples will be collected, where samples will be collected, what analyses will be conducted) and the rationale behind 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 how these parameters affect the conclusions.

Table 5-6. Examples of Sources of Data for an Exposure Assessment from EPA and other Federal Agencies

Source	Data Type	Scale	Description	Reference
U.S. EPA				
EPA – *Exposure Factors Handbook: 2011 Edition*	▪ Exposure factors	▪ Local ▪ State ▪ Regional ▪ National ▪ International	*The Exposure Factors Handbook* 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 to use for these factors. This document provides a summary of the available data on 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.	U.S. EPA (2011f) http://www.epa.gov/ncea/efh/pdfs/efh-complete.pdf
EPA – Expo-Box	▪ Exposure factors	▪ Local ▪ State ▪ Regional ▪ National ▪ International	Expo-Box is a compendium of exposure assessment tools with links to guidance documents, databases, models, reference materials and other related resources. Exposure assessment 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*.	http://www.epa.gov/risk_assessment/expobox/
EPA – National Human Exposure Assessment Survey (NHEXAS)	▪ Observational human exposure	▪ Local ▪ State ▪ Regional	NHEXAS addresses some of the limitations of single-chemical and single-media exposure route studies. 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.	http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=22424
EPA – Human Exposure Database System (HEDS)	▪ Observational human exposure	▪ National	HEDS is an integrated database system that contains chemical measurements, questionnaire responses, documents and other information related to EPA research studies of the exposure of individuals to environmental contaminants. The HEDS website contains a list of studies. Project information includes actual datasets, metadata and relevant documentation describing the studies.	http://www.epa.gov/heds/index.htm

Table 5-6. Examples of Sources of Data for an Exposure Assessment from EPA and other Federal Agencies (continued)

Source	Data Type	Scale	Description	Reference
U.S. EPA (continued)				
EPA – Total Exposure Assessment Methodology Study (TEAM)	▪ Observational human exposure	▪ Local	TEAM, conducted from 1979 to 1985, sought to develop 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.	Wallace (1987)
EPA – Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants Study (CTEPP)	▪ Observational human exposure	▪ State ▪ Regional	CTEPP 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. The research sought to identify the major pathways and sources through which children are exposed to chemicals. CTEPP, an observational human exposure measurement study, did not involve introducing chemicals into homes or daycare centers. Participants maintained normal daily routines during the study. The CTEPP website provides chapter-by-chapter files of data, which also are made available through HEDS.	http://www.epa.gov/heasd/research/ctepp.html
EPA – Detroit Exposure and Aerosol Research Study (DEARS)	▪ Observational human exposure	▪ State ▪ Regional	DEARS was designed to develop data 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 other air toxics. These data were correlated with information, such as blood pressure and heart rate, relevant to potential health effects.	http://www.epa.gov/dears/
EPA – Pesticide Handlers Exposure Database (PHED)	▪ Observational human exposure (occupational)	▪ Regional ▪ National	PHED is a database containing empirical exposure monitoring data for workers involved in the handling or application of pesticides in the field. The website features information on the data, worker exposure considerations and a PHED users guide.	http://www.epa.gov/pesticides/science/handler-exposure-data.html

Table 5-6. Examples of Sources of Data for an Exposure Assessment from EPA and other Federal Agencies (continued)

Source	Data Type	Scale	Description	Reference
U.S. EPA (continued)				
EPA – Relationship Between Indoor, Outdoor and Personal Air Study (RIOPA)	▪ Observational human exposure	▪ Regional	RIOPA quantified indoor and outdoor inhalation exposure to agents in three different areas of the United States. During the study, integrated indoor, outdoor and personal air samples were collected both for gas-phase and fine particulate matter (2.5 µm or smaller) analyses. Samples were analyzed for fine particulate matter mass, 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.	Weisel et al. (2005)
EPA – ExpoCast Database (DB)	▪ Observational human exposure ▪ Environmental ▪ Biological	▪ Local ▪ State ▪ Regional ▪ National	ExpoCastDB captures results from observational studies measuring potential exposure to environmental chemicals. It contains data from studies in which chemicals were measured in environmental and biological media. The database also provides access to data on chemical structure and physicochemical values.	http://www.epa.gov/nccct/expocast/
EPA – Air Quality System (AQS)	▪ Environmental	▪ Local ▪ State ▪ Regional ▪ 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 (QA)/quality control (QC) information. Data can aid in an exposure assessment of chemicals in air at varying geographic areas.	http://www.epa.gov/ttn/airs/airsaqs/
Centers for Disease Control and Prevention (CDC)				
CDC – NHANES	▪ Observational human exposure ▪ Biological	▪ National ▪ Regional	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 aged 60 years and older, African Americans and Hispanics.	http://www.cdc.gov/nchs/nhanes.htm

Table 5-6. Examples of Sources of Data for an Exposure Assessment from EPA and other Federal Agencies (continued)

Source	Data Type	Scale	Description	Reference
Centers for Disease Control and Prevention (continued)				
CDC – National Reports on Human Exposure to Environmental Chemicals	▪ Biological ▪ Biomonitoring	▪ National	The *National Report on Human Exposure to Environmental Chemicals (National Exposure Report)* is a series of ongoing assessments of the U.S. population's exposure to environmental chemicals using biomonitoring. Biomonitoring is the direct assessment of individuals' exposure to chemicals by measuring the chemicals or their breakdown products (metabolites) in blood or urine.	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.	http://www.cdc.gov/nchs/
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 RDC also hosts restricted data from a variety of groups within the U.S. Department of Health and Human Services (HHS).	http://www.cdc.gov/rdc/index.htm
CDC – Behavioral Risk Factor Surveillance System (BRFSS)	▪ Biological ▪ Health-related behaviors ▪ Human activity	▪ State ▪ National	BRFSS is an ongoing 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, D.C.; 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.	http://www.cdc.gov/BRFSS/

Table 5-6. Examples of Sources of Data for an Exposure Assessment from EPA and other Federal Agencies (continued)

Source	Data Type	Scale	Description	Reference
Centers for Disease Control and Prevention (continued)				
CDC – Agency for Toxic Substances and Disease Registry (ATSDR)	▪ Public health assessments ▪ Health consultations	▪ Local ▪ State ▪ 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.	http://www.atsdr.cdc.gov/COM/exposure.html; http://www.atsdr.cdc.gov/hac/PHAManual/toc.html; http://www.atsdr.cdc.gov/hac/pha/index.asp
NIOSH – National Occupational Exposure Survey (NOES)	▪ Observational human exposure	▪ National	From 1981 to 1983, NIOSH conducted NOES, which collected data on potential occupational exposures to chemical, physical and biological agents. The survey involved onsite visits to 4,490 establishments in 522 industry types employing approximately 1,800,000 workers in 377 occupational categories. Nearly 13,000 distinct potential exposure agents and more than 100,000 unique trade-name products were observed during these onsite visits.	http://www.cdc.gov/noes/
NIOSH – Health Hazard Evaluations (HHEs)	▪ Observational human exposure ▪ Environmental ▪ Biological	▪ Local	An HHE is a study of a workplace and potential exposures and hazards. It is performed to learn whether workers are exposed to hazardous materials or harmful conditions. In an HHE, NIOSH staff visit the workplace, meet with employer and employee representatives to discuss issues, tour the workplace, review records about exposure and health, interview or survey employees, measure exposures and conduct medical testing. At the end of this evaluation, NIOSH provides a written report to the employer and employee representatives.	http://www.cdc.gov/niosh/hhe/
NIOSH – Workplace Data and Statistics Gateway	▪ Observational human exposure ▪ Environmental ▪ Biological	▪ Local	NIOSH's *Workplace Data and Statistics Gateway* provides centralized access to NIOSH data collected in NIOSH research and surveillance studies. It also provides access to a range of CDC/NIOSH research and statistical tools and historical surveillance information.	http://www.cdc.gov/niosh/data/

Table 5-6. Examples of Sources of Data for an Exposure Assessment from EPA and other Federal Agencies (continued)

Source	Data Type	Scale	Description	Reference
U.S. Census Bureau				
U.S. Census Bureau – American FactFinder	▪ Demographics	▪ Census tract ▪ State ▪ Regional ▪ National	The Census Bureau's American FactFinder is an interactive application that supports the Economic Census, the American Community Survey, the 1990 Census, Census 2000 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.	http://factfinder2.census.gov/faces/nav/jsf/pages/index.xhtml
U.S. Census Bureau – Equal Employment Opportunity (EEO) Data Tool	▪ Demographics	▪ Census tract ▪ State ▪ Regional ▪ 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.	http://www.census.gov/people/eeotabulation/
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.	http://www.bls.gov/tus/
Occupational Safety and Health Administration (OSHA)				
OSHA (U.S. Occupational Safety and Health Administration) – Industry Profile for an OSHA Standard	▪ Observational human exposure	▪ State ▪ National	This database compiles OSHA citations for each OSHA standard issued by the federal or state OSHA during a specified fiscal year for particular industries.	http://www.osha.gov/pls/imis/industryprofile.html

Table 5-6. Examples of Sources of Data for an Exposure Assessment from EPA and other Federal Agencies (continued)

Source	Data Type	Scale	Description	Reference
U.S. Geological Survey (USGS)				
USGS – Toxics Program	▪ Environmental	▪ Local ▪ Regional ▪ National	The Toxics 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 waterbodies and other factors that could contribute to exposures.	http://toxics.usgs.gov/index.html)
USGS – National Water Information System	▪ Environmental	▪ Local ▪ Regional ▪ National	National Water Information System Mapper can provide information on the geological locations of water bodies that might be sources of exposure.	http://waterdata.usgs.gov/nwis
USGS – National Water Quality Assessment Program (NAWQA)	▪ Environmental	▪ Local ▪ State ▪ 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 were 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.	http://water.usgs.gov/nawqa/
USGS – Health Related Activities	▪ Environmental	▪ Local ▪ State ▪ National	The Human Consumption of Chemical Contaminants portion of this web page 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.	http://health.usgs.gov/bioacc_cont/water_sediment_tissue.html
USGS – National Stream Quality Accounting Network (NASQAN)	▪ Environmental	▪ Local ▪ Regional ▪ 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.	http://water.usgs.gov/nasqan

Table 5-6. Examples of Sources of Data for an Exposure Assessment from EPA and other Federal Agencies (continued)

Source	Data Type	Scale	Description	Reference
U.S. Geological Survey (continued)				
USGS – Sediment Data Portal	▪ Environmental ▪ Land use	▪ Local ▪ Regional ▪ 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.	http://cida.usgs.gov/sediment/
USGS – Environmental Health Sciences (EHS)	▪ Environmental data	▪ National	USGS provides information useful in characterizing the processes that affect the interaction among the physical environment, the 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 the 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.	http://www.usgs.gov/environhealth/
U.S. EPA/USGS – Water Quality Data Portal (WQP)	▪ Environmental ground water	▪ Local ▪ National	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 where samples were collected) and sample results (analytical data of collected samples).	http://www.waterqualitydata.us/
USGS - background levels of elements in soils and other surficial materials	▪ Environmental soil	▪ Local ▪ 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.	http://www.usgs.gov/fag/categories/9783/2566

Not exhaustive.

CHAPTER 6. COMPUTATIONAL MODELING FOR EXPOSURE ASSESSMENT

This chapter highlights basic computational modeling concepts for an exposure assessor to consider when using modeling approaches for an exposure assessment and provides an overview of modeling for exposure assessment. Specifically, it:

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

6.1. Principles and Definitions of Modeling

In EPA's *Guidance on the Development, Evaluation, and Application of Environmental Models* (U.S. EPA 2009c), the Agency adopted the National Academy of Sciences' (NAS) 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 the mathematics and making simplifying assumptions, as appropriate. Within an exposure assessment, computational models are tools used by the assessor to analyze and characterize processes that are too complex to be captured completely by empirical data.

In general, the modeling process within an exposure assessment might include interactions between 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 2009c). Depending on the analysis plan determined during the problem formulation phase of an exposure assessment (Section 3.2), exposure modeling might be used to estimate environmental concentrations, extend existing exposure information to refine exposure estimates, predict exposures for 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 1989; U.S. EPA 1992b; Williams et al. 2010). After the project team has identified the problem to be addressed by modeling, the specifications of the problem are determined, 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 is part of developing the analysis plan (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 is described in greater detail in *Guidance on the Development, Evaluation, and Application of Environmental Models* (U.S. EPA 2009c). In summary, this model guidance document recommends that model developers and users:

- Subject their model to credible, objective peer review;
- Assess the quality of the data they use;
- 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; and
- 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 (DQOs) to ensure that they are achieved (Section 5.2). An assessor might need to refine the model further or use a new model if these criteria are not met. The resources listed in Box 6-1 support the Agency's continued efforts to ensure the quality, transparency and reproducibility of the information in models used and disseminated by the Agency.

Box 6-1. Pertinent Resources for Modeling

- U.S. EPA (2002e) *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 (2009c) *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. http://www.epa.gov/quality.
- *Exposure Assessment Tools and Models* website. U.S. EPA. http://www.epa.gov/opptintr/exposure/.
- " "Publications, Technical Documents, and Guidance" Web page. *Radiation Protection* website. U.S. EPA. http://www.epa.gov/radiation/cleanup/pubs.html.

6.2. Selecting the Type of Model for Exposure Assessments

The process of model selection first involves identifying the type of model that is needed to meet the risk management objectives of the assessment and then determining the complexity of the model necessary to reach a decision. Once the type of model is defined, the assessor determines whether a model exists to meet those needs or a new model needs to be developed.

Appropriate model selection is critical for accurately estimating exposure concentrations. In most cases, assessors can choose from among several appropriate models for the populations and sources of interest. When selecting and using models, assessors need to collaborate with individuals experienced in modeling and 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 1988). Also equally critical is to choose appropriate default values for exposure information where data are missing or incomplete. The best model is less reliable without good data and appropriate default factors. A presentation of the rationale for selecting the model is essential to promoting transparency in the assessment (Section 6.2.1). A list of environmental modeling-related inventories and clearinghouses is provided in Table 6-1. Models range from simple to complex and users will typically begin with simpler models to screen out exposures of low concern (Section 6.2.2). Certain questions are also more amenable to simple models. For example, if the goal is to determine whether a level of a chemical in a product or observed to occur in an environmental medium is of low concern, a bounding analysis using a deterministic model might be sufficient. Certain goals will by necessity, however, require more advanced models. Questions concerning the fraction of the population affected by a source or the quantitative characterization of uncertainty immediately dictate the need for probabilistic models (Section 6.2.3).

6.2.1. Setting the Objectives for the Modeling Effort

Before using a model to estimate an exposure, an exposure assessor defines the exposure assessment goal(s) and describes how the model addresses assessment questions or hypotheses. The objective of the exposure assessment is the primary consideration in selecting a model. The objective of the modeling effort within the exposure assessment is to adequately represent the processes of greatest importance (U.S. EPA 2009a). Identifying these processes is a key part of developing the conceptual model (Section 3.2.2).

An exposure assessor, in collaboration with other project team members, develops a clear statement of what information the model will estimate and how this estimate will be used. This information is included in the exposure assessment plan, the modeling approach document or a standard operating procedure (SOP), depending on program, office or regional guidelines. The modeling approach needs to be consistent with known project constraints (e.g., schedule, budget). The information needs that the model will address are described in the exposure assessment's analysis plan, discussed in Section 3.1. Considerations include capturing variability over time, space or members of a population.

In setting the modeling objectives, exposure assessors need to consider how the model outputs will be used in the exposure assessment. Considerations include identifying population groups of concern; determining whether outputs need to be presented on a daily, quarterly, yearly or multiyear basis; deciding on the number of prediction years (i.e., lifetime or shorter timeframes); modeling based on location (e.g., on site, at the smoke stack, fence line, off site, indoor, in-vehicle, outdoor, residential); capturing variability over time, space or members of a population; and presenting model results appropriate for the intended purpose and audience.

Exposure assessors need to be aware that many available modeling applications could make exposure-modeling simulation appear deceptively simple. Any statistical modeling used to predict or estimate exposure is highly recommended to be conducted by, or in conjunction with, an expert in the discipline.

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

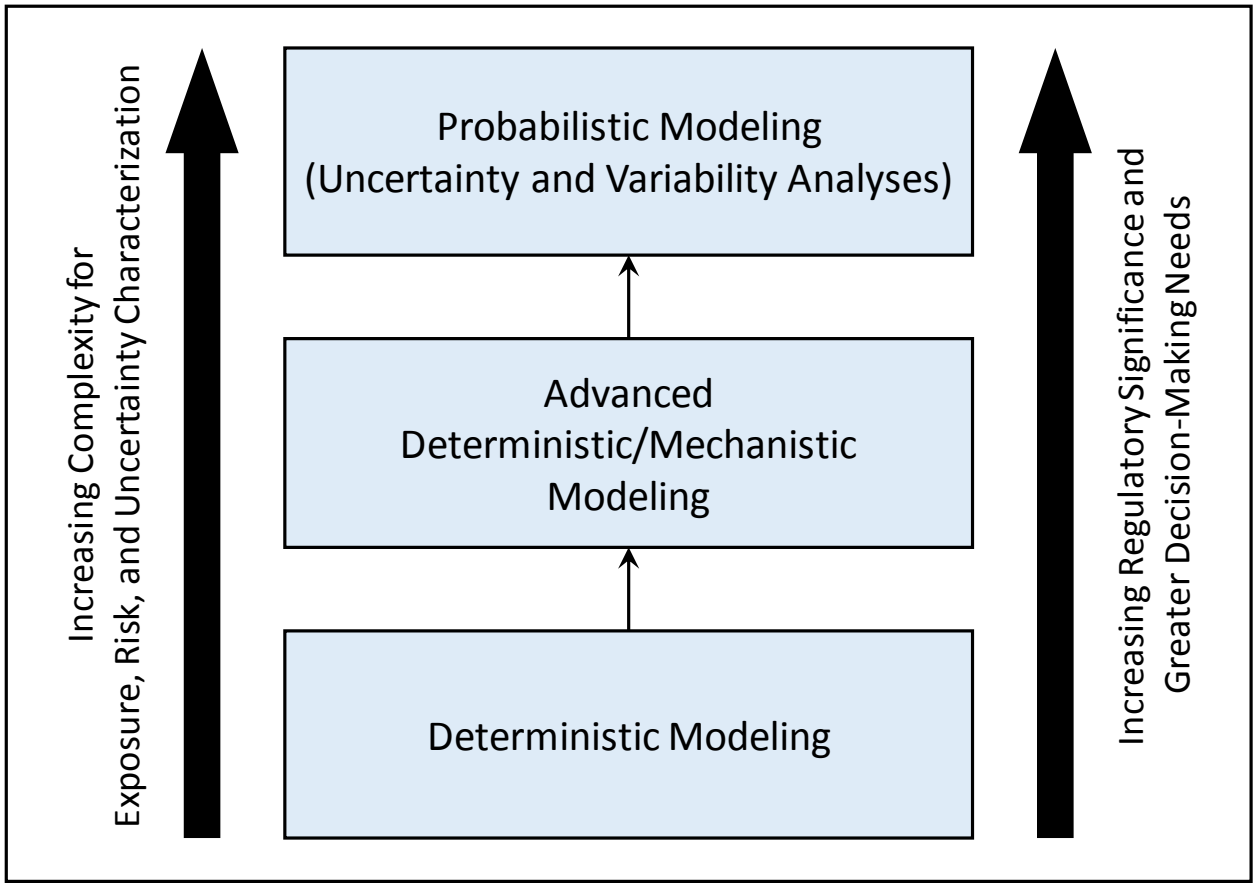
Source	Description	Types of Models and Information	URL
Registry of EPA Applications and Databases (READ)	Authoritative source of information about EPA information resources.	Models that are used, supported or funded by EPA.	http://ofmpub.epa.gov/sor_internet/registry/systmreg/home/overview/home.do
EPA 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 ground water, 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 (2012e) https://wiki.epa.gov/watershed2/index.php/The_Center_for_Subsurface_Modeling_Support_CCSMoS)
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.	http://www.epa.gov/ttn/chief/emch/index.html
An Overview of Exposure Assessment Models Used by the U.S. Environmental Protection Agency	Overview of exposure assessment models supported and used by EPA.	Models include 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.	http://www.epa.gov/ttn/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 that can be used in the development of Total Maximum Daily Loads, wasteload allocations and watershed protection plans.	http://www.epa.gov/athens/wwqtsc/index.html
Exposure Assessment Tools and Models	Website from which users can download or access models used by the Office of Pollution Prevention and Toxics in its programs.	Models used for prioritization, screening and detailed assessment of chemicals. Includes fate and transport, release and exposure assessment models.	http://www.epa.gov/oppt/exposure/

6.2.2. Level of Model Complexity

Based on the problem statement and system conceptualization developed jointly by the risk manager/decision maker, exposure assessor and modeler during the initial stage of the exposure assessment, a modeling methodology is developed. This methodology stipulates the degree of complexity of the model to be used. The computational models used at EPA in exposure assessment range from simple screening-level models to probabilistic models, based on both the complexity of the exposure assessment and regulatory considerations. Figure 6-1 illustrates that the complexity of the exposure and uncertainty characterization in an exposure assessment needs to increase to meet greater decision-making needs and regulatory significance, typically requiring selection of more complex models. A simplistic model with few input variables, however, can also include uncertainty and variability for probabilistic analyses. Figure 6-2 illustrates the difference between deterministic and probabilistic models, which are described below.

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 that is considered most critical to predicting human exposures, often using default or conservative assumptions. Screening-level exposure assessments that use screening-level models are developed routinely in certain EPA programs. 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 is the Office of Pollution Prevention and Toxics' (OPPT) use of the Exposure and Fate Assessment Screening Tool (E-FAST) to estimate the dermal, inhalation and ingestion exposure to pesticides of consumers and the general population (U.S. EPA 2007e). Assessors are encouraged to consult their programs to determine which screening-level models are used in their programs, and develop an understanding of their capabilities and limitations. Higher tier models provide more refined estimates for certain types of regulatory and decision-making needs. For instance, EPA conducted a probabilistic exposure assessment that evaluated potential exposure and risk to children from chromated copper arsenate-treated wood as part of the reregistration of the chemical (Zartarian et al. 2006).

Figure 6-1. A Tiered Approach for Modeling Analysis



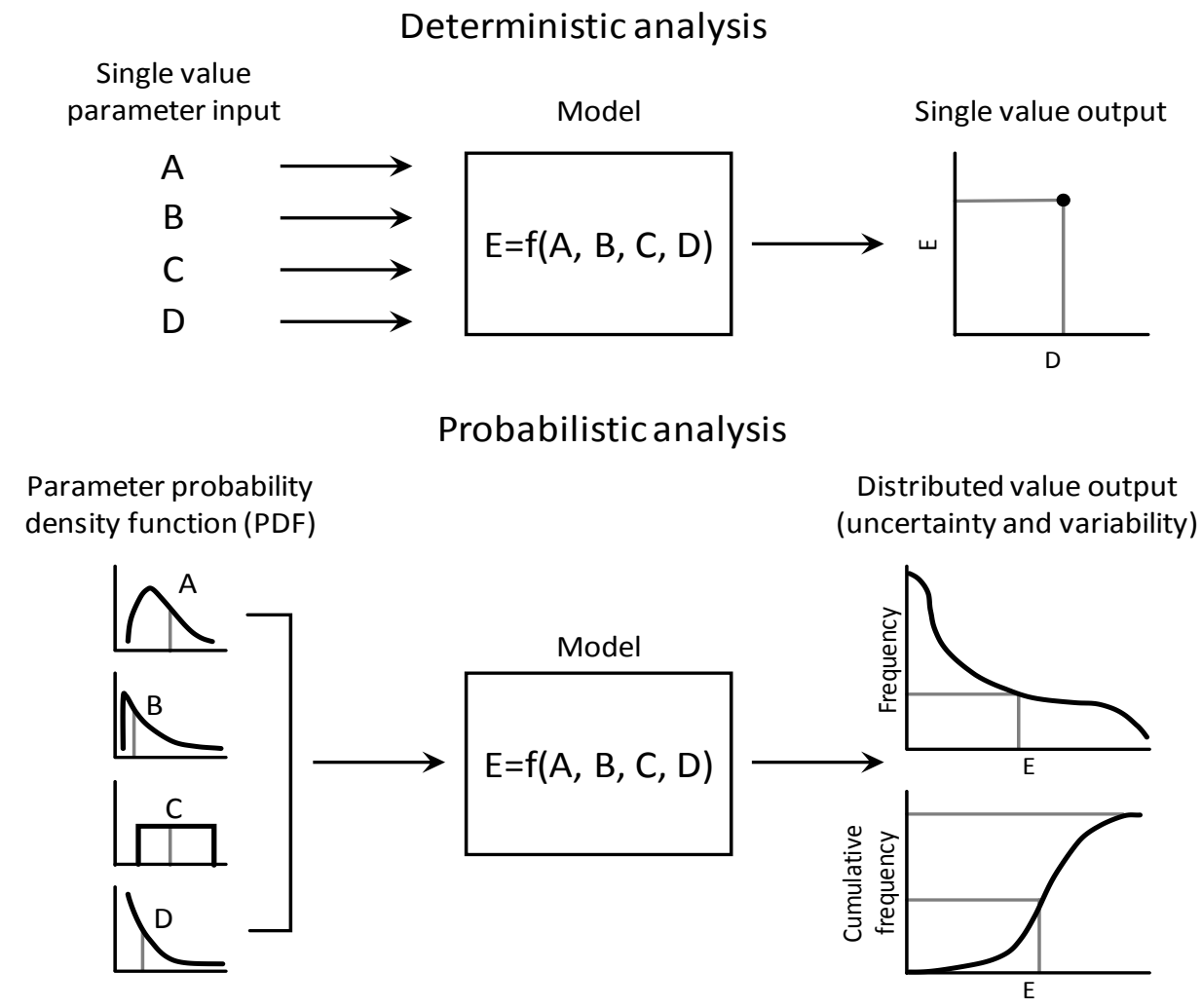
Adapted from Özkaynak et al.(2011)

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. Deterministic models, however, can be used to determine the range of possible outcomes. Some deterministic models are referred to as screening-level models either because of their limited spatial or temporal resolution or because they provide conservative estimates of exposure. Resources that support the use of screening-level models are listed in Box 6-2.

Screening-level models are used for screening or prioritization purposes, compliance-related decisions, regulatory considerations and other scientific applications. Screening-level models can be used to determine whether additional data are needed or to provide inputs required for further model refinement. Screening-level models also can be used to determine if the potential for exposure justifies an in-depth evaluation of the problem by using a more sophisticated exposure model.

Figure 6-2. Deterministic versus Probabilistic Analysis



Adapted from Maslia and Aral (2004)

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

- U.S. EPA (2001e) *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 (2009c) *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. http://www.epa.gov/oppt/exposure/. Provides access to the Office of Pollution Prevention and Toxics' (OPPT) screening-level models and documentation.

In a screening-level analysis, an exposure assessor generally relies on default values, which are point estimates for input parameters that are inherently broad in scope. These default values are selected so that analyses 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 evaluated is not a concern (U.S. EPA 2004b). Potential exposures based on the scenarios are identified and compared to screening values. Screening values include health-based values that are expressed as a dose (e.g., reference doses) and chemical concentrations in a specific medium (e.g., soil screening values).[14] The exposure assessor determines which exposure pathways, if any, require additional evaluation. Typically, exposures that exceed screening values are carried forward. 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.

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.

Probabilistic Models

Probabilistic exposure modeling (e.g., Monte Carlo analysis, Latin hypercube) represents a higher tier assessment method that provides statistical estimates of probable exposure to agents of interest. A probabilistic analysis considers the same exposure parameters (e.g., agent concentration, exposure duration, intake rate) as other types of exposure assessments but provides information on the range or distribution of exposures within a population rather than assigning a single number. The output of a probabilistic assessment is a probability distribution of exposures that reflects the combination of the probability distributions selected for one or more of the model inputs or parameters. The distributions are used to characterize the aspects of variability, uncertainty or both, depending on the sophistication of the method employed, in exposure estimates that are associated with model inputs and parameters. Box 6-3 lists examples of available resources for probabilistic assessments and models.

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. These assessments can include one-dimensional Monte Carlo analysis, as well as additional advanced multivariate or probabilistic analysis techniques. Some analyses might even involve simulations to evaluate temporal variability and spatial variability. Probabilistic risk assessment is employed when detailed statistical analysis is necessary to support sensitive decisions and help risk managers/decision makers distinguish among possible alternatives.

[14] When using chemical concentrations as screening values, an exposure assessor usually can compare an exposure point concentration (EPC) directly to the value. In this case, estimating the exposure quantitatively would not be necessary.

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. Risk Analysis 14: 53–73.
- U.S. EPA (1996d) *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 (1999a) *Report of the Workshop on Selecting Input Distributions for Probabilistic Risk Assessment*. EPA/630/R-98/004.
- U.S. EPA (2001g) *Risk Assessment Guidance for Superfund: Volume III – Part A. Process for Conducting Probabilistic Risk Assessment.* EPA/540/R-02/002.
- U.S. EPA (2005f) *Review of the National Ambient Air Quality Standards for Particulate Matter: Policy Assessment of Scientific and Technical Information.* EPA/452/D-03/001.
- *Probabilistic Model Evaluation* website. U.S. EPA. http://www.epa.gov/AMD/Research/Air/probalistic_model_eval.html.
- U.S. EPA (2014d) *Risk Assessment Forum White Paper: Probabilistic Risk Assessment Methods and Case Studies.* EPA/100/R-14/004.

Probabilistic approaches also can be used to identify data gaps where additional data collection might be necessary to reduce uncertainty and address variability. If data gaps are identified, an exposure assessor can address these gaps by collecting additional data or conducting additional statistical analyses, such as meta-analyses of existing data (Volstad et al. 2003; Weigel 2003).

Depending on the exposure assessment objectives, probabilistic methods of varying sophistication are available. Monte Carlo analysis is a widely used probabilistic method that uses computer simulations to combine multiple probability distributions. During the simulation, values of variables are selected randomly, and a quantitative exposure is estimated. This process is repeated to generate a series of exposure estimates that can be summarized with statistical analysis. In practice, assuming independence in the absence of data on correlations among input parameters contributes to uncertainty. In more complex simulations, parameters can be linked by conditional distributions or correlation coefficients. A one-dimensional Monte Carlo analysis characterizes uncertainty, variability or both related to model inputs (U.S. EPA 2001g).

Advanced Modeling Methods

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 2001g), 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 (Section 2.4.1) assumes that exposures are constant over time. Exposures at any

given moment, however, tend to fluctuate as individuals move from one microenvironment (e.g., outdoors, commuting) to another. Microexposure event analysis separately models the doses an individual receives while in each microenvironment for a period sufficiently short that exposures are reasonably constant. These individual doses are then summed to give 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, distributions that represent variability and data uncertainty are sampled using nested computational loops (MacIntosh et al. 1995). Varying parameter values over many iterations (e.g., 5,000 times) results in probability distributions that can be evaluated further with statistical analyses (e.g., evaluation of confidence limits surrounding the base-case variability distributions). In the more advanced probabilistic modeling of variability and uncertainty separately, bootstrap-based uncertainty analysis techniques described in Xue et al. (2006) for the Stochastic Human Exposure and Dose Simulation (SHEDS) model application to the chromated copper arsenate case study is one of the approaches used by EPA.
- **Geospatial Statistics.** This specialized branch of statistical analyses, a multivariate statistical tool, explicitly considers the location of data points. Geospatial statistics can be used to incorporate information about the spatial distribution of chemical concentration inputs and modeled exposure predictions (e.g., cities, states and regions).
- **Expert Judgment and Bayesian Analysis.** 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 not feasible or data are not yet available. The resulting information can inform decisions associated with the exposure assessment. Experts characterize the relationships, quantities, events or parameters of interest based on their professional judgment and expertise. These characterizations typically are expressed 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 applies 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 2011e). For Bayesian analysis, experts in a field construct distribution probabilities based on professional judgment and experience. These distributions can be updated as new data become available. Statistical analyses can be employed to quantify the value of the information stemming from the Bayesian analysis and the impact on uncertainty and variability evaluations (Bates et al. 2003; Gronewold et al. 2008). Expert elicitation can support probabilistic approaches when data are scarce or lacking.

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 addressed by the model and uncertainty introduced by the model. Note that models that are more complex 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 an exposure assessment process and to capture different processes in the source-to-exposure continuum. These models are described below. The emphasis here is physical-based deterministic or probabilistic models. Statistical models such as regression models based on available data, however, can be used to help estimate the distribution of exposures within a population, including central tendencies and percentiles, or to help quantify the relative significance of factors that can influence exposure levels. These include:

- **Fate and transport models**, which are used to 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 represent concentrations as potential exposures to receptors, although these estimates often are used as a proxy or surrogate for actual exposure or serve as inputs to other exposure models.
- **Integrated fate/transport-exposure models**, which include those models that yield both predicted ambient pollutant concentrations and predicted exposures.
- **Human exposure models**, which 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.
- **Dose estimation models**, which are 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 biological material.

Fate and Transport Models

Fate and transport models are used by exposure assessors to estimate the movement and alteration of contaminants as they are transported through environmental media (e.g., air, soil, water, ground water) (U.S. EPA 2012h). 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, as well as concentrations at specific locations (e.g., fence lines, locations for permit compliance, on site, off site).

Fate and transport models depict physical, chemical and biological processes. Physical processes include groundwater flow, volatilization and dispersion in air. Chemical processes include chemical oxidation and reduction, sorption to solid material and dissolution. Microbial degradation also can affect concentrations of chemicals in the environment and change the chemical nature of contaminants. Two examples of atmospheric fate and transport models used in the Agency are the spatially resolved point- and line-source-oriented AERMOD model with limited consideration of chemistry or removal processes (http://www.epa.gov/ttn/scram/dispersion_prefrec.htm#aermod) and the more complex multisource and larger spatial scale Community Multiscale Air Quality model (CMAQ) that incorporates physical chemical processes influencing the concentrations of various pollutants and

their species (http://www.epa.gov/amad/Research/RIA/cmaq.html). More detailed information on the use of fate and transport models is available through the resources listed in Table 6-1.

Integrated Fate/Transport-Exposure Models

Integrated fate/transport-exposure models combine (i.e., integrate) 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, ambient pollutant concentrations are integrated with location-specific representative human or demographic data along with relevant exposure factors (e.g., breathing rates, times spent indoors and outdoors) to estimate or predict human exposures using both atmospheric transport and diffusion models and human exposure models (e.g., SHEDS, Air Pollutants Exposure Model [APEX], Hazardous Air Pollutant Exposure Model [HAPEM]). The primary focus of these models is on integrating fate and transport parameters with exposure information for complex assessments. In addition, many integrated fate/transport-exposure assessment models provide estimates of potential or absorbed dose.

Although many of EPA's exposure models have been designed as standalone models, ongoing efforts in the Agency have focused on developing integrated modeling approaches. For example, 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 have been developed (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 that 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 2008b).

As indicated by the examples above, integrated fate/transport-exposure models generally are designed for a specific purpose (e.g., human inhalation exposures from hazardous air pollutants or fumigants, cumulative exposures). Detailed information on integrated fate/transport-exposure models can be obtained through the resources listed in Table 6-1.

Human Exposure Models

Human exposure models simulate and predict population exposure and dose distribution and assess variability in model inputs. An overview of these models is provided at the website,[15] *An Overview of Human Exposure Modeling at the U.S. EPA*'s *National Exposure Research Laboratory* and in journal publications (Furtaw Jr. 2001; Williams et al. 2010). EPA and other organizations have developed several human exposure models suited for inhalation exposure modeling for criteria air pollutants (e.g., SHEDS-Air, APEX) or other hazardous pollutants (e.g., HAPEM). In addition, EPA and several groups have developed similar but more complex probabilistic multimedia human exposure and dose models (e.g., SHEDS-Multimedia, Cumulative and Aggregate Risk Evaluation System [CARES™], LifeLine™, Calendex™) to accommodate additional chemicals (Price et al. 2001; Young et al. 2012). These models are

[15] http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=58356.

examples of microexposure event models. They couple environmental pollutant concentrations in specific environmental media/microenvironments (either modeled or measured) with estimates of the actual/assumed amount of time individuals spend in contact with these media/microenvironments to provide a robust characterization of exposure. The models simulate and track an individual's movements through space and time (and apportion the time of day spent in various activities or locations) to yield a time series or estimate of daily exposure to a pollutant. Detailed information on human exposure models can also be obtained through the resources listed in Table 6-1.

Estimates of Exposure Using Scenario Evaluation

In the planning and scoping phase of an exposure assessment, an assessor develops exposure scenarios of interest, as described in Section 3.1. 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 potential exposures might occur. An assessor determines chemical concentrations in a medium or location and links this information with individual or population exposures. 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 are then 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. This assumption is discussed in Section 6.3.4 on model uncertainty analysis. Generally, the closer to the point of contact (in both space and time) the concentration in the medium can be measured, the less uncertainty exists in an exposure concentration characterization. The change in the concentration over time can be estimated to 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 mentioned in Section 6.2.2 on microexposure event analysis). 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. 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 2011f);
- Consolidated Human Activity Database (CHAD; http://www.epa.gov/heasd/chad.html);
- American Time Use Survey (ATUS; http://www.bls.gov/tus/);

- Demographic data; and
- Survey statistics.

In the absence of more substantive information, participant-specific activity information is obtained 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 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 different environmental media and selected exposure factors, explicitly identifying the data requirements. Typically, a complete dataset is needed to estimate aggregate exposures using these algorithms. 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 residential surfaces that have been treated. These SOPs are used for product registration or reregistration in the United States and are intended to 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 2012i). Scenario evaluations also are commonly used in screening-level assessments in other EPA programs.

Another example of a scenario-based approach is EPA's *Example Exposure Assessment Scenarios Tool* website (U.S. EPA 2005b), which is designed to develop 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 2011f) 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. These estimates, however, are limited by the assumptions or boundary conditions used to derive them (boundary conditions are discussed in Section 5.2.2). To address this limitation, an assessor (1) evaluates an exposure equation under conditions when 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 microenvironmental method. The term microenvironment refers to surroundings (e.g., home, office, automobile) that can be 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 time segments and locations in which the assumption of uniform concentration is approximately true and then sums results for all time segments to estimate total exposure. 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

conducted during an exposure event. Although estimates of exposure concentration and time of contact still are derived indirectly by this method, the concentration and time of contact can be measured for each microenvironment. This process avoids much of the error caused by using average values when concentration varies widely along with time of contact. Tools such as Monte Carlo analysis also can be used to describe variability and parameter uncertainty. Additional discussion of variability and uncertainty analysis in probabilistic modeling is presented in Section 6.3.4.

Human Dose Models

Models have been developed that estimate dose from exposure data or estimate both exposure and dose from environmental data. Models also are used to estimate the severity of health effects from exposure to stressors.

Exposure and Dose Estimation Using Biomonitoring Data

Biomonitoring is the measurement or tracking of an agent or biomarker in an organism or in biological material, such as blood or urine, for monitoring exposure to an agent. It is an integrated measurement of exposure to a chemical from all sources and routes at a point in time. Biomarkers of exposure confirm that an individual has been exposed to a chemical and is 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). Biomonitoring data 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; Tan et al. 2005)]. A major 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. If available, simple reverse dosimetry models can be used to tie a biomarker concentration to an external dose. Chemicals or their metabolites commonly are used as biomarkers of human exposure in body fluids such as urine, blood, breath, hair and saliva. 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 these contaminants usually have longer half-lives (e.g., >1 month) in humans. The characteristics of a good biomarker of exposure include being sensitive, specific, biologically relevant, reliable, easy to collect, inexpensive and available (Metcalf and Orloff 2004). A good biomarker of exposure is useful as a surveillance tool and for helping quantify human exposures and absorbed doses of environmental chemicals (Sobus et al. 2010).

Forward Dosimetry

Forward and reverse dosimetry are two approaches for using biomonitoring data to provide quantitative estimates of human exposure to chemicals. Forward dosimetry is a process of using environmental measurements 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). Often, forward-based biomarker predictions and measured biomarker concentrations are not consistent. For example, when intake doses lead to predicted excreted amounts of a urinary biomarker (e.g., 10 ng/kg/day) that are lower than measured excreted biomarker amounts (e.g., 80 ng/kg/day), an exposure assessor needs to determine which of two possible problems exist: Either the model used to predict the biomarker is flawed or the assessor missed sources and pathways of exposure to this chemical. Tulve et al. (2011) published cumulative exposure estimates using forward dosimetry approaches. Illustrative examples and further discussion of the interplay between exposure estimation, biomonitoring data and these modeling methodologies are found in Tan et al. (2007) and Clewell et al. (2008). Examples of dose estimation using forward dosimetry are presented in Table 6-2.

Table 6-2. Examples of Modeling Exposure and Dose from Biomonitoring Data

Agent	Dosimetry Approach	Studies
Chlorpyrifos	Forward	Morgan et al. (2005)
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; 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 that is 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 can be used in reverse dosimetry analyses by rearranging parameters to estimate intakes based on biomarkers and modeling parameters. Other simple reverse dosimetry approaches use empirical measures, such as creatinine-corrected biomarker levels. Creatinine continuously is excreted from muscles and eliminated via urination. If exposure to a contaminant is continuous and the primary means of elimination of that contaminant is via urine, the creatinine correction approach can be used to estimate daily intake of that contaminant. Here, the urinary concentration of the contaminant is first divided by urine

creatinine concentration, yielding a creatinine-adjusted measure. Next, the creatinine-adjusted measure is multiplied by the daily creatinine output, yielding an estimate of daily contaminant elimination. By assuming steady-state exposure and urinary excretion, daily intake can be equated with daily urinary elimination. The creatinine correction approach has been used to estimate the intake of a variety of contaminants, including perchlorate (Blount et al. 2007), phthalates (Koch et al. 2003) and pesticides (Mage et al. 2004; Mage et al. 2008).

Blood concentrations of a biomarker generally are modeled with simple PK models and compared directly to measured biomarker values. Urine measurements are complicated by sample accumulation in the bladder; therefore, the timing of the accumulation period and urine volumes or normalized creatinine production rates are needed. Creatinine correction is the most common method for adjusting for variable dilutions in spot urine samples (Barr et al. 2005). Examples of exposure estimation using reverse dosimetry are presented in Table 6-2. Forward and reverse dosimetry approaches are complementary because the hypotheses raised by one analysis 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 can be used to predict concentrations of the chemical in a body matrix that is easily sampled, such as urine or blood. Toxicodynamic 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 can be used 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., a blood "volume of distribution"). The simplest PK model is a mass-balance model, which implicitly assumes steady state. Often, the goal of simple PK models is to compare predictions of concentrations in body matrices with analogous measurements reported in the literature. The standard one-compartment, first-order absorption model makes inherent assumptions about the absorption, distribution, metabolism and elimination (ADME) processes (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 2006b). 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). Important to note, however, is that although PBPK modeling can reduce uncertainty in internal dose estimates, reductions in uncertainty and increases in accuracy are not necessarily predetermined results. For use in risk assessments, PBPK models are recommended to:

- Have tissue-specific kinetics (e.g., distribution) for all relevant tissues, physicochemical properties of the chemical and chemical-specific ADME data;
- Contain a compartment that is associated with the target tissue, contain the target tissue or identify a surrogate for the target tissue;
- Have defensible physiological parameter values within the known plausible range; and
- Have undergone a thorough evaluation of their structure, implementation, appropriate application domain and predictive capability (U.S. EPA 2006b).

High-Throughput Exposure Models

The recent development of the ToxCast program has resulted in the generation of *in vitro* toxicity and bioactivity data on thousands of chemicals in commerce. Many of these chemicals have minimal *in vivo* toxicity data. The ToxCast data are currently being used to set screening levels of systemic dose that are associated with minimal levels of bioactivity (Thomas et al. 2013). These emerging findings have been proposed as the basis for prioritizing the need for animal testing and other purposes. To use these data properly requires screening estimates of the aggregate exposures to the chemicals. To meet this need, a new type of human exposure model is being created that will generate high-throughput screening exposure 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 model complexity, and a possible increase in the uncertainty in the model predictions, for the ability to be applied for thousands of chemicals.

The Stochastic Human Exposure and Dose Simulation-High Throughput model (SHEDS-HT) is an example of this type of model. It is based on probabilistic methods and algorithms developed under the SHEDS program, but the algorithms have been modified to 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 (near field 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, high-throughput screening heuristic models of exposure have been proposed (Wambaugh et al. 2014). This approach has produced predictive models of the median aggregate exposures based on use and property-related characteristics of chemicals and estimates of exposures inferred from the National Health and Nutrition Examination Survey (NHANES) biomonitoring program. In addition, a framework for using these NHANES-derived exposures to evaluate and calibrate estimates from multiple high-throughput models to form consensus high-throughput exposure predictions has been proposed (U.S. EPA 2014a).

6.3. Evaluation of Models

The Agency defines model evaluation as the process that generates information during the application of the model to determine whether a model and its analytical results are of sufficient quality to serve as the basis for a decision (U.S. EPA 2009c). Similarly, NAS defines model evaluation as the process of deciding whether and when a model is suitable for its intended

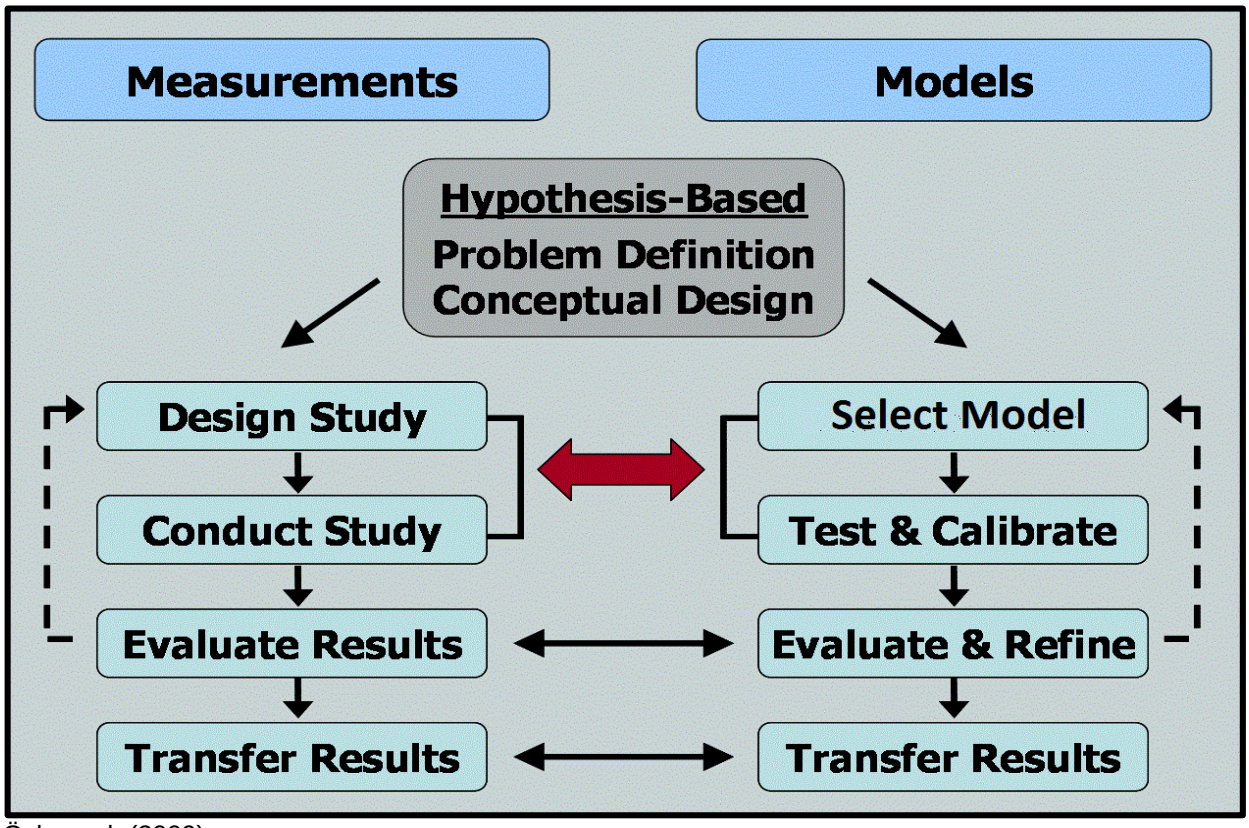
purpose and stipulates that this process is not a strict validation or verification procedure. Instead, it provides an objective assessment of the performance of the model for the stated purpose and increases the understanding of model strengths and limitations (NRC 2007).

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 (QA)/quality control (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 are, based on either deterministic model estimates or various statistics and percentiles of more advanced probabilistic models. Evaluation also considers the degree to which the model is based on generally accepted science and computational methods, whether the model fulfills its designed task and how well the model approximates observed conditions. For example, evaluating a fate and transport model that estimates concentrations at an exposure point might include verifying that the transport and transformation concepts are represented appropriately in the mathematical equations, verifying that the computer code is free from error by comparing the model output with data from laboratory microcosms and comparing field data to the modeling results under a variety of conditions and chemicals. The iterative use of models to evaluate and refine study designs is illustrated in Figure 6-3.

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 of the key components of EPA's exposure assessment models have been evaluated using different approaches and compared to available measurements. Some of the approaches to evaluate exposure assessment models include comparing the structure, model inputs and results of one model to another; comparing modeled estimates with measured or field data; and comparing modeled estimates with biomonitoring data. Comparing predictions against field data can model 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).

The process of model evaluation makes identifying the model's strengths and limitations and the most critical model parameters and assumptions possible. 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 a model is not to be used.

Figure 6-3. Iterative Use of Measurements and Models



Özkaynak (2009)

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 whether the assumptions, methods and conclusions derived from models are based on sound scientific principles and to check the scientific appropriateness of a model for informing a specific regulatory or risk-management decision (U.S. EPA 2009c). The latter objective is particularly important for applications of existing models for purposes other than those for which they were initially designed. Models frequently are used by, and sometimes have been developed in collaboration with, researchers and practitioners in academia, consulting, private industry and state and local governments, both nationally and internationally. A key consideration in using a model is transparency, including model documentation and communication among an exposure assessor, modeler and risk manager/decision maker in its application.

6.3.2. Attainment of Quality Assurance Objectives

For a chosen model, an exposure assessor determines whether the inputs required by the model are available, all parameters required by the model can be obtained or reasonable default values are available. After running the model, an exposure assessor needs to evaluate whether the model outputs meet the exposure assessment goal(s) and DQOs. If the outputs do not meet these goals, the model parameters might need to be adjusted or a different model might need to be selected and tested. All input data need to meet data quality acceptance criteria (Section 5.2.1).

The exposure assessor also conducts a data quality assessment to assess the type, quantity and quality of data to verify that the planning objectives, quality assurance project plan (QAPP) components and sample collection procedures are satisfied, and to confirm that the data are suitable for their intended purpose. EPA's five-step data quality assessment process is described on EPA's *Quality Management Tools – Data Quality Assessment* website.[16]

6.3.3. Qualitative and Quantitative Model Corroboration

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 2009c). Calibration accounts for spatial variation and temporal variation that are not represented by the model formulation; 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 Sensitivity and Uncertainty 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. See Chapter 8 for 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 at what level of detail. Model inputs and parameters typically include various sources of uncertainty. Important sources of uncertainty include 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 scale and exposed population of interest (Özkaynak et al. 2008). If the modeling approach omits any elements of the scenario of interest, the estimates could be biased. Uncertainty also might stem from extrapolating beyond conditions for which the model was constructed or calibrated. Model uncertainty is influenced by 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 (e.g., Cullen and Frey 1999).

Input and parameter uncertainty can be assessed using advanced statistical methods (e.g., Bayesian techniques) or more conventional one- or two-dimensional Monte Carlo methods, whereby model simulations are repeated using alternative sets of variability distributions for both

[16] http://www.epa.gov/QUALITY/dqa.html.

key inputs and parameters. Typically, a few hundred alternative exposure prediction distributions are generated that depict the uncertainty around the initial exposure distribution, for example the cumulative distribution function for exposures or dose (WHO 2008). Most one-dimensional 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 well and the extremes in the alternative uncertainty cumulative distribution function distributions, by capturing both the variability and uncertainty bounds within a one-dimensional simulation (WHO 2008). In more refined models that are based on two-dimensional Monte Carlo methods, variability is separated from uncertainty. Simplified two-dimensional Monte Carlo methods, as described in MacIntosh et al. (1995), can be considered if one decides to ignore 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). More recent and complex methods, however, apply the bootstrap-based uncertainty analysis technique, as described in Xue et al. (2006) for the SHEDS model application to the chromated copper arsenate case study.

Some of the fate and transport, human exposure and integrated fate/transport-exposure models can simulate stochastic processes, which allows for 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 that can simulate stochastic processes tend to be the higher tier exposure models and some of the integrated fate/transport-exposure models. For these models, such assessments usually are accomplished by performing univariate or multivariate Monte Carlo analyses, sensitivity analyses or contribution analyses or both. Exposure factors and chemical residue values in different environmental media are the most common model input parameters that are varied to address variability or uncertainty. One of the key challenges for integrated fate/transport-exposure models is the quantification of coupled model uncertainties resulting from propagation of errors from the different model components, which are linked during an integrated analysis. The impact of this problem has been evaluated in selected case studies (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 2009c). 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, decision 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 versus the benefit of having a more refined exposure assessment;
- Target additional analyses or data collection efforts; and
- 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 two. In the percentile scaling approach, first a reference or base (e.g., mean) value of the chosen variables is selected. Then, two more runs are conducted for each input at lower (e.g., 5th) and upper (e.g., 95th) percentiles of their distributional range. For each run and simulated individual, the modelers determine the mean outputs for each of these lower and upper percentile simulations and compare them to the reference or base case results. In addition, high/low ratios (e.g., the ratio of 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 each simulated individual's means of input variables and outputs are retained. This information is then used in stepwise regression models to examine the relationship between inputs and outputs of the model to determine 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 2001g). 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, Fourier amplitude sensitivity test and Sobol's method can be used to 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 2001g) and the World Health Organization's (WHO) *Uncertainty and Data Quality in Exposure Assessment* (WHO 2008) provide detailed guidance on conducting a sensitivity analysis. 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. Sensitivity analyses also can be performed across different models to determine whether some models are less sensitive to certain critical parameters. Uncertainty across models also can be examined, 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).

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

Observational human exposure measurement studies are used to quantify people's exposures to chemical, biological or physical agents or other stressors in their everyday environments during their normal daily activities. Such studies involve measurements of these 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 2008a; U.S. EPA 2009a; Zartarian et al. 2005).

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), and
- Conducting peer review and completing a final report (Section 7.5).

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 impact on exposure. Results from observational human exposure measurement studies have supported the regulatory work of Agency programs and contributed 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 regulatory standards have been exceeded. Observational human exposure measurement studies evaluate exposures, not absorption, distribution, metabolism and elimination (ADME) parameters or dose-response. Box 7-1 lists examples of observational human exposure measurement studies.

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

- U.S. EPA (1987b) Total Exposure Assessment Methodology Study (TEAM).
- Weisel et al. (2005) Relationship between Indoor, Outdoor, and Personal Air Study (RIOPA).
- U.S. EPA (2007g) Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants Study (CTEPP).
- U.S. EPA (2009d) National Human Exposure Assessment Survey (NHEXAS).
- U.S. EPA (2011a) Detroit Exposure and Aerosol Research Study (DEARS).

More information about these and other data sources can be found in Table 5-6.

Data generated in 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 (Section 6.2). Measured data are used as model inputs for model evaluation and optimization. Exposure and dose models then help identify key data needs that observational human exposure measurement studies can answer.

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 and risk assessments is limited because the potential clinical significance of biomonitoring results has been established for relatively few chemicals (ECETOC 2005; NRC 2006b). Barr and colleagues (2006) presented an overview of the concepts that need to be considered when using biomonitoring data. Sections 5.3.2 and 6.2.3 present additional information about the uses and limitations of biomonitoring data.

Although this chapter focuses on observational human exposure measurement studies, other types of research also can be conducted and used in exposure assessments. All human subjects research that is conducted by EPA scientists or supported by the EPA must go through several levels of approval. The specific path for review differs slightly depending on the origin of the

research, but all human subjects research projects must be approved by the Human Subjects Research Review Official (HSRRO) before any work involving human subjects can begin. The HSRRO's responsibility is to ensure that all research studies supported by EPA comply with EPA regulations concerning research with human subjects (40 CFR 26), EPA's Policy Order 1000.17 Change A1, and with best practices in ethics. A review and approval by an Institutional Review Board must precede a review request to the HSRRO.

In addition, all third-party research involving intentional exposure of a human subject to any substance that is submitted to EPA and/or considered in connection with any EPA decision under FIFRA or section 408 of the Federal Food, Drug and Cosmetic Act must meet additional standards as specified in 40 CFR 26. All third-party research involving intentional exposure of human subjects to a pesticide that is submitted to EPA and/or considered in connection with any EPA decision under other statutes must similarly meet these additional standards in 40 CFR 26. Among other provisions, these regulations may require review by the Human Studies Review Board (HSRB), an advisory board established under the Federal Advisory Committee Act, depending on the purpose and initiation date for the research. More information about the HSRB can be found at: http://www2.epa.gov/osa/human-studies-review-board. 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 data elements; sample size; data quality objectives (DQOs); criteria for selecting study location; eligibility criteria for study participants; sampling and analytical protocols; chain of custody, storage and data management; community involvement; human subjects guidelines; informed consent; recruitment; sample collection; sampling schemes; involvement of participants; compensation; database design; data analysis; and communication. These aspects of the study design are addressed in this chapter. Many other published articles and reports can help in 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. The number of participants, and the types of samples collected and analyzed, are strongly influenced by the available resources, participant burden, types of sampling methods and specificity of the measurements that need to be collected. 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. This might entail reducing the number of study participants, eliminating selected analytical procedures or modifying other components. When altering the study plan to meet resource constraints, the researchers consider whether the modified study plan is likely to

provide the quality of information necessary to meet the study objectives or consider other options for filling data or informational needs.

Burdens to both the participants and the field technicians also need to be considered during the planning process. 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/scientific question, the critical data elements are those pieces of information that need to be collected to achieve the objective/hypothesis or 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 (diameters 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 for testing hypotheses.

7.2.3. Determining Sample Size for Each Data Element

The sample size needed to meet the study objectives/hypotheses/scientific questions is determined statistically based on the desired outcome. Estimations of sample size are necessary to ensure that the probability of missing an important difference is small and to reduce unnecessary costs and waste (Devane et al. 2004). The number of participants enrolled in a study often is a compromise between the budget available for the study and the power that the study can achieve (Dupont and Plummer Jr. 1990; Kulldorff et al. 2004; Woodward 1999).

To determine the appropriate sample size for a study, the effect size is estimated. The effect size is a measure of the differences between populations and is used to assess whether the differences are statistically significant. If the effect size is large (e.g., the difference in the average fish consumption between a subsistence population and a landlocked population), the differences are easier to establish. Hence, a smaller study population would be needed to identify statistically significant results. Conversely, if the effect size is small (e.g., the difference in fish consumption between men and women), the differences are more difficult to establish. A larger study population would be needed to identify statistically significant results. If the true effect size already were known, variable parameters (e.g., average fish consumption) would be known and a study would be unnecessary. In determining the predicted effect size, data from a pilot study could be used (Devane et al. 2004).

The variability within the defined population also is important and needs to be considered in the sample size determination. 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/scientific questions. Criteria can include the location of the population group of interest, geographic or built environment considerations, the size of the cohort to be recruited and the time of year in which the study will be conducted. 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 an integral part of the technical study design. Eligibility criteria are used to select the type of person needed for an observational human exposure measurement study based on the study objectives/hypotheses/scientific questions. For example, an observational human exposure measurement study seeking to understand the variety of fruits and vegetables consumed by the elderly population in the United States would have very different eligibility criteria than 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 addressing scientific and ethical approaches for observational human exposure measurement studies can be found at EPA's website, *National Exposure Research Laboratory* (http://www.epa.gov/nerl/sots/). 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

Once the data quality criteria (discussed in Section 5.4) have been established, the methods available to meet these criteria can be identified. Observational human exposure measurement studies need to follow sampling and analytical protocols that are sufficiently accurate, precise and sensitive to meet the study objectives/hypotheses/scientific questions. Analytical and sample collection methods with demonstrated and acceptable performance parameters are selected. Many standard operating procedures (SOPs) have been developed and are available publicly in various Agency databases. For example, the *Human Exposure Database System* website (http://www.epa.gov/heds) contains analytical and ancillary data, including SOPs. Additional method development and testing might need to be performed prior to study implementation if existing or adequate methods are not available. If method development is required, acceptable performance parameters and evaluation criteria need to be determined before an analytical or sample collection method is deemed 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 to ensure that the sampling methods will be accurate, precise and sensitive and that modifications can be reevaluated if necessary. Analytical protocols are evaluated using 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 project plan (QAPP) (U.S. EPA 2001c; U.S. EPA 2012b). In combination, these procedures are used to track the movement of samples accurately before, during and after analysis and the storage and movement of the results.

Chain-of-custody forms (e.g., paper or electronic format) are used to 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 a website for training on chain-of-custody procedures for samples and data (http://www.apti-learn.net/LMS/EPAHomePage.aspx).

Sample storage procedures are developed to ensure adequate and proper 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.

Data management procedures are established 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 (http://www.epa.gov/fem/data_standards.htm). More information on the data analysis plan and database design is described in Section 7.2.13.

Section 5.6 provides 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 in which 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. Community involvement is a means 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 2008a). 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 some input into the decision-making process (U.S. EPA 2001h). Information and suggestions regarding community involvement in the Superfund process (U.S. EPA 2005g) might be generally applicable to community involvement in observational human exposure measurement studies. EPA's *Superfund Community Involvement Handbook* (U.S. EPA 2005g) provides specific information about community involvement.

Involving a community offers many advantages. Community representatives bring perspective, value and competence to a research project. Community representatives also bring to a study 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). More details on the importance of community involvement are presented in *Ethical Considerations for Research on Housing-Related Health Hazards Involving Children* (NRC and IOM 2005).

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 specify the issues to be studied, develop research questions in culturally sensitive ways and use 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 2008a; Williamson et al. 2005). This approach helps ensure that the research addresses the concerns, needs and priorities of the community in which it is conducted 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 of this document discusses community involvement in the planning and scoping phase of an exposure assessment.

7.2.9. Engaging Other Stakeholders

In some instances, researchers conducting an observational human exposure measurement study might ask stakeholders to participate in the planning and conduct of the 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 groups, advocacy groups, medical organizations, university partnerships, industry groups, nonprofit organizations and nongovernment and government organizations. Engaging other stakeholders in addition to community members might be necessary when planning an observational human exposure measurement study. The researchers and the community jointly decide which stakeholders are invited to participate in the planning process. Once stakeholders have been identified, they are invited to participate in planning the study. Beierle (2002) reported that the inclusion of 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/scientific questions of the research study and the persons recruited to participate in the study. Stakeholders engaged in

planning one observational human exposure measurement study might not be the same as those engaged in planning another. The Agency published *Stakeholder Involvement and Public Participation at the U.S. EPA: Lessons Learned, Barriers, and Innovative Approaches*, which reviews how EPA handles stakeholder involvement and public participation (U.S. EPA 2001h).

During the planning of an observational human exposure measurement study, meetings take place between the researchers, community members and stakeholders. These meetings are used to gather input from the stakeholders and to explain the purpose and approach of the study. Study announcements are released far enough in advance 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. Details on incorporating stakeholders in the research planning process are found on EPA's *Basic Information* website (http://www.epa.gov/environmentaljustice/basics/index.html).

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 home and work environments. Often, observational human exposure measurement studies provide the strongest available data that support regulatory action. Observational human exposure measurement studies can be complex in their design and implementation, addressing many scientific and ethical considerations. In conducting these studies, EPA scientists endeavor to apply the most current scientifically valid approaches, while recognizing the special responsibilities with regard to the ethical issues that sometimes arise when conducting these studies.

EPA has developed a document that examines both the scientific and ethical issues associated with observational human exposure measurement studies. *Scientific and Ethical Approaches for Observational Exposure Studies* (SEAOES) (U.S. EPA 2008a) 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 (http://www.epa.gov/hsrb/index.htm), reviewed and endorsed the document. Following the scientific and ethical approaches outlined in this document ensures that observational human exposure measurement studies are conducted with attention to the concerns of the participants. More information on the history of human subjects research can be found in the SEAOES document (Section 1.2 in U.S. EPA 2008a) and 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 study protocol and all associated documentation need to be approved by the appropriate Institutional Review Board (IRB). As directed by EPA Policy Order 1000.17 Change A1, approval normally includes an IRB from each participating organization and final approval by the Agency's Human Subjects Research Review Official (HSRRO), located in the Office of the Science Advisor. The HSRRO is responsible for reviewing and approving human subjects research at EPA prior to the recruitment of participants into a study. The *Office of the Science Advisor* website provides more information on this process (http://www2.epa.gov/osa/basic-information-about-human-subjects-research). Additional information on human subjects research and IRBs is available on the U.S. Department of Health and Human Services' (HHS) *Office for Human Research Protections* website (http://www.hhs.gov/ohrp/) and on the National Institutes of Health's *Bioethics Resources on the Web* website (http://bioethics.od.nih.gov/IRB.html). When the number of participants in an observational human exposure measurement study will be greater than 10, 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 (http://www.hhs.gov/ocio/policy/collection/index.html).

Effective recruitment is important to a successful study. Recruitment methods vary depending on the study design and the participants being selected, 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 2008a). 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, informed consent needs to be obtained before a person can participate in a research study. The informed consent documents and process need to be approved by the necessary IRBs prior to their use in the field. In studies where children old enough to have some understanding of the study are the participants, their assent needs to be obtained in addition to the consent of their parents or guardians. The age at which a child can provide his or her 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 and Shah 2003; Wendler 2006; Whittle et al. 2004).

Confidentiality and privacy also are key considerations in studies involving human subjects. The Privacy Act of 1974, the E-Government Act of 2002, the Federal Information Security Management Act, the Health Insurance Portability and Accountability Act (2003 Privacy Act) and policy and guidance issued by OMB outline restrictions and requirements associated with the use of 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, data collected during an observational human exposure measurement study and linked or linkable to an individual are required to be safeguarded. More information and resources are available at EPA's *Privacy Policy* website (http://www.epa.gov/privacy/policy/).

Determining appropriate compensation or incentives for participants in a research study can be complex. Compensation or incentives generally are offered 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 2008a). Compensation or incentives can take various forms, including monetary payments (e.g., cash, gift certificates), nonmonetary payments (e.g., gifts, valuable information), reimbursement for expenses associated with participating in the study 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

Environmental, biological, personal and exposure factor data and questionnaire information are obtained to understand potential exposures. Environmental samples are selected that account for exposure through the relevant routes and pathways based on the study objectives/hypotheses/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 that is 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 are directly related 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 consumed by the participant. 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 that the participant has engaged in during the period of interest that could account for exposures (Table 5-6 presents a discussion of EPA's Consolidated Human Activity Database [CHAD], the Pesticide Handlers Exposure Database [PHED] and other data sources). Biological samples are used to measure the absorbed dose of the chemical of interest (Sections 5.3.2 and 5.4.3 provide more discussion of the uses and limitations of biomonitoring).

Questionnaires are used to collect information on parameters that cannot be measured any other way, such as household demographic information or occupation. 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 document is a helpful tool for identifying the environmental, biological and personal samples; activity pattern data; and questionnaires that need to be collected in 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 (NCEA) *A Framework for Assessing Health Risk of Environmental Exposures to Children* (U.S. EPA 2006d) and the International Life Sciences Institute's risk assessment framework (Olin and Sonawane 2003).

7.2.12. Sampling Scheme

The sampling scheme is developed after the study objectives/hypotheses/scientific questions are identified, the technical study design is written and the types of samples to be collected are identified. The sampling scheme systematically details the samples that need to be collected in the field and usually includes the time, location and any other sample collection logistics (such as sample collection order). The sampling scheme might include information for both field samples and quality control (QC) samples. 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 are collected to assess collection and analytical precision. The QAPP contains the details on the quality assurance (QA) associated with the field study, including the QC samples and procedures used to assess the accuracy and precision of the sample collection and laboratory analysis. General information on the QAPP can be found on EPA's website (http://www.epa.gov/quality/qs-docs/g5-final.pdf; Section 5.2.1 presents more details about these requirements).

7.2.13. Data Analysis Plan and Database Design

The data analysis plan describes how the collected data are analyzed so that they address the objectives/hypotheses/scientific questions of the research study. The data analysis plan includes the objectives/hypotheses/scientific questions, the data relevant for evaluating each objective/hypothesis/scientific question and the statistical analyses that will be performed on the data. The data analysis plan is written in conjunction with the technical study design and sampling scheme. The data analysis plan also is used to design the database that contains sampling information, raw data and analysis results. Overall, details about the data requirements needed to address the objectives/hypotheses/scientific questions are an important component of the data analysis and need to be well documented.

The database houses the measurement data and all supporting documentation associated with sample collection and analysis. Developing the database is a critical component of the study and needs to be done as part of the planning and scoping process (Section 3.1). The Agency provides general guidance on designing, implementing and using databases (U.S. EPA 2011b; U.S. EPA 2012a), but in general, a database is specifically designed for each study with the help and guidance of the study's database manager. Agency guidance can be found at EPA's *Database and Software* website (http://www.epa.gov/epahome/data.html) and EPA's Forum on Environmental Measurements' *Environmental Data Standards* (http://www2.epa.gov/measurements) website.

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 to be entered in the database 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, the data generated during the pilot study (described in Section 7.3) are used to test the database design. 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 components. A pilot study has 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. A pilot study usually is conducted with only a few participants and is used to evaluate the field-readiness of the research personnel. The results and lessons learned from the pilot study also identify changes that need to be made in the implementation plan prior to the start of the full field study. Any special concerns or issues raised during the pilot study are addressed so that they do not affect the full field study. Using the approach of a pilot study followed by the full field study improves the chances for success of the field study. For example, multiple pilot studies were conducted prior to implementation of the Total Exposure Assessment Methodology Study (TEAM) study (Wallace 1987) and pilot studies were conducted in anticipation of the National Children's Study, as described on the "Methods Development and Pilot Studies" Web page of the *National Children's Study* website (http://www.nationalchildrensstudy.gov/research/methodspilot/).

7.3.1. Community and Stakeholder Involvement in the Pilot Study

Once the community and stakeholders are engaged in planning, their roles and responsibilities in the pilot study are defined. Examples of roles and responsibilities include serving as a consultant in planning the study, reviewing the pilot study results and providing resources.

Implementing the communication plan (Section 7.3.3) also is a component of the pilot study. The communication plan is developed in association with the research staff, community and stakeholders planning the design of an observational human exposure measurement study. 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, stakeholders) with an opportunity to give direct feedback about their experiences with the pilot study, including an in-depth view of what went well and where changes are needed. A debriefing with the community, 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 communicates the study components and the implementation plan, which describes the study execution, and contains all the details needed to conduct 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 (Chapter 9). The communication plan details what information to convey and to 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 that 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 discusses how information will be given to the community, the media, the stakeholders, the scientific community and other groups as deemed appropriate by the research staff. The community and stakeholders need to be consulted about what information they would like to receive and in what format.

Chapter 9 provides guidance on communication considerations in exposure assessments.

7.4. Planning and Executing a Full Field Study

All components of the pilot study discussed throughout this chapter are used to plan and execute 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 DQOs, 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 QAPP (Section 5.2.1);
- The data analysis plan specifies the analyses of the collected data (multimedia samples and questionnaire information) in relation to the study objectives/hypotheses/scientific questions; and
- The communication plan—developed by the project team, community members and stakeholders—specifies what data to convey and to whom and in what format.

7.5. Peer Review and Completion of the Final Report

Peer review is an integral component throughout the design, implementation and completion of an observational human exposure measurement study. The peer-review process ensures that the data generated and information disseminated about the study meet the highest quality and ethical standards (U.S. EPA 1998; U.S. EPA 2000a; U.S. EPA 2015). Any documents associated with the study could be subjected to peer review, but typically only the study design and final documents, such as reports and journal articles, are peer reviewed. EPA's *Peer Review Handbook* (U.S. EPA 2015) provides a comprehensive guide for organizing and conducting peer reviews in accordance with EPA's updated peer review and peer involvement policy statement (U.S. EPA 2015).

CHAPTER 8. UNCERTAINTY AND VARIABILITY IN EXPOSURE ASSESSMENT

Decision uncertainty is a broad category of uncertainty that includes the lack of complete knowledge about the facts. It also encompasses how decision criteria (as represented by data) relate to each other and help answer the decision question. Typically, discussions about uncertainty focus on data uncertainty and variability. Decision uncertainty includes data uncertainty and variability. Data uncertainty includes sampling, observational, modeling and scenario uncertainties (Section 5.5). Decision uncertainties also include uncertainties about the relationships among the chosen data and values and judgment uncertainties that affect the assessment of each decision alternative based on those data/values/judgments. All these sources of uncertainty can contribute to the choice of a decision alternative. Decision uncertainty pertains to the decision criteria and the relationship among those criteria that, if understood differently, could result in a risk manager's/decision maker's making a different decision.

Decision criteria are represented by data. Data uncertainty is a component of decision uncertainty that—together with variability—can influence exposure assessment results and decisions based on those results. Decision uncertainty, like data uncertainty and variability, is inherent in the exposure assessment process. It is introduced by the assumptions, methods, models and data used to assess exposures. Generally, when assessors need a better understanding of actual exposures, potential exposure impacts and appropriate risk management decisions, they seek to characterize data uncertainty and variability. Understanding and characterizing decision uncertainty can require an assessor to work with risk managers/decision makers and other stakeholders to frame the context of the question being answered. In this chapter, a distinction is made between data uncertainty (the type of uncertainty typically addressed) and decision uncertainty. Consequently, when organizations and documents clearly are referring to data uncertainty, this term is used. If the uncertainty includes both data and decision uncertainty, the term "uncertainty" is used.

When considering uncertainty and variability in an exposure assessment, questions that can be asked include: Would results or decisions be different if different assumptions were made or different data were used? When uncertainty is understood, what level of uncertainty is appropriate for the decision? For example, uncertainty might lead an assessor to assume a worst-case scenario in an exposure assessment, which results in a conservative estimate of risk. A change in one or more input parameters within the range supported by the data might lead to a different risk management decision. If so, an exposure assessor might consider spending additional time and resources (e.g., collection of additional data, additional data analyses, more advanced statistical analyses of data) to refine input parameters and reduce uncertainty. Inherent in this process are ongoing discussions between an exposure assessor and risk manager/decision maker regarding the assumptions, the results and their influence on the risk-management/decision-making process. This ongoing discussion enables an assessor and risk manager/decision maker to determine how to weigh the available resources against the benefits of a more refined assessment to achieve the assessment goals.

The process for conducting an uncertainty and variability evaluation can range from simple screening methods to complex statistical analyses. To help an assessor distinguish between uncertainty and variability and conduct an appropriate evaluation, this chapter:

- Defines uncertainty and variability and describes the differences between the two (Section 8.1);
- Outlines the basic considerations that will influence the uncertainty and variability evaluation (Section 8.2);
- Describes the process for conducting an uncertainty and variability evaluation using a tiered approach (Section 8.3); and
- Introduces considerations in communicating information about uncertainty and variability to risk managers/decision makers and stakeholders (Section 8.4).

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. Some relevant uncertainty and variability terminology is listed in Box 8-1.

EPA consistently has addressed the need to characterize uncertainty in risk estimates. This history is described in more detail in National Research Council (NRC) and EPA documents (Clinton 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 1996d; U.S. EPA 1997a; U.S. EPA 2001g; U.S. EPA 2004b; U.S. EPA 2011i; U.S. EPA 2012j). In addition, the International Programme on Chemical Safety (IPCS)/World Health Organization (WHO) has developed guidance on characterizing and communicating uncertainty in exposure assessment and has emphasized the importance of both data and decision uncertainty evaluations in its 10 guiding principles for an uncertainty evaluation (WHO 2008).

8.1. Terminology

The distinction between data uncertainty and variability is important for both conducting an exposure assessment and communicating its results. According to NRC (2009), data uncertainty refers to the lack of, incomplete or incorrect information, whereas variability refers to true differences in attributes resulting from heterogeneity or diversity in an individual or population.

The following sections expand on these definitions and describe the different types of data uncertainty, decision uncertainty and variability that can be present in an exposure assessment.

Many types of uncertainty exist. This *Guidelines for Human Exposure Assessment* describes data and decision uncertainty associated with evaluating exposure scenarios, conducting sampling or measurement studies and carrying out observational studies or modeling efforts.

Box 8-1. Uncertainty and Variability Terminology

- **Data uncertainty**
  The lack of knowledge about factors affecting exposure; uncertainty can lead to inaccurate or biased estimates of exposure. Uncertainty can be reduced with additional information. Data uncertainty describes how well the data used in the assessment are understood. Data uncertainty is a component of decision uncertainty.
- **Decision uncertainty**
  The lack of knowledge about the decision context. Specifically, it is the lack of knowledge about the adequacy of the analysis design to answer the decision question(s), factors selected for the analysis and influence of those factors on the decision options that affect the choice of the decision option. Decision uncertainty is a broad category of uncertainty that can include data uncertainty, sampling uncertainty, model uncertainty and uncertainty about the values/judgments used to arrive at the exposure assessment conclusions. Decision uncertainty cannot always be reduced, but risk managers/decision makers who work to understand the context in which they are making a decision can better determine the robustness of choosing one alternative over another.
- **Variability**
  The heterogeneity of the diversity of potential exposures in a population that represents true heterogeneity or diversity (e.g., the amount of water consumed on a daily basis by an individual or population, which can vary based on age; residence in geographic areas with varying weather conditions; activity patterns, including getting more or less exercise). Variability can be better understood, but not reduced, with additional information.
- **Sensitivity analysis**
  Any systematic, commonsense technique used to understand how exposure and risk estimates and, in particular, risk-based decisions depend on uncertainty and variability in the factors contributing to exposure and risk.
- **Probabilistic risk assessment**
  A range of techniques (e.g., Monte Carlo analysis, Latin hypercube) used to:
  - Identify the sources of the uncertainty that most greatly influence the effect of concern,
  - Define or estimate distribution parameters (mean, variance) and any correlations with other parameters, and
  - Combine uncertain and variable parameters (or treat them separately) and estimate the distribution of effects by using the laws of mathematical statistics or Monte Carlo analysis.
- **Monte Carlo analysis**
  A probabilistic risk assessment technique that can provide a probability function of estimated exposure using repeated random sampling from the distribution of values for each parameter in a generic (exposure or dose) equation to derive an estimate of the distribution of exposures or doses in the population.
- **Expert elicitation**
  A multidisciplinary process that gathers input from outside experts to characterize uncertainty and fill data gaps when traditional scientific research is not feasible or data are not yet available.

U.S. EPA (2011e; 2012k)

Table 8-1 elaborates on the errors that can result from these types of uncertainty, which EPA defines as the following:

- **Exposure Scenario Uncertainty:** Uncertainty in an exposure assessment that occurs when the information regarding the exposure scenario is limited or inadequate. For example, using an exposure assessment relying on information from a study conducted in the southwestern United States can introduce uncertainty when it is used to evaluate

activity patterns in New England. The WHO (2008) defines scenario uncertainty as the "uncertainty in specifying [an] exposure scenario that is consistent with the scope and purpose of the assessment."

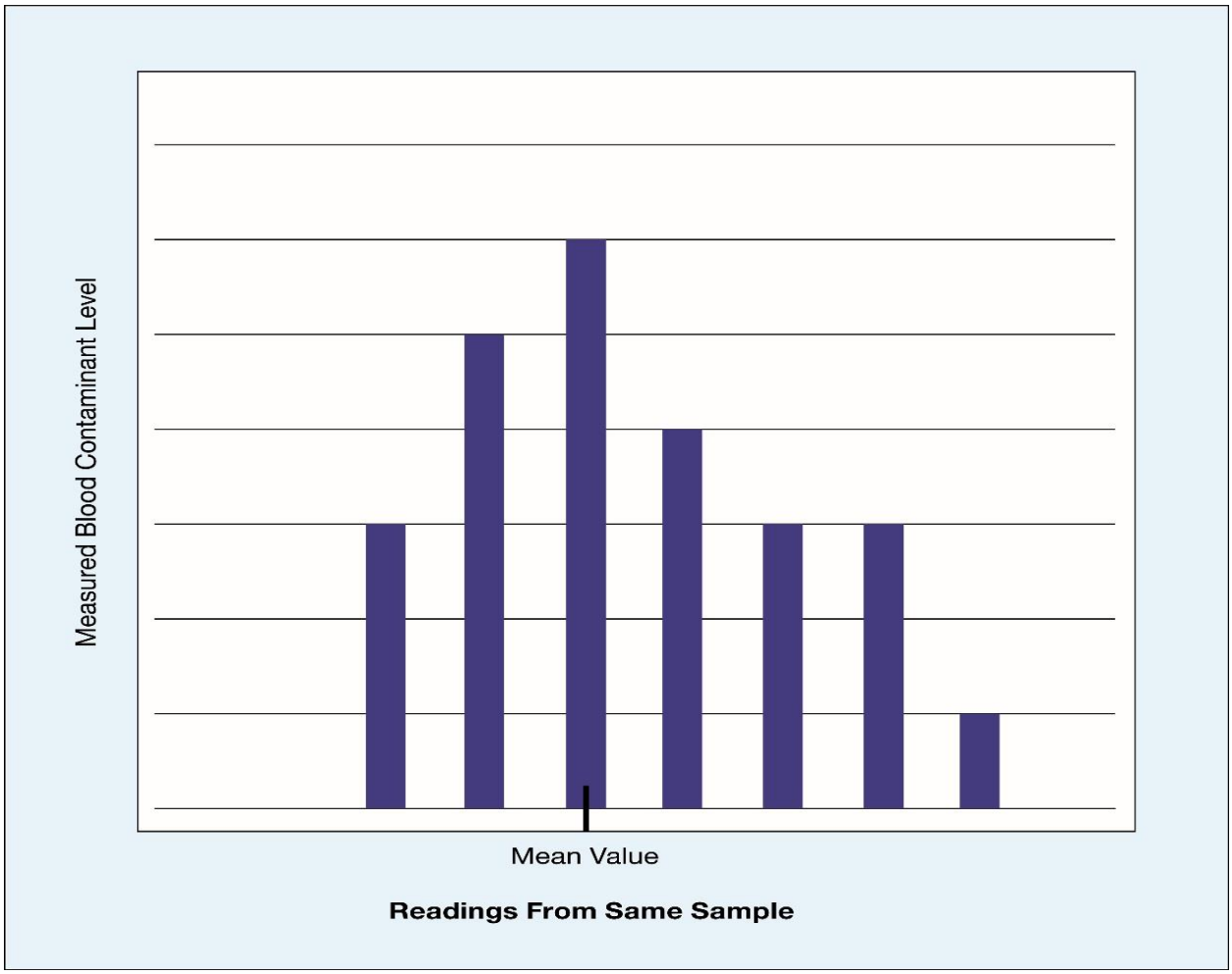
Table 8-1. Types of Uncertainty and Contributing Errors

Type of Uncertainty	Type of Error Causing Uncertainty	Description or Example
Exposure scenario	Misclassification	Failure to adequately identify exposure routes, exposure media and exposed population
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	Use of alternative data for a parameter instead of direct analysis of exposure (e.g., use of population figures 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	Use of a small sample of individuals to estimate risk to exposed workers
	Nonrepresentativeness	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	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	Use of alternative variables for ones that cannot be measured (e.g., using wind speed at the nearest airport 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 assembler put them together)
	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)

U.S. EPA (2004b)

- **Sampling or Measurement Uncertainty.** Uncertainty in sampling or measurement data that is associated with data collection or analysis methods. Sample location, sample number and analysis methods are sources of sampling uncertainty. For example, sampling methods and analyses are unlikely to produce the same reading every time, even when measuring the same sample. This adds to the overall uncertainty of an exposure assessment (Figure 8-1). Sampling uncertainty also is introduced when surrogate data are used to represent an exposure or when data are not representative of the exposures. Other organizations use the term "parameter uncertainty" to describe this type of uncertainty (WHO 2008).
- **Observational or Model Uncertainty.** Gaps in the scientific theory that is required to make predictions based on causal inferences. Model uncertainty is unavoidable and difficult to quantify because modeling uses mathematical or statistical formulas to capture complex processes (e.g., chemical releases, environmental fate and transport, biological activity). Section 6.3.4 presents a discussion about how to address model uncertainty.

Figure 8-1. Example of Sampling Uncertainty Resulting from Data Analysis Limitations



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 2004b). The uncertainty in an exposure assessment often is reduced by using more or better data. Uncertainty analysis is the process by which the sources of uncertainty in an assessment are identified and an estimate made of 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 risk assessment, to describe uncertainty by presenting a range of possible exposures and risks.

The term "inherent uncertainty" also is used in risk assessment. It describes the factors that are not resolvable with either more time or better science. Typically, inherent uncertainty cannot be described qualitatively or quantified; instead, it is a component of natural variability (Section 8.1.3). This chapter does not discuss inherent uncertainty in detail because the impact of inherent uncertainty on an exposure assessment is difficult to evaluate and cannot be resolved.

8.1.2. Decision Uncertainty

Regardless of whether data uncertainty has been reduced, risk managers/decision makers are confronted with decision uncertainty. Decision uncertainty pertains to understanding the decision context. This includes deciding whether the analysis has been adequately characterized to answer the question(s) posed (e.g., Were the appropriate data used?) and understanding the relationships among the factors that are relevant to the decision options. In understanding these relationships, making two distinctions is essential. The first distinction to be made, which requires analytical expertise, is the determination of the significance of those decision factors 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 the determination of the relative importance of those decision factors, which is the role of a risk manager/decision maker/stakeholder. Determining relative importance means explicitly and transparently expressing how those factors need to be balanced or valued. The relative importance of decision factors is a reflection of the values of the risk manager/decision maker/stakeholder and is determined by the risk manager/decision maker through a process that includes input from the stakeholders. Decision uncertainty associated with evaluating exposure scenarios, conducting sampling or measurement studies and carrying out observational studies or modeling efforts are described in this *Guidelines for Human Exposure Assessment*.

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 rather than in pursuit of a universal scientific truth.

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 other 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? In other words, does the risk manager/decision maker feel comfortable making a decision with the currently available data?
Will using a combined dataset be a problem?	If the data were of one type or another, would it change the risk-management decision?
Does the risk manager/decision maker need to understand the current data better?	What is the relationship between the currently available data and the management decision options being considered? For example, are the conditions expected to change significantly in the future?
How is the relative attractiveness of the 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 attractiveness 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 to 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 2004b). In exposure assessment, variability represents the range of possible outcomes resulting from 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 geographic areas). Variability affects the precision of exposure estimates and the degree to which results can be generalized. Types of variability that are encountered in exposure assessment include human (intra- and interindividual), spatial and temporal. 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 2004b). Human variability consists of intra- and interindividual variability. Intra-individual variability refers to the changes that occur in one person over time. These changes 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. Similar to intra-individual variability, these differences can arise from differences in physiological or behavioral characteristics.

Spatial 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 provided by ground water 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 uncertainty and variability evaluation provides the assessor with an opportunity to evaluate the accuracy and effectiveness of an exposure assessment as a whole, as well as its components (e.g., conceptual models, modeling approaches). An uncertainty evaluation will not eliminate all uncertainty, but it can help an assessor address questions that arise about an exposure assessment, its results 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) can change potential exposures (e.g., eliminating exposure via direct contact with soil).

Many of the questions that arise during an exposure assessment can be answered by an uncertainty and variability evaluation (e.g., What are the sources of uncertainty?) or can influence the methods selected for conducting the evaluation (e.g., Does one specific exposure scenario substantially contribute to the total exposure?). This section discusses this consideration and provides examples of questions for an assessor to address when planning and implementing an evaluation. Because an assessor addresses uncertainty and variability throughout an exposure assessment, questions and considerations are presented for the planning and scoping process, implementation (i.e., gathering data and estimating exposure) and results steps of an exposure assessment.

8.2.1. Planning and Scoping for Characterizing Uncertainty and Variability

As described in Chapter 3, 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. EPA (2004b)[17] provides a sample of questions to ask during planning and scoping to characterize uncertainty and variability, including:

- Will a quantitative analysis improve the assessment?
- What are the major sources of uncertainty?
- What are the major sources of variability within the individual/lifestage/group/population?

[17] U.S. EPA (2004b) primarily addresses data uncertainty. This list of sample questions is applicable to both data and decision uncertainty.

- What time and resources are available for conducting an evaluation?
- What level of effort is warranted for this project?
- Will a quantitative estimate of uncertainty improve the decision?
- Will a quantitative estimate of the variability of a specific exposure parameter improve the decision?
- How will the uncertainty and variability analysis affect the regulatory decision?
- How available are the skills (e.g., statistical expertise) and experience needed to perform the analysis?
- Have the weaknesses and strengths of the methods involved been evaluated?
- How will the uncertainty analysis be communicated to the risk managers/decision makers and stakeholders?

Communicating with risk managers/decision makers, stakeholders and community members during the planning and scoping phase also can identify questions that might influence the uncertainty and variability evaluation. Communication (Section 9.3.1) between an assessor and risk manager/decision maker is important for identifying potential areas where additional research or resources might be useful in an exposure assessment. Anticipating these concerns during the planning and scoping phase can help an assessor be responsive to risk manager/decision maker and stakeholder needs.

8.2.2. Gathering Data and Estimating Exposure

Data uncertainty and variability contribute to the overall uncertainty and variability of an exposure assessment. Understanding specific data concerns can highlight some of the limitations of estimated exposures. 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 site- or project-specific data, an assessor will rely on existing datasets, such as those in the *Exposure Factors Handbook: 2011 Edition* (U.S. EPA 2011f). These documents provide an important reference for evaluating potential exposure parameters 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 and often can address these issues. The extent of the evaluation depends on many factors, including the type of assessment, the data quality objectives (DQOs) and data availability. In these situations, an assessor balances the cost of conducting more sophisticated uncertainty and variability evaluations (e.g., probabilistic risk assessment, advance modeling) with the benefits reaped from the information. In most instances, spending more resources to obtain more certain data is important only if the new information would change a risk manager's/decision maker's choice. Whether a particular level of uncertainty is acceptable is a matter of context, values and regulatory policy (Jamieson 1996a; Stahl and Cimorelli 2005).

8.2.3. Conveying Uncertainty when Presenting Results

Transparency in communicating 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 because of the potential complexity of the evaluation. 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. *Risk Assessment Guidance for Superfund*, Volume III, Part A, Chapter 6 (U.S. EPA 2001g) provides specific information on communicating uncertainty and variability to many audiences, such as risk managers/decision makers, stakeholders and the public. Section 6.4 of this guidance provides key factors for successful communication of probabilistic risk assessment, including early and continuous involvement of stakeholders, a well-developed communication plan, good 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 2001g). Chapter 9 provides additional information about communication considerations for the overall exposure assessment. EPA's *Risk Characterization Handbook* (2000c) is another resource for information about communicating results to risk managers/decision makers and others (e.g., community groups).

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

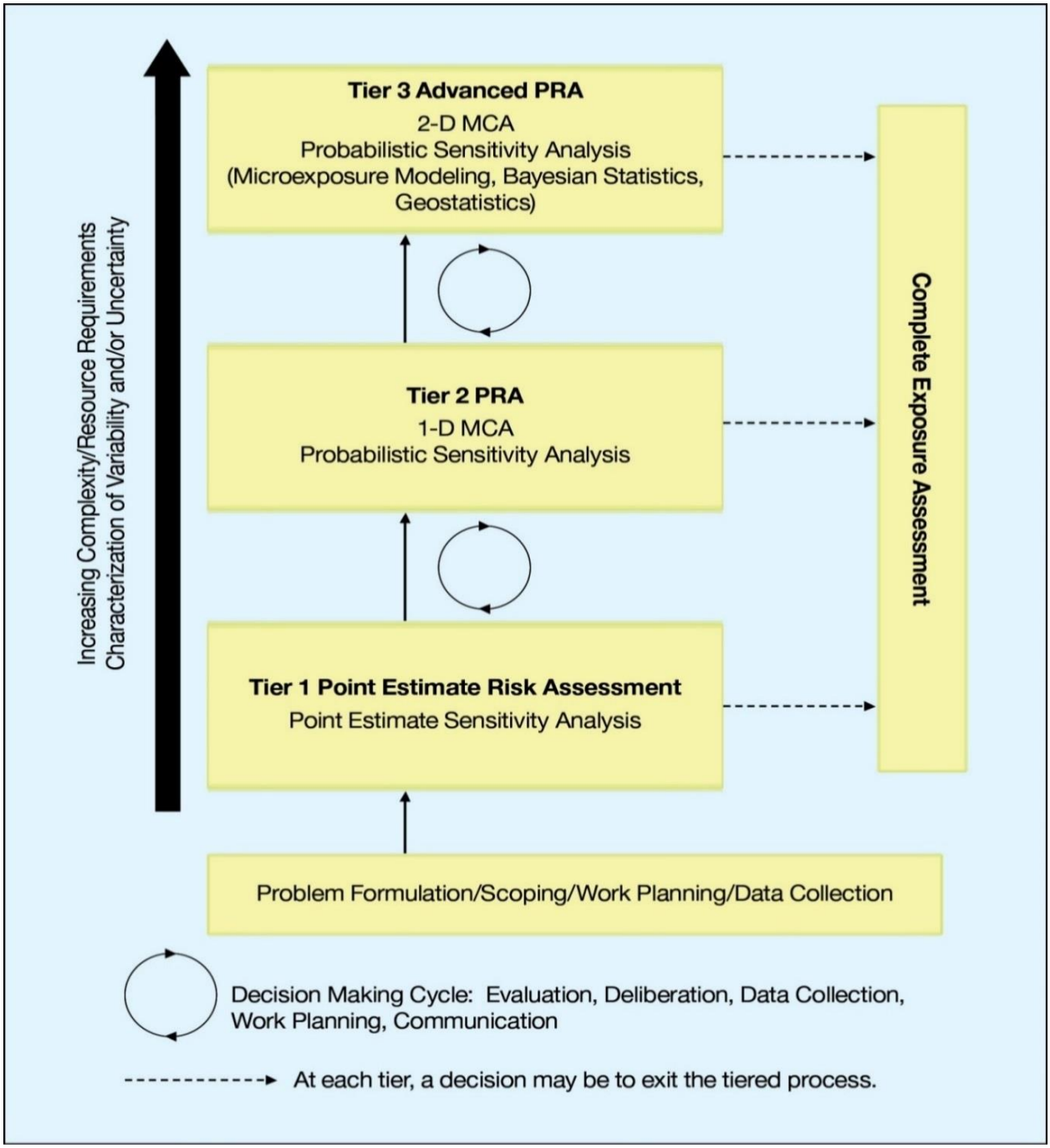
Uncertainty and variability evaluations are increasing in complexity as evaluation tools (i.e., modeling capabilities) grow more sophisticated. Not all exposure evaluations, however, require the most complex evaluation possible. EPA has emphasized the use of a tiered approach to conducting uncertainty and variability evaluations. The level of complexity of the evaluation is related to the complexity of the assessment and the potential use of the exposure information in the risk management decision. In its simplest form, this approach involves starting with basic screening methods and sequentially employing more sophisticated methods as needed to support the decision (U.S. EPA 2004b).This section describes the tiered approach to data uncertainty and variability evaluations and discusses the methods most commonly used for each tier. Important to note, however, is that evaluation methods can be used during more than one tier of an evaluation. Assessors need to identify and use the methods that best meet their needs.

In moving through each tier—from simple to complex—an assessor determines whether additional evaluations are required or whether the uncertainty (data and decision) and variability have been addressed or reduced to an acceptable level. This process involves:

- Selecting input parameters for an exposure assessment;
- Developing a deterministic analysis to identify potential exposures to provide a baseline for a sensitivity analysis and more sophisticated analyses;
- Conducting a sensitivity analysis to characterize the impacts of uncertainty or variability on exposure assessment outcomes; and
- Implementing analyses to refine the input parameters to an exposure assessment and address uncertainty and variability in the assessment.

This process, although presented linearly here, is iterative and related to each tier. 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 of the evaluation (e.g., one-dimensional Monte Carlo analysis). Figure 8-2 illustrates EPA's tiered approach.

Figure 8-2. Schematic Diagram of Tiered Approach to Data Uncertainty



Note: MCA = Monte Carlo analysis; PRA = probabilistic risk assessment
Adapted from U.S. EPA (2004b)

Figure 8-2 also provides examples of the most commonly used methods for each tier (e.g., point estimates or deterministic analysis, one-dimensional Monte Carlo analysis, two-dimensional Monte Carlo analysis). Assessors are encouraged to consult with their programs to identify preferred evaluation tools and default input parameters (e.g., drinking water intake, body weight). 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; Jamieson 1996b; Renn 1986; Stahl and Cimorelli 2005).

8.3.1. Selecting Input Parameters

For each parameter of an exposure assessment (e.g., chemical concentration, exposure duration), a range of potential values exists. As a data uncertainty and variability evaluation becomes more sophisticated, an assessor will revisit and, as necessary, refine these parameters to improve how conditions are represented.

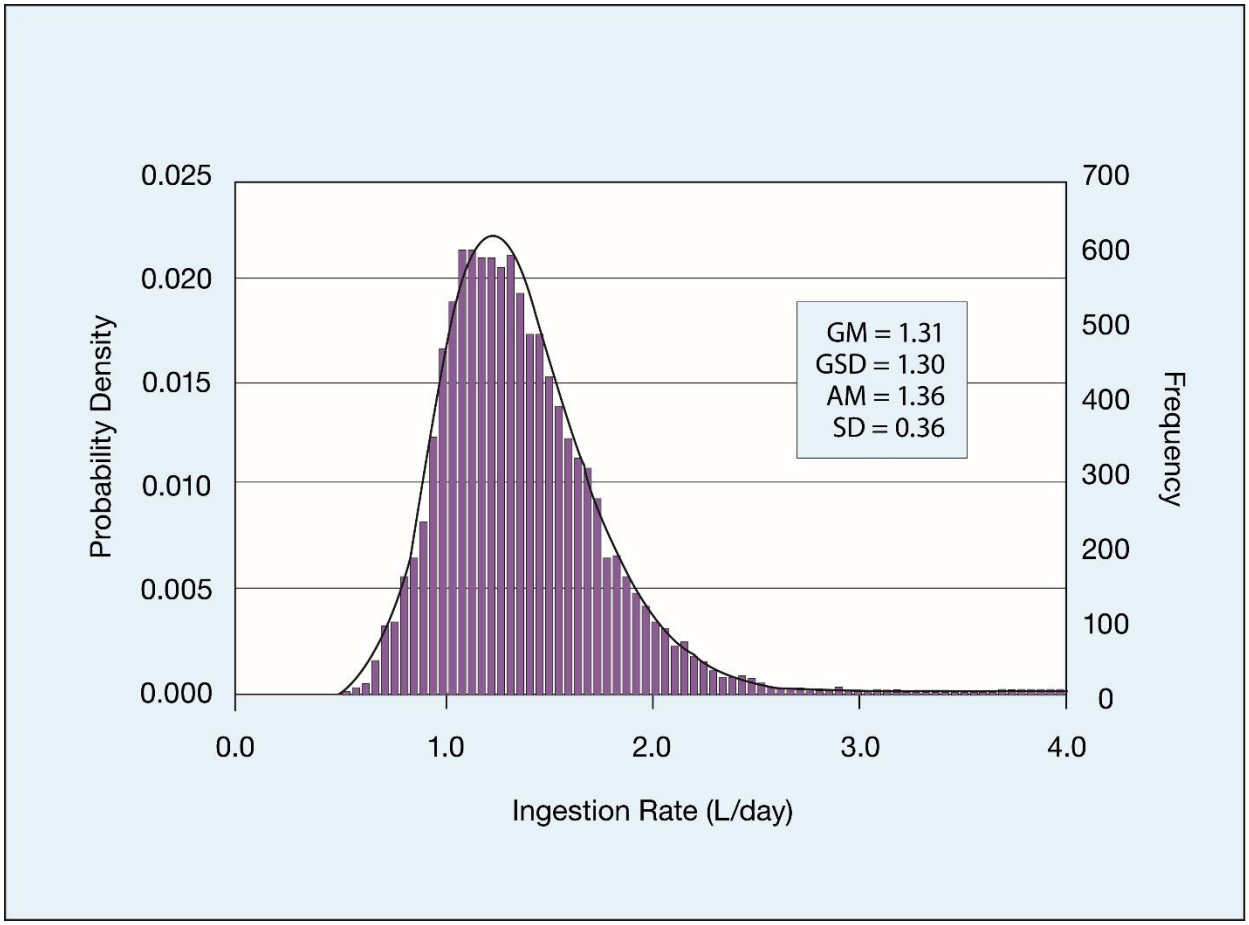
At the beginning of an exposure assessment, an assessor often uses a screening-level approach (Section 8.3.2) to gain an overall understanding of exposures. At the screening level, an assessor typically selects a single data point estimate to represent a central tendency, maximum or other exposure level.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

If after completing the screening-level evaluation an assessor determines that additional refinement of the input parameters is necessary, he or she advances to the next step in the process and conducts a sensitivity analysis (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).

Based on the sensitivity analysis, one approach an assessor might take is to select the maximum and minimum values for the variables that most influence the assessment as input parameters. These values are used to estimate the upper and lower bounds of exposure, referred to as an interval. An assessor might assume a uniform distribution across this interval or a skewed distribution, based on professional judgment. Additional data uncertainty in an exposure assessment, however, is introduced by these assumptions (WHO 2008). In addition to simply 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 or 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, a probabilistic risk assessment approach can be used to refine the input parameters. In these instances, 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 2001g). For example, a probability distribution for drinking water intake would represent the range of possible intake rates and spread of the values within the range (Figure 8-3).

Figure 8-3. 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 not necessary. 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 that were conducted to refine the exposure assessment. The accuracy of the probability distribution also depends on the quality of the input data (Section 5.2). 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 2011f). Once an appropriate dataset is identified, statistical analyses are conducted to develop the probability distributions (U.S. EPA 2001g; U.S. EPA 2004b). For example, Appendix B of EPA's *Risk Assessment Guidance for Superfund, Volume III – Part A, Process for Conducting Probabilistic Risk Assessment* (U.S. EPA 2001g) 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. More information on these tools is provided in Section 6.3.4

8.3.2. Screening Analyses

Screening-level analyses serve as the first tier of a data uncertainty and variability evaluation. These analyses often are used to screen out exposure scenarios or pathways that are not expected to pose much 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 2004b).

Screening-level analyses typically are used 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. These default values are selected so that analyses 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 evaluated is not a concern (U.S. EPA 2004b).

The basic process for conducting a screening-level analysis includes:

- Selecting point estimates for input parameters. These estimates likely will be based on default values, but location- or scenario-specific data can be used, if available.
- Estimating potential exposures based on the scenarios identified.
- Comparing the estimated exposure to screening values. Screening values include health-based values that are expressed as a dose (e.g., reference doses) and chemical concentrations in a specific medium (e.g., soil screening values).[18]
- Determining which exposure pathways, if any, require additional evaluation. Typically, exposures that exceed screening values are carried forward. In some cases, an assessor might carry forward or eliminate a scenario for further evaluation based on community concerns, stakeholder input or other factors.

This process most commonly is followed using a deterministic approach. This approach entails developing a point estimate of exposure and using point estimates of toxicity to calculate a hazard quotient (noncarcinogenic effects) or risk level (carcinogenic effects). An assessor also can use probabilistic risk assessment approaches during the screening-level analysis. These approaches, however, are used more often when refining an exposure assessment (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 (SOPs).

[18] When using chemical concentrations as screening values, an assessor usually can compare an exposure point concentration (EPC) to the value directly. In this case, estimating the exposure quantitatively would not be necessary.

8.3.3. Conducting a Sensitivity Analysis to Better Characterize Uncertainty

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 2001g). 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. For decision uncertainty, the sensitivity analysis is a process of placing all relevant data in the decision context so that 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 sensitivity need not be sequential. For example, while performing data uncertainty analysis, conducting decision uncertainty analyses is advisable. An assessor uses the results of the analyses to determine when additional sampling data no longer need to be collected or more time-consuming probabilistic analyses need to be performed.

Identifying the parameter(s) driving uncertainty and variability in the results of an exposure assessment allows an assessor to:

- Prioritize sources of data uncertainty, decision 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 versus the benefit of having a more refined exposure assessment;
- Target additional analyses or data collection efforts; and
- Assist in model development and refinement by highlighting key input parameters.

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 2001g). 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 2001g) and WHO's *Uncertainty and Data Quality in Exposure Assessment* (WHO 2008) provide detailed guidance on conducting a sensitivity analysis. EPA programs might implement specific procedures for conducting sensitivity analyses. Assessors need to consult with their programs and follow their SOPs.

In some cases, the sensitivity analysis is a low-cost procedure that uses basic calculations to evaluate the relative contribution of the various exposure parameters. In other cases, a more intensive and complicated sensitivity analysis is required. This complexity usually arises when multiple sources of uncertainty and variability influence an exposure assessment outcome. These sources can be linked; in other words, changes to one source might impact another source (U.S. EPA 2001g).

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

- The uncertainty and variability have been defined such that an exposure assessment is sufficient to support decisions, or
- The uncertainty and variability affect the outcome of an exposure assessment to the degree that the assessment is insufficient to support decisions.

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 2001g).

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

If a sensitivity analysis indicates that the uncertainty and variability in an exposure assessment have the potential to 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 (for example, Figure 8-2). At the screening level, an assessor might decide to move to statistical analyses of the data (e.g., 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 advanced modeling approaches. Important to remember is that these approaches cannot address inherent uncertainty. In addition, although they can help improve an assessor's understanding of exposure variability, they cannot reduce variability.

Refining an exposure assessment can require considerable time and effort. For example, additional data collection efforts might be required (Section 5.4.2). As discussed in Section 8.2.2 on gathering data, an assessor balances 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. Deterministic approaches, as discussed in the description of the screening-level analyses (Section 8.3.2), most likely are used during the lower tier stages of an evaluation. An assessor more commonly will use a probabilistic risk assessment or advanced modeling approaches during upper-tier or more complex evaluations.

Role of Probabilistic Risk Assessment in Uncertainty Analyses

Probabilistic risk assessment is a statistical method that yields a probability distribution for risk, generally by assigning a probability distribution to represent variability or data uncertainty in one or more parameters of an exposure assessment. This approach is employed when detailed statistical analysis is necessary to support sensitive decisions and help risk managers/decision makers distinguish among possible alternatives. Probabilistic approaches also can be used to identify data gaps where additional data collection might be necessary to reduce uncertainty and address variability. If data gaps are identified, an assessor can address these gaps by collecting additional data (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). Resources for probabilistic risk assessment are listed in Box 8-2.

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. Risk Analysis 14: 53-73.
- U.S. EPA (1996d) *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 (1999a) *Report of the Workshop on Selecting Input Distributions for Probabilistic Risk Assessment*. EPA/630/R-98/004.
- U.S. EPA (2001g) *Risk Assessment Guidance for Superfund: Volume III – Part A, Process for Conducting Probabilistic Risk Assessment.* EPA/540/R-02/002.
- U.S. EPA (2014d) *Risk Assessment Forum White Paper: Probabilistic Risk Assessment Methods and Case Studies*. EPA/100/R-14/004.

Depending on the exposure assessment objectives, probabilistic risk assessment methods of varying sophistication are available. A Monte Carlo analysis is a widely used probabilistic method that employs computer simulations to combine multiple probability distributions in a quantitative exposure assessment. During the simulation, variables are selected randomly and a quantitative exposure is estimated. This process is repeated many (e.g., 10,000) times. The output is a series of exposure estimates that can be summarized with statistical analysis (e.g., mean, quartiles). Most commonly, the input parameters are assumed to be independent (i.e., the value of one parameter is not linked to the value of another). In more complex simulations, parameters can be linked by 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 uncertainty and variability and is considered an advanced modeling method (U.S. EPA 2001g).

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 not feasible or data are not yet available. The resulting information can inform decisions associated with the assessment. Each expert characterizes the relationships, quantities, events or parameters of interest based on professional judgment and expertise. These characterizations typically are expressed 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 applies 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).

8.4. Communicating the Results of the Uncertainty and Variability Evaluation

Effectively communicating about uncertainty and variability concepts, evaluation tools and impacts on an exposure assessment can be difficult. Risk managers/decision makers and stakeholders likely will have preconceptions and biases that influence their interpretations of the evaluation. Ultimately, an assessor seeks to communicate the information effectively so that informed decisions about risks to health, safety and the environment can be made (WHO 2008). Section 3.2.2 and Chapter 9 provide details about how to communicate the overall exposure assessment process effectively.

WHO (2008) has identified questions for an assessor to consider and address when discussing the results of an uncertainty and variability evaluation with the public, including:

- 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 different 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 more complex analyses for others. These analyses will differ quite markedly in the level of sophistication, quality of data and amenability to quantitative expressions of uncertainty (both data and decision). The rationale for applying a specific method in a specific situation is outlined clearly 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 that describe when and how to use a specific tool, as well as resources that define 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 remember that, although decisions about data collection and additional analyses can be influenced by resources (i.e., time and cost constraints), stakeholders usually are less concerned about these constraints. They might lose confidence in decisions that appear to be 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 the trust and confidence of a risk manager/decision maker and stakeholder (WHO 2008).

Chapter 6 of EPA's *Risk Assessment Guidance for Superfund: Volume III – Part A, Process for Conducting Probabilistic Risk Assessment* (U.S. EPA 2001g) and Chapter 6 of WHO'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, Dalkmann et al. 2004; Davies et al. 1987; Illing 1999; Jamieson 1996a; Jamieson 1996b; Sarewitz 2004; Stahl and Cimorelli 2005.) Chapter 9 presents additional guidance for communication in exposure assessments.

CHAPTER 9. PRESENTING AND COMMUNICATING RESULTS

Communication of exposure assessment results is shaped by the assessment's purpose (e.g., conducting a risk assessment, measuring status and trends, drafting mitigation strategies, making regulatory decisions, conducting epidemiological studies). This chapter highlights the communication of the results of an exposure assessment in the context of characterizing risk. It presents:

- An overview of communication in an exposure assessment (Section 9.1);
- Characterizing the results of an exposure assessment (Section 9.2);
- Audiences for communication (Section 9.3);
- Communication products (Section 9.4);
- Ethical issues (Section 9.5); and
- Additional resources for communication and stakeholder involvement (Section 9.6).

This chapter provides an overview of exposure communication. The reader is referred to the many references throughout this chapter for more detailed information.

9.1. Overview of Communication in Exposure Assessment

The National Research Council (NRC) observes that the products of a risk assessment are, among other things, communication products (NRC 2009):

> "Their value lies in their contribution to the objectives of the decision-making function, including their effects on the primary risk manager/decision maker and other interested parties who participate in the decision or otherwise use the information that the products convey. Although the effort expended in the process is largely scientific, the critical final process in risk assessment is ultimately communication."

These principles also apply to communicating the results of an exposure assessment. Carrying out this "critical final process" of communication can be a difficult task because of the complexity of the information to be conveyed, inherent uncertainty and varying needs of the different audiences, including scientists, risk managers/decision makers, various stakeholders, the media and the public (WHO 2008). High-quality communication improves the ability of the risk manager/decision maker to make informed decisions in the face of "substantial, inevitable, and irreducible uncertainty"; improves other stakeholders' understanding; and fosters public interest (e.g., fairness, transparency) in the decision-making process (NRC 2009).

An effective communication strategy begins during the early phases of the assessment process (i.e., during planning and scoping and problem formulation) (NRC 2009). Chapter 3 presents

guidance on establishing a dialogue with stakeholders in the early phases of an exposure assessment. Establishing a relationship early in the process can facilitate communication with stakeholders later. This can often be facilitated by communication experts in EPA's Office of Public Affairs and the communication staffs within each region and program (http://www2.epa.gov/aboutepa/about-office-public-affairs-opa).

Since the publication of EPA's 1992 *Guidelines for Exposure Assessment* (U.S. EPA 1992c), risk communication has evolved in theory and practice. This evolving maturity is reflected in the transition from the Agency's inception, which relied on a one-way presentation of the information, to the partnering with stakeholders and other interested parties starting with the inception of the project through the risk management decision (Santos 2007). EPA adopted the *Seven Cardinal Rules of Risk Communication* as a policy guidance document in 1988. These principles uphold the importance of dialogue with the community and other interested stakeholders and recognize that stakeholders might hold a more complicated view of risk than do technical experts (Covello and Sandman 2001). EPA recognizes the role of the public in risk management and actively engages the public in many of its decision-making processes.

9.2. Results of an Exposure Assessment: Exposure Characterization and Risk Characterization

An exposure assessment results in a value or distribution of expected values and a range of uncertainty (WHO 2008). Exposure characterization is the narrative that provides the discussion, analysis and conclusions to synthesize these 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 9.2.1 presents information on developing the exposure characterization as part of the overall risk assessment. Section 9.2.2 presents the key elements of an exposure characterization in detail.

9.2.1. Development and Use of an Exposure Characterization in Characterizing Risk

In practice, an individual characterization is written for each component of the risk assessment (hazard assessment, dose-response assessment, exposure assessment) to carry forward the key findings, assumptions, limitations and uncertainty. The set of these individual characterizations provides the informational basis for writing the results of an integrated risk characterization analysis. 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; what assumptions were made and what data uncertainty exists; and can include insights about where policy choices (e.g., value judgments) will need to be made.

Often these assessments lead to some form of regulatory decision. Regulatory decisions are policy decisions. Ideally, they are supported by rigorous analysis of quality scientific data. The strength behind the regulatory action is based on the amount and quality of the data and its analysis. 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 is based on the quality of the exposure characterization. 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). Ideally, the risk characterization will restate the scope of the assessment, express results clearly, articulate major assumptions and uncertainty, identify reasonable alternative interpretations and separate scientific conclusions from policy judgments (U.S. EPA 2000c).

This document reiterates EPA's risk characterization policy (U.S. EPA 2000c), which calls for conducting risk characterizations in a manner that is consistent with the principles listed below. 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.** The products from the assessment need to be understood readily by readers inside and outside the assessment process. Documents need to be concise and free of jargon and include understandable tables, graphs and equations.
- **Consistency.** The assessment needs to be conducted and presented in a manner consistent with EPA policy and guidance.
- **Reasonableness.** The assessment needs to be based on sound judgment, 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, these principles need to have been applied in all steps of the process (U.S. EPA 2000c).

Communication is an ongoing process that starts at conception of the assessment. When developing the problem formulation, the risk manager/decision maker specifies to the other members of the project team the question(s) that needs to be answered. Additionally, the assessors and risk managers/decision makers need to effectively communicate the questions to be addressed and the approach that will be taken to the stakeholders and the public. As discussed in Chapter 3, as appropriate, stakeholder input can begin with the planning and scoping process and problem formulation and continue through to the final assessment employing the TCCR principles. In doing so, the assessor(s) needs to be aware of the multiple audiences to ensure clarity and transparency for all users of the assessment.

Box 9-1 presents excerpts from EPA's policy for risk characterization (U.S. EPA 2000c).

9.2.2. Elements of an Exposure Characterization

An exposure characterization is a summary explanation of an exposure assessment. Ideally, an exposure characterization:

- Provides the statement of purpose, objective(s), scope, level of detail and approach used in the assessment, including key assumptions;
- Presents the estimates of exposure and dose by pathway and route for individuals/lifestages/groups/populations in a manner appropriate for the intended exposure characterization;

- 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; and
- Communicates the results of an exposure assessment to the project team in a manner that can be used to facilitate the integration of the exposure characterization with the other assessment elements, to develop a risk characterization.

Box 9-1. EPA's Policy for Risk Characterization Relevant to an Exposure Assessment

Policy Statement:

Each risk assessment prepared in support of decision making at EPA includes a risk characterization that follows the principles and reflects the values outlined in this policy. A risk characterization is prepared in a manner that is clear, transparent, reasonable and consistent with other risk characterizations of similar scope prepared across programs in the Agency. Further, discussion of risk in all EPA reports, presentations, decision packages and other documents needs to be substantively consistent with risk characterizations in risk assessments. The nature of the risk characterization will depend upon the information available and regulatory application of the risk information and resources (including time) available. In all cases, however, the assessment identifies and discusses all major issues associated with determining the nature and extent of the risk and provides commentary on any constraints limiting fuller exposition.

Key Aspects of Risk Characterization:

- **Bridging risk assessment and risk management/decision making.** As the interface between risk assessment and risk management/decision making, options are developed using the risk characterization and based on consideration of all relevant factors, scientific and nonscientific.
- **Discussing confidence and uncertainty.** Key scientific concepts, data and methods (e.g., use of animal or human data for extrapolating from high to low doses, use of pharmacokinetics data, exposure pathways, sampling methods, availability of chemical-specific information, quality of data) are discussed. To ensure transparency, risk characterizations include a statement of confidence in the assessment that identifies all major uncertainties along with commentary on their influence on the assessment, consistent with the *Science Policy Council Handbook: Risk Characterization* (U.S. EPA 2000c).
- **Presenting several types of risk information.** Information is presented on the range of exposures derived from exposure scenarios and use of multiple risk descriptors (e.g., central tendency, high-end individual risk, population risk, important lifestages), consistent with terminology in the *Science Policy Council Handbook: Risk Characterization*; Agency risk assessment guidelines; and program-, office- and region-specific guidance. In decision making, risk managers/decision makers use risk information appropriate to their program legislation.

U.S. EPA (2000c)

Along with explaining why the assessment was conducted and presenting the findings, an exposure characterization presents a conclusion about whether the questions posed were answered and what degree of confidence the assessor has in those answers. The characterization also notes whether an exposure assessment brought to light additional or perhaps more appropriate questions, whether these questions were answered and the degree of confidence the assessor has in those answers. A good exposure assessment recapitulates the components of the problem formulation and other relevant aspects of the planning and scoping process.

In presenting exposure and dose estimates, important source(s), significant pathway(s) and routes of exposure from the source to the individual/lifestage/group/population are identified and quantified as laid out in the conceptual model, and reasons for excluding any individual/lifestage/group/population from the assessment are discussed. If the exposure distribution is known, a variety of exposure descriptors and, where possible, the full population distribution are presented. Risk managers/decision makers are given 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 [MEI]) or other descriptors as appropriate to the risk assessor's needs (Section 5.3). If the distribution is not known, the scenario hypotheses can be presented and characterized to the extent possible to provide context for the exposure estimates. Ideally, an exposure characterization links the purpose of the assessment with specific risk descriptors, which in turn are presented in such a way as to facilitate construction of a risk characterization.

Finally, 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 about improving the quality of the assessment. For this reason, an exposure characterization identifies key data gaps that can help focus further efforts to reduce uncertainty.

9.2.3. Formats for Exposure Characterization

EPA does not require a set format for exposure characterization reports, but some individual programs within the Agency have specific format requirements. As an example, EPA's Office of Solid Waste and Emergency Response (OSWER) has developed standardized methods for presenting exposure information, described in the *Risk Assessment Guidance for Superfund Part D* (U.S. EPA 2001f). The tables in this reference provide an approach to summarizing and presenting information consistently. They help organize information on the exposure point concentration (EPC), including statistics used, exposure variables for specific lifestages (e.g., children, adolescents, adults), toxicity values, calculated cancer risks and estimates of noncancer health hazards.

EPA's *Risk Characterization Handbook* (2000c), Appendices B through E, presents several examples of exposure characterizations as part of risk characterization case studies. EPA's Office of Research and Development (ORD) also provides templates for presentations at conferences, public meetings and other venues. Other EPA programs also might have specific formats for communicating results (e.g., oral, written). Assessors need to consult with their programs and follow their standard operating procedures (SOPs).

9.2.4. Communicating Uncertainty

A recurring theme in the conduct of a risk assessment, and one that is most evident in the exposure component, is the uncertainty associated with the modeling or measurement data. One of the most challenging aspects of communication is the presentation of uncertainty (NRC 2009). Absence of a discussion of uncertainties in the assessment deprives the audience of the full complement of information, including a discussion of the level of confidence and a distribution of the measurements or model output (Stirling 2010). Addressing uncertainties in the assessments is an essential but often a challenging task particularly to an audience with a wide range of technical expertise (Spiegelhalter et al. 2011; Visschers et al. 2009). The most

appropriate method for addressing uncertainty depends on the nature of the assessment and the audience (IOM 2013).

In general, presentation of uncertainty, in the form of probability, in a numeric (e.g., tabular) format can lead to a more accurate perception of risk than can a graphical presentation or a narrative. Numerical presentation has the advantage over graphic and narrative presentation because it enables readers to conduct their own calculations more readily. Numerical presentation of information requires, however, that the audience have the background to interpret the significance of the results, and numerical presentation of the information often fails to hold the audience's attention (IOM 2013).

Narrative or verbal presentation of uncertainty has the advantage of introducing uncertainty in the normal flow of the data description without diverting the attention of the audience. These presentation types therefore might hold the audience's attention better than numerical information such as values presented in a tabular form. Narrative is limited, however, by its ability to contrast data for different treatments or across studies and often relies on subjective interpretation when employing terms such as "rare" or "unlikely" (IOM 2013).

Graphics provide a more visually appealing presentation of the data and can hold the attention of the audience more effectively. The variety of formats provides options for adapting a graph to its purpose. A quality graph can readily illustrate effects and present central tendencies along with their distributions (uncertainties). A limitation of graphs is their inability to convey a level of precision and the lack of capability to extract information directly for additional analysis. Furthermore, graphs can evoke emotion and promote a more risk adverse attitude (Spiegelhalter et al. 2011). Whether using a graphics or numerical table, the item needs to be self-explanatory: capable of communicating the critical information without reliance on the narrative to explain the main message. For additional information on the use of graphics, Helsel and Hirsch (1993); Lipkus (2007); Slovic (1986); Slovic et al. (1979); and Tufte (1997; 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 a mutually exclusive situation. Rather, these can be used in concert to improve communication. Certainly, a table or graph is often used to support a narrative in the presentation.

9.3. Audiences for Communication of an Exposure Assessment

The potential audiences for an exposure assessment are wide ranging: risk assessors, risk managers/decision makers, peer reviewers, stakeholders, the scientific community, study participants, community members and members of the press. EPA (2000c) notes that the requirement for transparency means that EPA assessments need to be conducted "as if in a fishbowl"; therefore, the number of audiences potentially can be limitless and can include almost anyone. Assessors need to be aware that their communication, particularly with outside groups but also internally, could become a matter of public record. The website www.plainlanguage.gov provides useful guidance on communicating with a variety of different audiences.

Sections 9.3.1 through 9.3.3 present considerations for communication to risk managers/decision makers, stakeholders and the media; Section 9.4 describes communications products that can be developed to meet a variety of communications needs.

9.3.1. Risk Managers/Decision Makers

The principal issues of communication occur with the integration of the exposure assessment into the risk characterization. Once the risk characterization is complete (including the exposure characterization), the focus turns to communicating the results to the risk manager/decision maker. 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 2000c). Because of the way these risk management/decision-making factors can affect different cases, risk managers/decision makers need to reach consistent, but not necessarily identical, decisions on a case-by-case basis. Consequently, that a chemical with a specific risk characterization might be regulated differently under different statutes is entirely possible and appropriate. This *Guidelines for Human Exposure Assessment* is not intended to provide guidance on the nonscientific aspects of risk management decisions.

9.3.2. Stakeholders

Possible stakeholders (Sections 3.1.3, 7.2.8 and 7.2.9) in an exposure assessment include study participants, residents of the community in which the assessment took place, community groups, interested members of the public, industry groups, states and tribes. Chapter 7 provides guidance on communicating results to study participants. Chapter 3 describes 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 questions that they want answered and the way in which they wish to receive the results of the 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."

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.

Section 9.6 lists additional resources that assessors can use for effective communication about exposures and their associated risks.

9.3.3. Press/Media

The mass media influences people's perception of risk, so the project team needs to understand the media's strengths and limitations as a tool for risk communication (U.S. EPA 2007j). Covello

and Sandman (2001) conducted research that focused on the news media and found that journalists:

- Report highly selectively about risk and tend to emphasize unusual, dramatic, confrontational, negative or sensational situations;
- Tend to focus their attention on issues that play to "outrage factors" that the public uses in evaluating risks: dreaded events, risks to future generations, involuntariness, unclear benefits, inequitable distribution of risks and benefits, potentially irreversible effects and cases where trust is lacking;
- Pay much less attention to stories about risks that affect many more people each year but are less dramatic (e.g., heart disease, diabetes);
- Often make substantial omissions or present oversimplified, distorted or inaccurate information (e.g., inadequate statistics on general cancer rates for purposes of comparison; insufficient information on detection, treatments and other protective measures) in many of their stories about risk.

Table 9-1 lists general guidelines to help communicate effectively with the media (and other audiences); additional resources are provided in Section 9.6.

9.4. Communication Products and Strategies

The technical exposure characterization is consistent with the level of detail and complexity of the assessment conducted. The subsequent products, however, need to be tailored in terms of depth and detail to meet the needs of the audience.

First-level risk managers/decision makers, for example, might be technically oriented, but might have little time to review details. For this audience, a good 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 (which probably would accompany the summary for first-level managers). Higher-level managers and policy makers might have less technical expertise than first-level managers, so technical terms and more sophisticated content (e.g., equations) often are removed from risk characterization communication products intended for this audience. For senior Agency officials, providing an abstracted product of one page or less with little or no technical detail might be appropriate. Note, however, that summarizing and simplifying does not mean creating simplistic products (U.S. EPA 2000c).

For nontechnical audiences, especially the public, a "plain English" approach is important; little or no technical detail is necessary. Communication products for nontechnical, public audiences might include fact sheets, slide presentations, press releases, *Federal Register* notices, newsletters, site- or community-specific Web pages, public meetings and hotlines.

An exposure assessor ensures that appropriate Agency clearance procedures are followed for all communication products related to the exposure assessment. Documents and other communications products need to be dated and replaced (e.g., on websites) as updates become available.

Table 9-1. General Guidelines for Good Risk Communication

Good Communication	Poor Communication
Clearly state and estimate the risk (e.g., "We have a serious and immediate problem requiring attention.").	Exaggerate or minimize the risk (e.g., "It's time to panic." "No one has anything to worry about.").
Use clear, nontechnical language. Write at an eighth-grade reading level if communicating with the public.	Use technical language/jargon (e.g., using too many acronyms: "For the RfD, go to EPA's IRIS.").
Use credible sources: government agencies, scientific experts and reliable news sources (Associated Press, Reuters, etc.).	Use noncredible sources: lobbying groups or industries.
Listen to the audience. Assume that if one communicates in a clear, appropriate manner, the audience will understand.	Ignore the audience's concerns. Adopt a "they won't understand anyway" mentality.
Remain calm. Do not become agitated or defensive.	Get angry: "That's a stupid question."
Keep messages brief. The main message needs to be about 25–30 words (or 10 seconds).	Make messages long-winded, droning on with long lists.
Balance a negative statement with three positive statements.	Use an overload of negative statements and words like "no," "never" and "nothing."
Place the most important messages first and last.	Hide the most important message in the middle of the speech.
Use visual aids and graphics (e.g., charts, videos, pictures, graphs).	Use impersonal statistics: "The chance of one having an exposure of more than 50 ppb is about 1 in 100."
Repeat messages three times to make sure the most important points are remembered.	Mention an important message in passing: "Oh, by the way, the hurricane warning is effective immediately."
Speak with a serious tone. It will give the impression of taking the audience seriously.	Add humor. It can often be received as flippant or be misunderstood as a lack of concern.

U.S. EPA (2007j)

Communication strategies begin before an exposure assessment is conducted and continue throughout the process (*Superfund Community Involvement Handbook* U.S. EPA 2005g). When appropriate, early and continuous communication with the community provides the opportunity for an exposure assessor to learn about the community's concerns, identify potential sources of exposure data, establish a relationship with local and state environmental and health agencies and work with local and state elected officials. This initial coordination also provides insights into community preferences for communication (e.g., availability sessions, local newspapers, blogs).

For assessments that are to be explained to the public, a communication strategy often is essential. A communication strategy includes the key messages to be disseminated and the audiences, format, timing and frequency for distributing the messages. 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."

Section 9.6 presents resources prepared by EPA and other organizations for developing communication strategies. 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 2011d). These tools can be an effective component of a communication strategy for an exposure assessment.

9.5. Ethical Issues in Communication

As described in Chapter 7, prior to implementing any study involving human subjects, the study protocol and all associated documentation, including the plan for returning results to the participants and community, need to be approved by the necessary Institutional Review Boards (IRBs). Agency researchers have developed a document on scientific and ethical approaches for observational human exposure measurement studies (U.S. EPA 2008a). This document also addresses strategies for effective communication. New technical developments in exposure assessment have raised new ethical questions regarding the communication of study results. Little guidance is available, for example, regarding the reporting of biomonitoring data to individuals in instances when the scientific basis is limited for understanding the health implications of these data. Approaches that restrict reporting to aggregate results might be challenged by advocacy organizations and others, which could, in turn, require consideration of the ethical responsibilities associated with communicating individual and community-level data (Morello-Frosch et al. 2009). It is critical for an exposure assessor to understand the ethical considerations that apply when using existing datasets, as is consideration of the recommendations the researchers make regarding the use of their data, including specific confidentiality protections.

9.6. Additional Resources for Communication

In addition to the resources cited above, the array of published literature on risk communication and public involvement is extensive (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; Morgan and Martinez 1992; North 1997; Thompson and Bloom 2000).

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