

## CHAPTER 1

### OVERVIEW OF PROBABILISTIC APPROACH TO RISK ASSESSMENT

#### 1.0 INTRODUCTION

This chapter is intended for risk managers and risk assessors as an overview of the probabilistic approach to risk assessment in the context of the Superfund program at the U.S. Environmental Protection Agency (EPA). The goals of this chapter are to provide the reader with information about (1) the role of risk assessment in the Superfund program; (2) the basic concepts of probabilistic risk assessment (PRA); (3) important policies and guiding principles for PRA, as outlined throughout this guidance; and (4) the next steps that will be undertaken in the Superfund program to provide guidance on PRA.

Section 1.1 (1.1.1–1.1.3) describes the role of risk assessment from three perspectives, including the role of risk assessment in areas external to EPA, Agency-wide, and within Superfund. Section 1.1 (1.1.4) also introduces PRA and identifies its place in the Superfund program. Section 1.2 introduces the basic concepts of PRA, including the key terms of variability, uncertainty, Monte Carlo analysis (MCA), and reasonable maximum exposure (RME). PRA concepts are presented using a comparison between PRA and the traditional point estimate approach. Sections 1.2.4 and 1.3 summarize the advantages and disadvantages of PRA and point estimate risk assessment. Section 1.4 provides a summary of policies and guiding principles for using PRA in the Superfund program. EPA's policies on conducting PRA are highlighted throughout the guidance using pointers and are linked to more detailed policy discussions in other chapters in the guidance. Section 1.5 outlines the organization of this document and provides a brief summary of the content of each subsequent chapter and appendix. Section 1.6 presents EPA's next steps for PRA implementation in the Superfund program.

Key terms used throughout this guidance include: Probabilistic Risk Assessment (PRA), Monte Carlo Analysis (MCA), Probability Density Function (PDF), Cumulative Distribution Function (CDF), Reasonable Maximum Exposure (RME), Sensitivity Analysis, Tiered Approach, Variability, Uncertainty, and Preliminary Remediation Goal (PRG). Terms and their definitions are identified in an exhibit at the beginning of each chapter. Terms and definitions relevant to Chapter 1 are presented in Exhibit 1-1. In addition, a glossary of terms used throughout the guidance is given in Appendix E.

EXHIBIT 1-1

DEFINITIONS FOR CHAPTER 1

Central Tendency Exposure (CTE) - A risk descriptor representing the average or typical individual in a population, usually considered to be the mean or median of the distribution.

Confidence Interval - A range of values that are likely to include a population parameter. Confidence intervals may describe a parameter of an input variable (e.g., mean ingestion rate) or output variable (e.g., 95<sup>th</sup> percentile risk). When used to characterize uncertainty in a risk estimate, it is assumed that methods used to quantify uncertainty in the model inputs are based on statistical principles such as sampling distributions or Bayesian approaches. For example, given a randomly sampled data set, a 95% confidence interval for the mean can be estimated by deriving a sampling distribution from a Student's t distribution.

Confidence Limit - The upper or lower value of a confidence interval.

Countably Infinite - Used to describe some discrete random variables, this term refers to a set of numbers that can be counted with integers (e.g., one, two, three) and that has no upper limit. Examples include the number of tosses required for a coin to show a head—we can count each toss, but it is possible that at least one more toss is needed. The number of dust particles in a volume of air is another example. Countably finite implies there is an upper limit (e.g., days of work per year).

Credible Interval - A range of values that represent plausible bounds on a population parameter. Credible intervals may describe a parameter of an input variable (e.g., mean ingestion rate) or output variable (e.g., 95<sup>th</sup> percentile risk). The term is introduced as an alternative to the term confidence interval when the methods used to quantify uncertainty are not based entirely on statistical principles such as sampling distributions or Bayesian approaches. For example, multiple estimates of an arithmetic mean may be available from different studies reported in the literature - using professional judgment, these estimates may support a decision to describe a range of possible values for the arithmetic mean.

CTE Risk - The estimated risk corresponding to the central tendency exposure.

Cumulative Distribution Function (CDF) - Obtained by integrating the PDF, gives the cumulative probability of occurrence for a random independent variable. Each value  $c$  of the function is the probability that a random observation  $x$  will be less than or equal to  $c$ .

Expected Value of Information (EVOI) - The expected increase in the value (or decrease in the loss) associated with obtaining more information about quantities relevant to the decision process. EVOI is a measure of the importance of uncertainty in risk and the potential for changing a risk management decision if uncertainty is reduced (see Appendix D).

Frequency Distribution or Histogram - A graphic (plot) summarizing the frequency of the values observed or measured from a population. It conveys the range of values and the count (or proportion of the sample) that was observed across that range.

Monte Carlo Analysis (MCA) or Monte Carlo Simulation - A technique for characterizing the uncertainty and variability in risk estimates by repeatedly sampling the probability distributions of the risk equation inputs and using these inputs to calculate a range of risk values.

Numeric Stability - Stochastic variability, or "wobble" associated with random sampling, calculated as the average percent change in the model output after rerunning Monte Carlo simulations with the same set of input assumptions. Used as a metric for evaluating the adequacy of the number of iterations in a MCA.

Parameter - A value that characterizes the distribution of a random variable. Parameters commonly characterize the location, scale, shape, or bounds of the distribution. For example, a truncated normal probability distribution may be defined by four parameters: arithmetic mean [location], standard deviation [scale], and min and max [bounds]. It is important to distinguish between a variable (e.g., ingestion rate) and a parameter (e.g., arithmetic mean ingestion rate).

Point Estimate - In statistical theory, a quantity calculated from values in a sample to estimate a fixed but unknown population parameter. Point estimates typically represent a central tendency or upper bound estimate of variability.

EXHIBIT 1-1

DEFINITIONS FOR CHAPTER 1—*Continued*

Point Estimate Risk Assessment - A risk assessment in which a point estimate of risk is calculated from a set of point estimates for exposure and toxicity. Such point estimates of risk can reflect the CTE, RME, or bounding risk estimate depending on the choice of inputs.

Probabilistic Risk Assessment (PRA) - A risk assessment that yields a probability distribution for risk, generally by assigning a probability distribution to represent variability or uncertainty in one or more inputs to the risk equation.

Probability Density Function (PDF) - A function representing the probability distribution of a continuous random variable. The density at a point refers to the probability that the variable will have a value in a narrow range about that point.

Probability Distribution - A mathematical representation of the function that relates probabilities with specified intervals of values for a random variable. Also called a *probability model*.

Probability Mass Function (PMF) - A function representing the probability distribution for a discrete random variable. The mass at a point refers to the probability that the variable will have a value at that point.

Random Variable - A variable that may assume any value from a set of values according to chance. Discrete random variables can assume only a finite or countably infinite number of values (e.g., number of rainfall events per year). A random value is continuous if its set of possible values is an entire interval of numbers (e.g., quantity of rain in a year).

Reasonable Maximum Exposure (RME) - The highest exposure that is reasonably expected to occur at a site (U.S. EPA, 1989a). The intent of the RME is to estimate a conservative exposure case (i.e., well above the average case) that is still within the range of possible exposures.

Remedial Investigation/Feasibility Study (RI/FS) - Studies undertaken by EPA to delineate the nature and extent of contamination, to evaluate potential risk, and to develop alternatives for cleanup.

RME Risk - The estimated risk corresponding to the reasonable maximum exposure.

Sensitivity Analysis - Sensitivity generally refers to the variation in output of a model with respect to changes in the values of the model's input(s). Sensitivity analysis can provide a quantitative ranking of the model inputs based on their relative contributions to model output variability and uncertainty. Common metrics of sensitivity include:

- ▶ Pearson Correlation Coefficient - A statistic  $r$  that measures the strength and direction of linear association between the values of two quantitative variables. The square of the coefficient ( $r^2$ ) is the fraction of the variance of one variable that is explained by the variance of the second variable.
- ▶ Sensitivity Ratio - Ratio of the change in model output per unit change in an input variable; also called *elasticity*.
- ▶ Spearman Rank Order Correlation Coefficient - A "distribution free" or nonparametric statistic  $r$  that measures the strength and direction of association between the ranks of the values (not the values themselves) of two quantitative variables. See Pearson (above) for  $r^2$ .

Stochastic Dominance - Implies no intersection between two or more CDFs. For example, if the CDF for A and B do not overlap and the CDF for A is greater than the CDF for B, then at every cumulative percentile, the value of A is greater than that of B. Therefore, it can be stated that distribution A stochastically dominates distribution B. It should be noted that even when the CDFs for A and B do not overlap, the PDFs for A and B can overlap.

Uncertainty - Lack of knowledge about specific variables, parameters, models, or other factors. Examples include limited data regarding the concentration of a contaminant in an environmental medium and lack of information on local fish consumption practices. Uncertainty may be reduced through further study.

Variability - True heterogeneity or diversity that characterizes an exposure variable or response in a population. Further study (e.g., increasing sample size,  $n$ ) will not reduce variability, but it can provide greater confidence (e.g., lower uncertainty) in quantitative characterizations of variability).

## 1.1 THE ROLE OF RISK ASSESSMENT IN SUPERFUND

The role of risk assessment in the Superfund program today is built upon a foundation of scientific and management principles, policies, and laws that have been established over the past two decades. Since the enactment of the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) in 1980 the risk assessment policies and guidance documents have evolved to reflect advances in science and changes in federal regulations.

### 1.1.1 RISK ASSESSMENT IN THE UNITED STATES

Risk assessment has a long history beginning in 1940. In 1983, the National Research Council published *Risk Assessment in the Federal Government: Managing the Process* (NRC, 1983) which outlines the four steps of risk assessment (hazard identification, dose-response, exposure assessment, and risk characterization) that are used today.

The NRC addressed three main objectives in risk assessment: (1) assessment of the benefits of separating the analytical process of risk assessment from the regulatory process of risk management; (2) consideration of the feasibility of creating a single regulatory agency for the purpose of conducting all government risk assessments; and (3) consideration of the feasibility of creating uniform guidelines for risk assessment (NRC, 1983).

The Committee concluded that regulatory agencies should maintain a conceptual distinction between risk assessment and risk management, and develop uniform inference guidelines in risk assessment for use by all federal regulatory agencies. The Committee also recommended that Congress establish a Board on Risk Assessment Methods in order to ensure that risk assessment procedures be continuously reviewed and modified as the science advances. The Committee rejected the proposal for a single federal risk assessment agency based on inadequate evidence to show that one administrative structure would be more advantageous (NRC, 1983).

Since 1983, there have been ongoing advancements in the field of risk assessment. These include: (1) a continued increasing role for risk assessment in the decision-making process of many regulatory agencies, as exemplified by several bills introduced by the 103<sup>rd</sup> and 104<sup>th</sup> Congresses in 1994-1995; (2) an increased awareness of the need for uncertainty analysis and for quantifying and communicating uncertainties in risk estimates (*Science and Judgement in Risk Assessment*, NRC, 1994); (3) guidance about more inclusive approaches to risk assessment, as exemplified by environmental health legislation such as the Food Quality Protection Act (FQPA) of 1996 and the Presidential/Congressional Commission on Risk Assessment and Risk Management (1997); and (4) setting the stage for a more open decision-making process through stakeholder involvement in the risk management process, as outlined in *Improving Risk Communication* (NRC, 1989).

### 1.1.2 RISK ASSESSMENT AT EPA

EPA has refined the risk paradigm through deliberations of the Risk Assessment Forum, Science Policy Council, and other Agency-wide bodies. Such deliberations have led to consensus in guidance, policies, and memoranda that respond to the requirements set out by various environmental statutes. Individual offices have also developed regulations, guidance, and other supporting documents to aid in the implementation of particular environmental statutes.

In 1986, EPA issued final guidelines relating to risk assessment for cancer, mutagenic effects, developmental effects, exposure assessment, and chemical mixtures. Since 1986, EPA has updated or issued revised final guidelines for developmental toxicity, exposure assessment, reproductive toxicity, neurotoxicity, and ecological risk assessment; and is now revising carcinogen risk assessment guidelines. (See <http://www.epa.gov/ncea/raf/rafguid.htm> for details on *guidelines*.)

Other notable documents that guide risk assessment at EPA include:

- *Framework for Ecological Risk Assessment* (U.S. EPA, 1992b)
- *Guidelines for Ecological Risk Assessment* (U.S. EPA, 1998)
- *Guidance for Risk Characterization* (U.S. EPA, 1995a)
- *Policy for Risk Characterization* (U.S. EPA, 1995c)
- *Policy on Evaluating Health Risks to Children* (U.S. EPA, 1995d)
- *Policy for Use of Probabilistic Analysis in Risk Assessment* (U.S. EPA, 1997g)
- *Use of Probabilistic Techniques (including Monte Carlo Analysis) in Risk Assessment* (U.S. EPA, 1997g)
- *Guidance on Cumulative Risk Assessment. Part 1. Planning and Scoping* (U.S. EPA, 1997e)
- *Risk Characterization Handbook* (U.S. EPA, 2000)

### 1.1.3 RISK ASSESSMENT IN SUPERFUND

The activities and publications described above have provided a strong foundation for the development of risk assessment guidance on conducting human health—and ecological risk assessments in the Superfund program. EPA uses risk assessment (NRC, 1983, 1994) to carry out CERCLA, as amended by the Superfund Amendments and Reauthorization Act of 1986 (SARA). Under CERCLA/SARA, EPA's Superfund program is authorized to protect human health and the environment from current and potential threats posed by releases of hazardous substances, pollutants, or contaminants. The blueprint for the Superfund program is the National Oil and Hazardous Substances Pollution Contingency Plan (NCP) (U.S. EPA, 1990). Among other things, the NCP calls for the identification and mitigation of environmental impacts at hazardous waste sites, and for the selection of remedial actions to protect human health and the environment. An important part of the NCP is the implementation of a Remedial Investigation and Feasibility Study (RI/FS), which is designed to support risk management decisions within the Superfund program. A risk assessment is an integral part of the RI/FS, and is

generally conducted at a site to determine the need for action and to ensure that a selected remedy will be protective. The NCP also establishes some benchmarks for protectiveness and lays out nine criteria (some risk-based) against which each cleanup option should be evaluated (see Exhibit 1-2).

Guidance for risk assessment in the Superfund program has been developed to facilitate consistent site-specific responses. Early major guidance documents developed by EPA included: *Risk Assessment Guidance for Superfund (RAGS): Volume I. Human Health Evaluation Manual (HHEM) (Part A, Baseline Risk Assessment)* (U.S. EPA, 1989a) and *Risk Assessment Guidance for Superfund. (RAGS): Volume II. Environmental Evaluation Manual* (U.S. EPA, 1989b). *RAGS Volume I: Part A* provides an approach for conducting site-specific baseline (i.e., without remediation or institutional controls) human health risk assessments. *RAGS Volume II*, aimed at site managers, provides a framework for considering environmental effects at sites. More recently, EPA developed guidance for conducting ecological risk assessments within the Superfund program. This guidance, *Ecological Risk Assessment Guidance for Superfund: Process for Designing and Conducting Ecological Risk Assessments* (U.S. EPA, 1997a), discusses scientific methods and stakeholder input.

Over the years, the Superfund program has expanded RAGS to include the following documents relating to human health:

- *RAGS Volume I, Part B: Development of Risk-based Preliminary Remediation Goals (Risk Equations and Parameters)* (U.S. EPA, 1991b)
- *RAGS Volume I, Part C: Risk Evaluation of Remedial Alternatives* (U.S. EPA, 1991c)
- *RAGS Volume I, Part D: Standardized Planning, Reporting, and Review of Superfund Risk Assessments* (U.S. EPA, 2001a)
- *RAGS Volume I, Part E: Supplemental Guidance for Dermal Risk Assessment* (U.S. EPA, 2001b)

Additional ecological guidance documents include:

- *Role of the Ecological Risk Assessment in the Baseline Risk Assessment*. OSWER Directive No. 9285.7-17 (U.S. EPA, 1994a)
- *Issuance of Final Guidance: Ecological Risk Assessment and Risk Management Principles for Superfund Sites*. OSWER Directive 9285.7-28 P (U.S. EPA, 1999)
- *The Role of Screening-Level Risk Assessments and Refining Contaminants of Concern in Baseline Risk Assessments*. 12<sup>th</sup> Intermittent Bulletin, ECO Update Series. (U.S. EPA, 2001d)

**EXHIBIT 1-2**

**NINE CRITERIA FOR EVALUATION OF  
CLEANUP ALTERNATIVES (U.S. EPA, 1990)**

*Threshold Criteria*

1. Overall protection of human health and the environment
2. Compliance with ARARs

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*Balancing Criteria*

3. Long-term effectiveness and permanence
4. Reduction in toxicity, mobility, or volume through treatment
5. Short-term effectiveness
6. Implementability
7. Cost

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*Modifying Criteria*

8. State acceptance
9. Community acceptance

This document (*RAGS Volume 3: Part A*) provides guidance for probabilistic approaches for both human health and ecological risk assessment.

The Superfund program has also issued supplementary documents, including:

- *Human Health Evaluation Manual, Supplemental Guidance: "Standard Default Exposure Factors"* (U.S. EPA, 1991a)
- *Supplemental Guidance to RAGS: Calculating the Concentration Term* (U.S. EPA, 1992d)
- *Role of the Baseline Risk Assessment in Superfund Remedy Selection Decisions* (U.S. EPA, 1991d)
- *Use of IRIS (Integrated Risk Information System) Values in Superfund Risk Assessment* (U.S. EPA, 1993)
- *Final Soil Screening Guidance, May 17, 1996. Soil Screening User's Guide* (U.S. EPA, 1996)
- *Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites* (U.S. EPA, 2001c).

EPA will continue to develop Superfund guidance and tools to improve the practice of risk assessment. Superfund guidance documents are available from EPA's Superfund publications web site (<http://www.epa.gov/superfund/pubs.htm>).

The role of risk assessment in Superfund, described above, can be summarized by a number of principles that are followed and developed in *RAGS Volume 3: Part A*, including:

- The Superfund risk assessment process should rely on early problem formulation, planning, and scoping for improved remedial investigations and feasibility studies, risk assessments, and risk management decisions.
- The use of a tiered process in Superfund risk assessment and management is beneficial in that it promotes an efficient allocation of resources and improved decision-making.
- Early and continuing involvement of stakeholders throughout the Superfund risk assessment process provides an opportunity to build stakeholder trust and meet stakeholder needs, which can result in improved risk assessments and faster, more-informed risk management decisions.

#### **1.1.4 PROBABILISTIC RISK ASSESSMENT AND ITS ROLE IN SUPERFUND**

*RAGS Volume I* (U.S. EPA, 1989a) and supporting guidance describe a point estimate approach to risk assessments in the Superfund program. Point estimate risk assessments use single values (point estimates) to represent variables in a risk equation. The output of the risk equation in a point estimate risk assessment is, therefore, a point estimate of risk, which can be a central tendency exposure (CTE) estimate of risk (e.g., the average expected risk) or reasonable maximum exposure (RME) estimate of risk (e.g., the risk expected if the RME was to occur), depending on the input values used in the risk equation. *RAGS Volume 3: Part A* describes a probabilistic approach to risk assessment. Probabilistic risk assessment uses probability distributions for one or more variables in a risk equation in order to quantitatively characterize variability and/or uncertainty. The output of a PRA is a probability

distribution of risks that reflects the combination of the input probability distributions. If the input distributions represent variability, then the output risk distribution can provide information on variability in risk in the population of concern. If the input distributions reflect uncertainty, then the output risk distribution can provide information about uncertainty in the risk estimate. Information from a PRA can be used to make statements about the likelihood of exceeding a risk level of concern, given the estimated variability in elements of the risk equation. Since the results of point estimate methods generally do not lend themselves to this level of risk characterization (e.g., quantitative uncertainty assessment), PRA can provide unique and important supplemental information that can be used in making Superfund risk management decisions at Superfund sites.

Monte Carlo Analysis (MCA) is perhaps the most widely used probabilistic method in PRA. MCA is a specific probabilistic method that uses computer simulation to combine multiple probability distributions in a risk equation (see Section 1.2.2 for further discussion of Monte Carlo simulation). Monte Carlo methods have been in use in modeling since 1946 when Stanislaw Ulam used MCA to conduct uncertainty analysis at Los Alamos during the conceptual stage of the hydrogen bomb project. The history of the use of MCA (from the 1940s to the present) can be found in Rugen and Callahan, 1996.

The application of probabilistic analysis to human health and ecological risk assessment is a relatively recent development that was facilitated by development of statistical sampling techniques to obtain a probabilistic approximation to the solution of a mathematical equation and/or model, and increased speed and capacity of modern computers which can support the intensive computational requirements of MCA. Desktop computers and commercial software are currently available which enable risk assessors to make, in minutes, PRA calculations that only a few years ago would have required days.

The potential value of PRA to support risk-based decisions has become increasingly apparent over the last several years. This has prompted the need for appropriate policy and guidance documents that define the role of PRA in the Superfund program and that promote and facilitate the highest quality and consistent application of PRA in the Program where appropriate. EPA previously issued guidance that addresses the use of quantitative uncertainty analysis in risk assessment. *RAGS Volume I* (U.S. EPA, 1989a) and the *Final Guidelines for Exposure Assessment Guidelines* (U.S. EPA, 1992a) emphasize the importance of assessing variability and uncertainty in risk estimates conducted in the Superfund program. Guidance is also available for characterizing the 95% upper confidence limit (UCL) for the mean exposure concentration (U.S. EPA, 1992d, 1997f). At the regional level, EPA Regions 3 and 8 issued guidance on the appropriate use of probabilistic methods in risk assessment (U.S. EPA, 1994b, 1995e). The importance of adequately characterizing variability and uncertainty is addressed in the 1995 memorandum on *Risk Characterization Policy and Guidance* (U.S. EPA, 1995b). In the spring of 1997, EPA released the memorandum, *Use of Probabilistic Techniques (including Monte Carlo Analysis) in Risk Assessment* (U.S. EPA, 1997g). According to the Policy Statement of the memorandum, probabilistic analysis techniques, "given adequate supporting data and credible assumptions, can be viable statistical tools for analyzing variability and uncertainty in risk assessments." As such, a PRA, "will be evaluated and utilized in a manner that is consistent with other risk assessments submitted to the Agency." Along with this Policy Statement, the Agency released a set of guiding principles for use and review of probabilistic analyses (U.S. EPA, 1997g). Hence, both RAGS and Agency-wide guidance emphasize the importance of review of the scientific and technical merit of a probabilistic analysis to determine whether or not the assessment is of sufficient quality to support a remedial decision.

Currently, EPA's Office of Emergency and Remedial Response (OERR) is implementing PRA as part of its Superfund reform activities. This guidance, *RAGS Volume 3: Part A*, provides risk assessors with comprehensive guidance on when and how it may be appropriate to conduct PRAs using Monte Carlo analysis within the Superfund program. It describes basic concepts in PRA, an approach for conducting MCA, and EPA's policy for implementing PRA in the Superfund program. The Agency also intends to supplement this guidance with additional examples and case studies in PRA (see Section 1.6).

## 1.2 BASIC CONCEPTS OF PROBABILISTIC RISK ASSESSMENT

This section describes what a PRA is and compares and contrasts it to the more familiar point estimate methods for human health risk assessment (U.S. EPA, 1989a) and ecological risk assessment (U.S. EPA, 1997a). A risk assessment performed using probabilistic methods is very similar in concept and approach to the point estimate method, with the main difference being the methods used to incorporate variability and uncertainty into the risk estimate. A variety of modeling techniques can be used to characterize variability and uncertainty in risk. This guidance focuses on MCA, perhaps the most common probabilistic method that risk assessors will encounter. Basic concepts on how to use MCA to propagate variability and uncertainty in exposure through a risk model are presented. Many of the concepts presented in this guidance are applicable to other probabilistic approaches to risk assessment.

At some sites, probabilistic analysis can provide a more complete and transparent characterization of the risks and uncertainties in risk estimates than would otherwise be possible with a point estimate approach. However, a PRA is not necessary or desirable for every site. The tiered approach presented in Chapter 2 highlights important scientific and management decisions for determining if PRA is appropriate at a specific site. The decision to perform PRA is appropriate only after the risk assessor and the remedial project manager (RPM) at the site determine whether a PRA will enhance decision making at the site. If a PRA is conducted, the assumptions and inputs to the probabilistic model should be sufficiently documented so that the results can be independently reproduced.

An essential concept in PRA that will be important throughout this section and the rest of the guidance is the distinction between "variability" and "uncertainty". *Variability* refers to true heterogeneity or diversity. For example, among a population that drinks water from the same source and with the same contaminant concentration, the risks from consuming the water may vary. This may be due to differences in exposure (i.e., different people drinking different amounts of water, having different body weights, exposure frequencies, and exposure durations) as well as differences in response (e.g., genetic differences in resistance to a chemical dose). Differences among individuals in a population are referred to as inter-individual variability, while differences for one individual over time are referred to as intra-individual variability.

*Uncertainty* occurs because of a lack of knowledge. For example, we can be very certain that different people drink different amounts of water, but we may be uncertain about how much variability there is in water intakes among the population. Uncertainty can often be reduced by collecting more and better data, while variability is an inherent property of the population being evaluated. Variability can be better characterized with more data, but it cannot be reduced or eliminated.

Sometimes there can be confusion about whether data are representative of variability or uncertainty, especially when the distinction depends on how the problem is framed. For example, one of

the exposure variables that may be considered in a risk assessment of workers exposed via inhalation to an indoor air contaminant is the fraction of time spent indoors on site. Assume that time-activity information is available from surveys of a representative population of workers. This data set may be used to define a probability distribution (e.g., empirical, normal) that characterizes inter-individual variability in exposure times among workers. Sources of uncertainty would include the choice of the probability distribution used to characterize variability, as well as the parameter estimates that are based on a finite data set. Using the same data set, uncertainty in a parameter, such as the arithmetic mean exposure time, may also be defined by a probability distribution. Efforts to clearly distinguish between variability and uncertainty are important for both risk assessment and risk communication. Section 1.2.4 and Chapter 3, Section 3.4 present an overview of the different sources of uncertainty. Guidance on selecting and fitting probability distributions is given in Appendices B and C, and advanced methods for characterizing both variability and uncertainty are discussed in Appendix D.

### 1.2.1 WHAT IS PRA?

Probabilistic risk assessment is a general term for risk assessments that use probability models to represent the likelihood of different risk levels in a population (i.e., variability) or to characterize uncertainty in risk estimates.

A risk assessment performed using probabilistic methods would rely on the same fundamental exposure and risk equations as do point estimate approaches. U.S. EPA guidance, including *RAGS Volume I: Part A* (U.S. EPA, 1989a), the *Standard Default Exposure Factors Guidance* (U.S. EPA, 1991a), *Supplemental Guidance for Developing Soil Screening Levels* (U.S. EPA, 2001c), and *Ecological Risk Assessment Guidance for Superfund: Process for Designing and Conducting Ecological Risk Assessments* (U.S. EPA, 1997a) present methods for estimating risk using standardized exposure and risk models. Examples of typical exposure and risk equations that would be used in risk calculations, in this case, for a drinking water exposure scenario, are provided in Exhibit 1-3:

EXHIBIT 1-3

CANCER AND NONCANCER RISK MODELS

Exposure Model:

Cancer Risk Model:

Noncancer Risk Model:

$$CDI = \frac{C \times IR \times EF \times ED}{BW \times AT}$$

$$Risk = CDI \times CSF$$

$$HQ = \frac{CDI}{RfD}$$

CDI	=	chronic daily intake of the chemical (mg/kg-day)
C	=	concentration of the chemical in an exposure medium (e.g., mg/L)
IR	=	ingestion rate (e.g., L/day for water, mg/day for soil, etc.)
EF	=	exposure frequency (days/year)
ED	=	exposure duration (years)
BW	=	body weight (kg)
HQ	=	hazard quotient
AT	=	averaging time (equal to ED x 365 days/year for noncarcinogens and 70 years x 365 days/year for carcinogens)
CSF	=	cancer slope factor (linear low-dose cancer potency factor) for the chemical (mg/kg-day) <sup>-1</sup>
RfD	=	reference dose for the chemical for assessing noncancer health effects (mg/kg-day)

In the point estimate approach, a single numerical value (i.e., point estimate) is chosen for each variable shown in Exhibit 1-3. For example, point estimates may include a drinking water ingestion rate of 2 L/day and a body weight of 70 kg for an adult. Based on the choices that are made for each individual variable, a single estimate of risk is calculated. In the probabilistic approach, inputs to the risk equation are described as *random variables* (i.e., variables that can assume different values for different receptors in the population) that can be defined mathematically by a probability distribution. For continuous random variables, such as those in Figure 1-1 (body weight), the distribution may be described by a PDF, whereas for discrete random variables (e.g., number of fish meals per month), the distribution may be described by a probability mass function (PMF). The key feature of PDFs and PMFs is that they describe the range of values that a variable may assume, and indicate the relative likelihood (i.e., probability) of each value occurring within that range for the exposed population. For example, the distribution of tap water ingestion (mL/day) among the general U.S. population might be characterized by a lognormal distribution with a log-mean of 6.86 and a log-standard deviation of 0.575 (Table 3-11 of U.S. EPA 1997b). One might use a PDF to show how approximately half the population drinks more than 1 L/day of tap water, but only 10% of the population drinks more than 2 L/day. After determining appropriate PDF types and parameter values for selected variables, the set of PDFs is combined with the toxicity value in the exposure and risk equations given in Exhibit 1-3 to estimate a distribution of risks. Guidance on selecting and fitting distributions for variables in risk equations is provided in Appendix B.

In human health risk assessments, probability distributions for risk should reflect variability or uncertainty in exposure. In ecological risk assessments, risk distributions may reflect variability or uncertainty in exposure and/or toxicity (see Sections 1.4 and 1.4.1, Item 3).

A continuous probability distribution can be displayed in a graph in the form of either a PDF or corresponding CDF; however, for clarity, it is recommended that both representations be presented in adjacent (rather than overlaid) plots. Figure 1-1 illustrates a PDF and CDF for a normal probability distribution for adult body weight. Both displays represent the same distribution, but are useful for conveying different information. Note that it is helpful to include a text box with summary statistics relevant to the distribution (e.g., mean, standard deviation). The types of information that PDFs and CDFs are most useful for displaying are presented in Exhibit 1-4.

**EXHIBIT 1-4**

**USE A PDF AND CDF TO DISPLAY:**

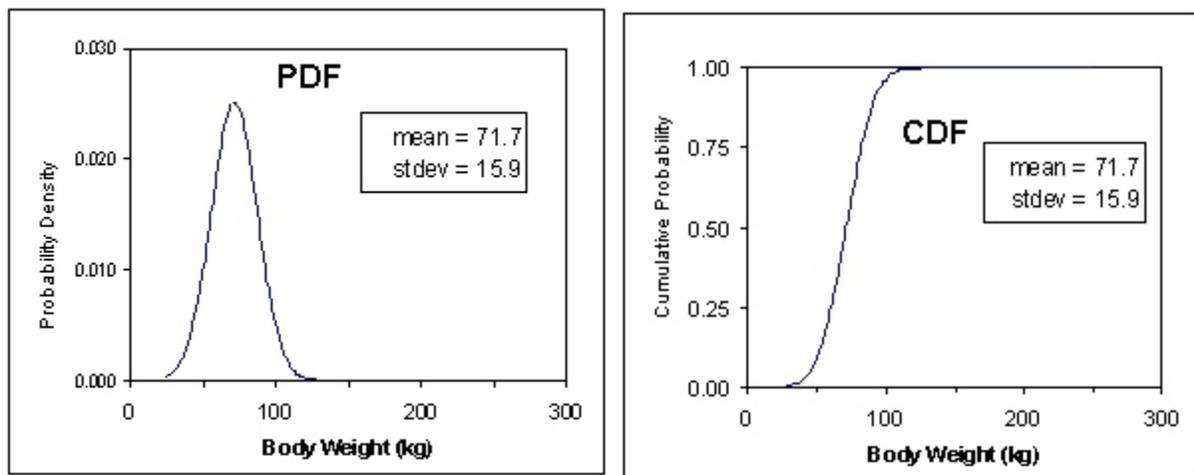
**PDF**

- The relative probability of values
- The most likely values (e.g., modes)
- The shape of the distribution (e.g., skewness, kurtosis, multimodality)
- Small changes in probability density

**CDF**

- Percentiles, including the median
- High-end risk range (e.g., 90<sup>th</sup> to 99<sup>th</sup> percentiles)
- Confidence intervals for selected percentiles
- Stochastic dominance (i.e., for any percentile, the value for one variable exceeds that of any other variable)

Source: U.S. EPA, 1997g



**Figure 1-1.** Example of a normal distribution that characterizes variability in adult body weight (males and females combined). Arithmetic mean=71.7 kg, standard deviation=15.9 kg (Finley and Paustenbach, 1994). Body weight may be considered a continuous random variable. The left panel shows a bell-shaped curve and represents the PDF, while the right panel shows an S-shaped curve and represents the CDF. Both displays represent the same distribution (including summary statistics), but are useful for conveying different information.

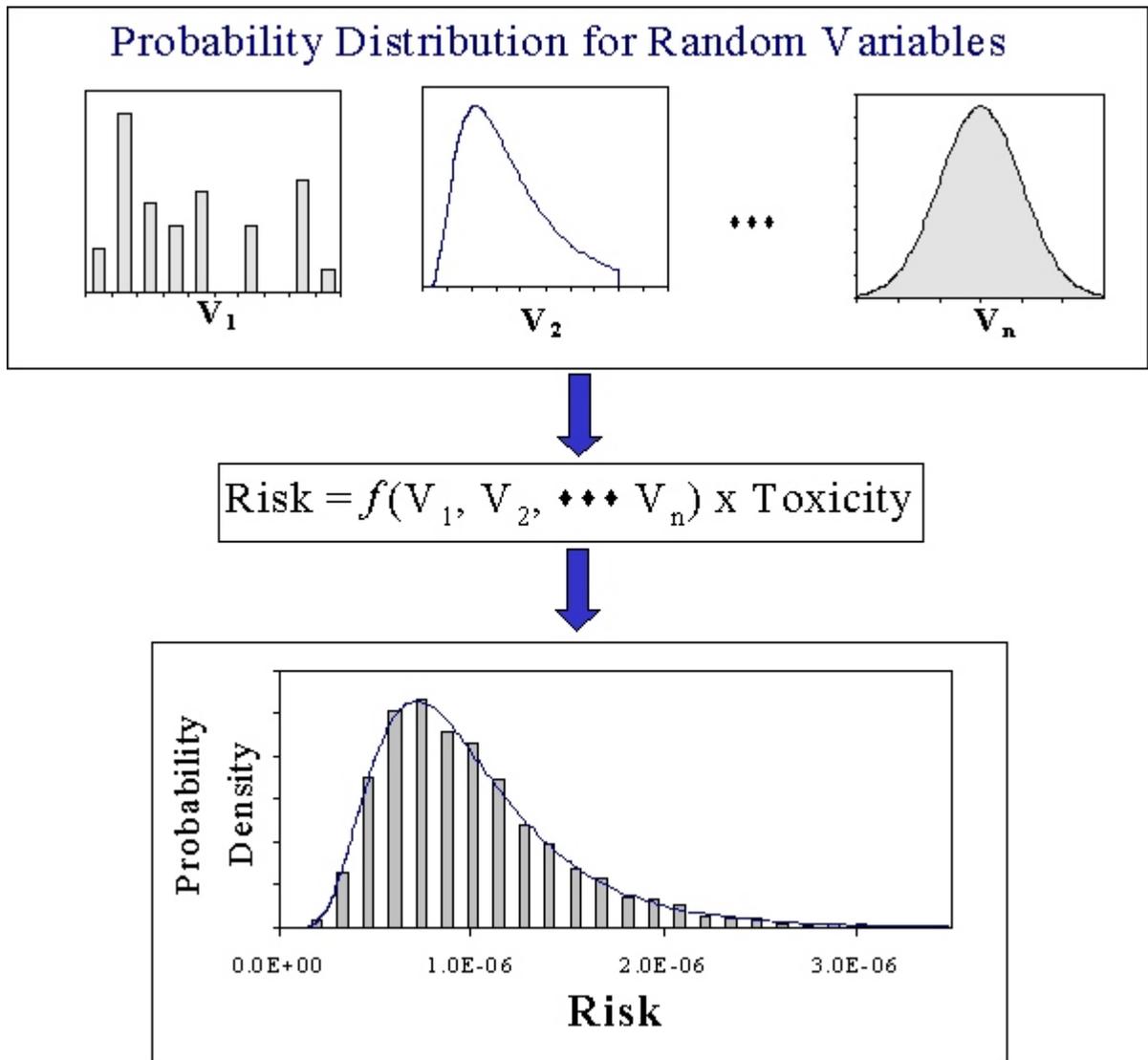
The CDF for risk can be especially informative for illustrating the percentile corresponding to a particular risk level of concern (e.g., 95<sup>th</sup> percentile=1E-06). A text box may also be included on the graph to highlight important summary statistics, such as the parameters of the input distribution, or selected percentiles of the output distribution for risk. For example, a clear description of the parameters for the probability distribution should be given, as well as an indication of whether the distribution represents variability or uncertainty.

### 1.2.2 WHAT IS A MONTE CARLO SIMULATION?

Perhaps the most common numerical technique for PRA is Monte Carlo simulation. Monte Carlo simulation has been widely used to explore problems in many disciplines of science as well as engineering, finance, and insurance (Rugen and Callahan, 1996). The process for a Monte Carlo simulation is illustrated in Figure 1-2. In its general form, the risk equation can be expressed as a function of multiple exposure variables ( $V_i$ ) and a toxicity term:  $Risk=f(V_1, V_2, \dots V_n) \times Toxicity$ . Solutions for equations with PDFs are typically too complex for even an expert mathematician to calculate the risk distribution analytically. However, numerical techniques applied with the aid of computers can provide very close approximations of the solution. This is illustrated here for the simplified case in which the assessment variables are statistically independent, that is, the value of one variable has no relationship to the value of any other variable. In this case, the computer selects a value for each variable ( $V_i$ ) at random from a specified PDF and calculates the corresponding risk. This process is repeated many times (e.g., 10,000), each time saving the set of input values and corresponding estimate of risk. For example, the first risk estimate might represent a hypothetical individual who drinks 2 L/day of water and weighs 65 kg, the second estimate might represent someone who drinks 1 L/day and weighs 72 kg, and so forth. Each calculation is referred to as an iteration, and a set of iterations is called a simulation.

☞ *A convenient aid to understanding the Monte Carlo approach for quantifying variability is to visualize each iteration as representing a single individual and the collection of all iterations as representing a population.*

Each iteration of a Monte Carlo simulation should represent a plausible combination of input values (i.e., exposure and toxicity variables), which may require using bounded or truncated probability distributions (see Appendix B). However, risk estimates are not intended to correspond to any one person. The “individuals” represented by Monte Carlo iterations are virtual and the risk distributions derived from a PRA allow for inferences to be made about the likelihood or probability of risks occurring within a specified range for an exposed human or ecological population. A simulation yields a set of risk estimates that can be summarized with selected statistics (e.g., arithmetic mean, percentiles) and displayed graphically using the PDF and CDF for the estimated risk distribution. Often the input distributions are assumed to be independent, as shown in Figure 1-2. More complex Monte Carlo simulations can be developed that quantify a dependence between one or more input distributions by using conditional distributions or correlation coefficients (see Appendix B, Section B.5.5 for a discussion of correlated input distributions).



**Figure 1-2.** Conceptual model of Monte Carlo analysis. Random variables ( $V_1, V_2, \dots, V_n$ ) refer to exposure variables (e.g., body weight, exposure frequency, ingestion rate) that are characterized by probability distributions. A unique risk estimate is calculated for each set of random values. Repeatedly sampling ( $V_i$ ) results in a frequency distribution of risk, which can be described by a PDF. In human health risk assessments, the toxicity term should be expressed as a point estimate. In ecological risk assessment (see Sections 1.4 and 1.4.1) the toxicity term may be expressed as a point estimate or as a probability distribution.

The rapid evolution in computing power has greatly reduced concerns among regulators regarding the number iterations needed in MCA.

☞ *While this guidance does not prescribe specific criteria or set an arbitrary “minimum” number of iterations needed for PRA, a general rule of thumb is that a sufficient number of iterations should be run to obtain numerical stability in percentiles of the output (e.g., risk distribution) that are important for decision making.*

Numerical stability refers to the stochastic variability, or “wobble” associated with random sampling, and can be evaluated by running multiple simulations with the same set of input assumptions and calculating the average percent change in a specified percentile of the output (e.g., Maddalena et al., 2001). For example, it may be determined that 5,000 iterations are sufficient to achieve numerical stability in the 50<sup>th</sup> percentile, but insufficient for the 95<sup>th</sup> percentile risk estimate when a criteria of  $\pm 1\%$  is applied for multiple simulations. As discussed in Section 1.4, one of the eight conditions specified by EPA for the acceptance of PRA is that the numerical stability of the output be presented and discussed, since it will vary depending on what percentile of the risk distribution is evaluated. While some commercial software now have a feature to automatically stop simulations after a specified criterion for numerical stability is achieved (Burmester and Udell, 1990), care should be taken to understand how this criterion is implemented across the entire range of the output distribution.

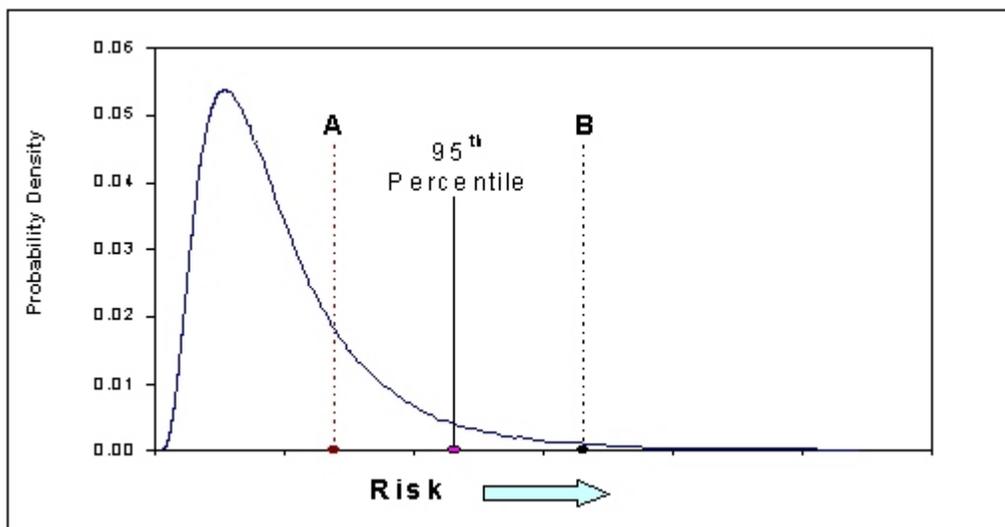
### **1.2.3 WHY IS VARIABILITY IMPORTANT IN RISK ASSESSMENT? HOW IS IT ADDRESSED BY THE POINT ESTIMATE AND PROBABILISTIC APPROACHES?**

As noted previously, variability refers to true heterogeneity or diversity that occurs within a population or sample. Factors that lead to variability in exposure and risk include variability in contaminant concentrations in a medium (air, water, soil, etc.), differences in ingestion rates or exposure frequencies, or in the case of ecological assessments, inter- and intra-species variability in dose-response relationships. *Risk Assessment Guidance for Superfund Volume I* (Section 6.1.2 of U.S. EPA, 1989a) and the *NCP Preamble* (U.S. EPA, 1990) state that human health risk management decisions at Superfund sites will generally be based on an individual that has RME. Likewise, RME estimates of risk are the most appropriate basis for decision making using an ecological risk assessment. Use of the RME and CTE risk descriptors in ecological risk assessment are discussed in Chapter 4. The intent of the RME is to estimate a conservative exposure case (i.e., well above the average case) that is still within the range of possible exposures based on both quantitative information and professional judgment (Sections 6.1.2 and 6.4.1 of U.S. EPA, 1989a). In addition, the Agency released guidance in 1992 (U.S. EPA, 1992c) recommending the inclusion of a “central tendency” exposure estimate to an individual, as well as a high-end exposure estimate, in the risk assessment. Generally, the CTE is considered to be a measure of the mean or median exposure. The difference between the CTE and the RME gives an initial impression of the degree of variability in exposure or risk between individuals in an exposed population.

Depending on assessment needs at a site, a range of point estimates of risk can be developed to represent variability in exposures. To support the evaluation of RME risk estimates using the point estimate approach described in Section 1.3, the Superfund program developed guidance with recommended default values for exposure variables as inputs to the risk equations (U.S. EPA, 1992a, 1996, 1997a, 2001d). These standardized values are a combination of average (e.g., body weight, skin surface area) and high-end exposure assumptions (e.g., drinking water intake, exposure duration). A

CTE risk estimate is based on central estimates (e.g., mean, 50<sup>th</sup> percentile) for each of the exposure variables. Available site-specific data on plausible mean and upper range values for exposure variables should be used to support CTE and RME risk estimates. The point estimate approach to risk assessment does not determine where the CTE or RME risk estimates lie within the risk distribution. For example, the RME risk estimated with the point estimate approach could be the 90<sup>th</sup> percentile, the 99.9<sup>th</sup> percentile, or some other percentile of the risk distribution. Without knowing what percentile is represented by the RME risk estimate, the risk manager might be unsure about the likelihood of the RME risk occurring or being exceeded in the receptor population and about what level of remedial action is justified or necessary to achieve the protective objectives of CERCLA.

In a PRA, distributions used as inputs to the risk equations can characterize the inter-individual variability inherent in each of the exposure assumptions. By characterizing variability with one or more input distributions, the output from the Monte Carlo simulation is a distribution of risks that could occur in that population (Figure 1-3). The central tendency of the risk distribution (e.g., arithmetic mean, geometric mean, 50<sup>th</sup> percentile) may be characterized as the CTE risk estimate. Similarly, the high-end of the risk distribution (e.g., 90<sup>th</sup> to 99.9<sup>th</sup> percentiles) is representative of exposures to the RME individual. In addition to providing a better understanding of where the CTE and RME risks occur in the distribution, a PRA can also provide an estimate of the probability of occurrence associated with a particular risk level of concern (e.g., cancer risk of 1E-05). A PRA that quantifies variability can be used to address the question, “What is the likelihood (i.e., probability) that risks to an exposed individual will exceed 1E-05?” Based on the best available information regarding exposure and toxicity, a risk assessor might conclude, “The estimated distribution for variability in risk across the target population indicates that 10% of the individuals exposed under these circumstances have a risk exceeding 1E-05.” This type of evaluation can be achieved using a technique known as one-dimensional Monte Carlo Analysis (1-D MCA). Guidelines for interpreting the high-end of the risk distribution in terms of the RME risk estimate are discussed further in Section 1.4.1 and Chapter 7.



**Figure 1-3.** Example of a probability distribution for risk illustrating the 95<sup>th</sup> percentile and two different risk levels of concern (A and B). Assuming the 95<sup>th</sup> percentile corresponds to the RME, the need for remedial action depends on how the RME risk compares with the risk level of concern. For Case A (RME > level of concern), remedial action may be warranted. For Case B (RME < level of concern), remedial action may be unnecessary.

The agreement (or lack of agreement) between the results of the point estimate calculations and the PRA calculations is expected to vary as a function of the form of the exposure or risk model and the attributes of the input variables. In general, if the terms in the denominator of the exposure or risk equation have low variability and do not approach zero, then the CTE point estimate is likely to agree quite well with the arithmetic mean from the PRA simulation, and the RME point estimate is likely to correspond to the high-end of the risk distribution (see discussion of RME range in Section 1.2.5). However, if the exposure or risk model has terms in the denominator that are a significant source of variability, or if the terms approach zero, then the agreement between the point estimate values and the PRA values may be more substantial. In addition, since the RME point estimate of risk reflects a combination of central tendency and high-end input values, it is difficult to anticipate what percentile of a distribution of variability it represents.

☞ *If results of PRA calculations differ substantially from point estimate calculations, a risk manager may benefit from understanding the reasons for the differences and the relative strengths of the different approaches.*

Since point estimate and PRA approaches may yield different estimates of CTE and RME risks, the two approaches also may support different risk management decisions. This does not imply that either approach is invalid. Likewise, a correspondence between the point estimate and PRA results does not imply a greater accuracy or certainty in the modeling assumptions and inputs. Simply stated, PRA, based on the same risk equations and data as the point estimate approach, provides a different means of characterizing variability and uncertainty. Potential sources of variability and uncertainty in risk estimates should be identified, discussed, and to the extent practicable, quantified. Advantages and disadvantages of PRA and point estimate risk assessment are discussed in Section 1.2.4 and 1.3.

#### **1.2.4 WHY IS UNCERTAINTY IMPORTANT IN RISK ASSESSMENT? HOW IS UNCERTAINTY ADDRESSED BY THE POINT ESTIMATE AND PROBABILISTIC APPROACHES?**

Uncertainty derives from a lack of knowledge. Various taxonomies of uncertainty relevant to risk assessment have been presented (Finkel, 1990; Morgan and Henrion, 1990; Cullen and Frey, 1999). U.S. EPA guidance, including the *Final Guidelines Exposure Assessment Guidelines* (U.S. EPA, 1992a), *Exposure Factors Handbook* (U.S. EPA, 1997b,c,d), and *Guiding Principles for Monte Carlo Analysis* (U.S. EPA, 1997g) describe a variety of different types of uncertainty in risk assessment as well as modeling strategies for quantifying uncertainties. Potential sources of uncertainty in risk assessment can be divided into one of three broad categories:

- (1) *Parameter uncertainty* - uncertainty in an estimate of an input variable in a model. In PRA, this may refer specifically to a statistical concept of uncertainty in estimates of population parameters (e.g., arithmetic mean, standard deviation) from random samples, due to the quality, quantity, and representativeness of available data as well as the statistical estimation method.
- (2) *Model uncertainty* - uncertainty about a model structure (e.g., exposure equation) or intended use, including the relevance of simplifying assumptions to the endpoint of the risk assessment, the choice of probability distribution to characterize variability, and interpolation or extrapolation beyond the scale used to calibrate a model from empirical data.

- (3) *Scenario uncertainty* - uncertainty regarding missing or incomplete information to fully define exposure. This may include descriptive errors regarding the magnitude and extent of chemical exposure or toxicity, temporal and spatial aggregation errors, incomplete analysis (i.e., missing exposure pathways), and potential mis-specification of the exposed population or exposure unit.

Sources of uncertainty described by these categories are important because they can influence risk management decisions in both point estimate and probabilistic risk assessment. As additional sources of uncertainty are quantified and included in the risk assessment, uncertainty in risk estimates may appear to increase, suggesting there may be little confidence in a risk management decision. This situation may appear to be counterintuitive for those managers who expect confidence to increase as uncertainty is quantified. However, as discussed below and in Chapter 6 (see Section 6.4.2), uncovering and quantifying these sources of uncertainty may help to provide perspective, and make the decisions using the tiered process more transparent. In PRA, there are a variety of methods that can be used to effectively quantify uncertainty as well as communicate confidence in risk estimates (see Chapter 3, Section 3.4; Chapter 6, Section 6.4, and Section 6.5).

Parameter uncertainty may be the most readily recognized source of uncertainty that is quantified in site-specific risk assessments at hazardous waste sites. Parameter uncertainty can occur in each step of the risk assessment process from data collection and evaluation, to the assessment of exposure and toxicity. Sources of parameter uncertainty may include systematic errors or bias in the data collection process, imprecision in the analytical measurements, inferences made from a limited database when that database may or may not be representative of the variable under study, and extrapolation or the use of surrogate measures to represent the parameter of interest.

In the point estimate approach, parameter uncertainty is addressed in a qualitative manner for most variables. For example, the uncertainty section of a point estimate risk assessment document might note that a soil sampling plan yielded a small sample size that may not be representative of overall contaminant concentrations and, as a result, the risk estimate may over- or under-estimate actual risk. Uncertainty in the concentration term is addressed quantitatively to a limited extent in a point estimate approach by using the 95% UCL for the arithmetic mean concentration in both CTE and RME risk estimates; this accounts for uncertainty associated with environmental sampling and site characterization (U.S. EPA, 1992d, 1997f). The 95% UCL is combined in the same risk calculation with various central tendency and high-end point estimates for other exposure factors.

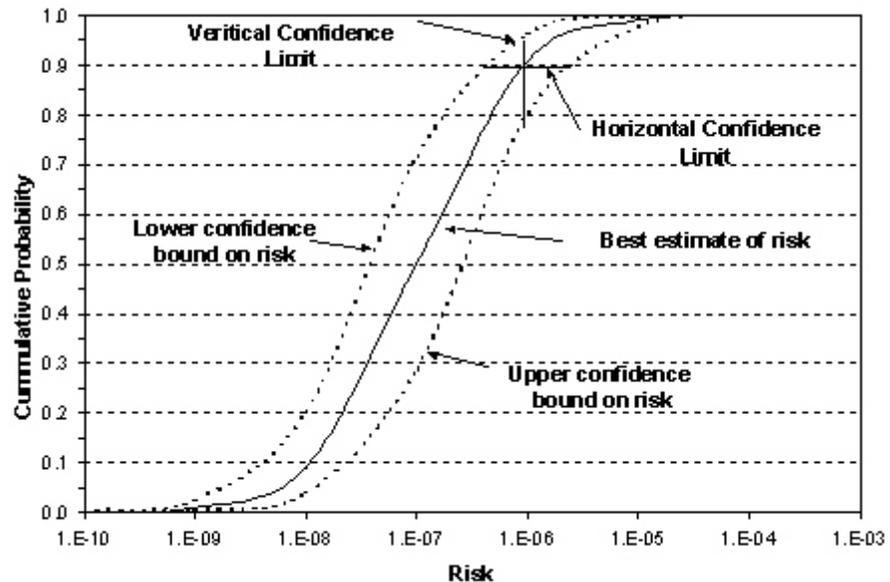
Some examples of the models that EPA uses in the risk assessment process are the equations used to calculate exposure and risk, the linearized multistage model used to estimate cancer dose-response relationships, and media-specific models to estimate contaminant concentrations. All models are simplified, idealized representations of complicated physical or biological processes. Models can be very useful from a regulatory standpoint, as it is generally not possible to adequately monitor long term exposure for populations at contaminated sites. However, models that are too simplified may not adequately represent all aspects of the phenomena they were intended to approximate or may not capture important relationships among input variables. Other sources of model uncertainty can occur when important variables are excluded, interactions between inputs are ignored, or surrogate variables that are different from the variable under study are used.

In most probabilistic assessments, the first step of analysis is usually an analysis of variability in exposure or risk. However, PRA methods may also be used to characterize uncertainty around the best estimate of the exposure or risk distribution. This is done using "2-dimensional" MCA (2-D MCA) (see Appendix D). One convention that has been used to distinguish between probability distribution functions for variability

and uncertainty is to use subscripts "v" and "u" to indicate PDFs that characterize variability (PDF<sub>v</sub>) or uncertainty (PDF<sub>u</sub>). Figure 1-4 shows an example of the results of this type of 2-D MCA. This analysis can provide a quantitative measure of the *confidence in the fraction of the population with a risk exceeding a particular level*; which is sometimes referred to as a *vertical confidence interval* (Figure 1-4). For example, a conclusion based on this type of output might be, "While the best estimate for the variability distribution for risk across the target population indicates that 10% of the individuals exposed under these circumstances have a risk exceeding 1E-06, the uncertainty is such that we can only be reasonably certain (e.g., 95% sure) that no more than 20% of the exposed population has a risk that exceeds 1E-06."

Additionally, the output from a 2-D MCA can provide a quantitative measure of the *confidence in the risk estimate* for a particular fraction of the population; which is sometimes referred to as a *horizontal confidence interval*. This type of output might support the following type of conclusion, "While the best estimate for the variability distribution for risk across the target population indicates that 10% of the individuals exposed under these circumstances have a risk exceeding 1E-06, the uncertainty is such that we can only be reasonably certain (e.g., 95% sure) that the risk for this group of individuals does not exceed 2E-06." The term "confidence interval" is used loosely in this context to convey information about uncertainty; however, it is not the same as a statistical confidence interval that one might obtain by estimating a population parameter from a sample. The vertical and horizontal bars shown in Figure 1-4 represent a range of possible estimates for the percentile given one or more sources of uncertainty that were included in the simulation. If the target audience for this graphic has a greater understanding of statistics, it may be less confusing if alternative phrases are used to describe the results, such as "credible interval" or "probability band".

In general, one should avoid developing input distributions to a PRA model that yield a single risk distribution that intermingles, or represents both variability and uncertainty. By separately characterizing variability and uncertainty, the output from a PRA will be easier to understand and communicate. A number of tools can aid in evaluating the uncertainty in estimated distributions for



**Figure 1-4.** Illustration of "Vertical" and "Horizontal" Confidence Intervals (or limits) on a risk estimate. This type of output can be produced from a 2-D MCA in which probability distributions of uncertainty are introduced into the risk equation. See Chapter 3 and Appendix D for further discussion of 2-D MCA in quantitative uncertainty analysis.

variability. Both simple and very complex approaches have been applied to this problem. Two basic methods for quantifying variability and parameter uncertainty simultaneously are described in Exhibit 1-5. PRAs that use these approaches can provide quantitative estimates of uncertainty in percentiles of the risk distribution based on confidence intervals or credible intervals for one or more parameter estimates. Techniques for characterizing both variability and uncertainty in PRA are discussed in more detail in Chapters 3, 4, 5, and 7, and Appendices A, C, and D.

A common apprehension concerning the utility of PRA is that it may require more information and data than are available to generate credible PDFs. Risk assessors may feel that they can't specify a PDF because they don't have enough information to choose a distribution type, estimate parameters, or evaluate the representativeness to the site population of concern. However, if sufficient information exists to support a meaningful point estimate evaluation (i.e., if some sort of central tendency and upper bound values are available for each input variable), then it is usually possible to perform a screening level, or preliminary 1-D MCA that may provide additional useful information regarding variability. Likewise, an initial two-dimensional analysis may be performed that does not require collection of any new data, but simply characterizes uncertainty in the existing data. The results of such a 2-D MCA can help to identify the main sources of uncertainty in the risk results, and can support decisions to collect more data and/or proceed with additional tiers of analysis in order to improve the assessment. As with a preliminary 1-D MCA, the decision to conduct a more advanced probabilistic analysis does not always result in added data requirements.

#### EXHIBIT 1-5

##### QUANTIFYING VARIABILITY AND UNCERTAINTY

###### 1. Single source of uncertainty

Run multiple one-dimensional Monte Carlo simulations (1-D MCA) in which each simulation uses a different point estimate for a parameter selected from an uncertainty distribution, combined with PDFs for one or more variables. For example, separate simulations can be run in which the mean of the exposure concentration variability distribution is represented by either the 95% lower or upper confidence limit on the mean. A comparison of the output of these simulations would provide a partial characterization of the quantitative impact of uncertainty in the mean exposure concentration on the risk estimate (provided that certain conditions hold; i.e., risk increases with increasing exposure concentration) (see Chapter 3, Section 3.3.1).

###### 2. Multiple sources of uncertainty

Run a single two-dimensional Monte Carlo simulation (2-D MCA), in which separate probability distributions are specified for variability and parameter uncertainty and values from these distributions are randomly selected and used in each iteration of the Monte Carlo simulation (see Appendix D).

Use of probabilistic methods (e.g., MCA) to propagate variability and uncertainty through risk models offers five key advantages over point estimate approaches in addressing uncertainty in risk estimates:

- (1) Probabilistic methods may often provide a more complete and informative characterization of variability in exposure or risk than is usually achievable using point estimate techniques.
- (2) Probabilistic methods can provide a more quantitative expression of the confidence in risk estimates than the point estimate approach.

- (3) Sensitivity analysis methods using PRA may help risk assessors to better identify influential exposure factors.
- (4) Probabilistic methods can account for dependencies between input variables (e.g., body weight and skin surface area).
- (5) Probabilistic methods provide quantitative estimates of the expected value of additional information that might be obtained from data collection efforts (Morgan and Henrion, 1990). The importance of quantifying uncertainty in an *expected value of information* (EVOI) framework is discussed in Appendix D.

Since both point estimate and probabilistic approaches in risk assessment are applied to the same conceptual models (i.e., the same exposure and risk models), uncertainties in the conceptual model are generally addressed in the same manner. If other models are available to explain or characterize a given phenomenon, the risk estimates associated with each of those conceptual models could be compared to determine the sensitivity of the risk to the uncertainty in the choice of a model (see Chapter 2 and Appendix A). For example, when deciding on a contaminant concentration term for tetrachloroethylene in groundwater for a residential exposure assessment 10 years in the future, it would be appropriate to compare and contrast several fate and transport models and their results before deciding on a concentration term.

### **1.2.5 REASONABLE MAXIMUM EXPOSURE AT THE HIGH-END**

Risk management decisions at Superfund sites should be based on an estimate of the risk to a reasonably maximum exposed receptor, considering both current and future land-use conditions. The RME is defined as the highest exposure that is reasonably expected to occur at a site. In general, risks corresponding to the 90<sup>th</sup> to 99.9<sup>th</sup> percentiles of the risk distribution estimated from a PRA are considered plausible high-end risks, and the RME risk should be selected within this range (see Section 1.2.4, Section 1.4.1, and Chapter 7 for further discussion). In comparison with point estimate risk assessments, PRA can provide the entire range of estimated risks as well as the likelihood of values within the range (i.e., the frequency distribution)

As noted in Chapter 7, estimates of risk become more uncertain at very high percentiles (e.g., the 99.9<sup>th</sup>), so results of PRA calculations at these extreme values should be used with caution. Risk frequency distributions toward the 99.9<sup>th</sup> percentile may be numerically unstable due to the uncertainties embedded in the input exposure assumptions. This guidance recommends that a risk manager select the RME in consultation with a risk assessor. One item for discussion should be the numerical stability of the high-end RME risk value (i.e., a stable value on the frequency distribution within the high-end range that could be reproduced in successive Monte Carlo simulations.)

### **1.3 ADVANTAGES AND DISADVANTAGES OF POINT ESTIMATE AND PROBABILISTIC APPROACHES**

As discussed in Chapter 2, a PRA should not be conducted until adequate point estimate calculations have been completed. Once this has been done, the potential benefits of proceeding to a PRA evaluation should be based on an understanding of the potential advantages and limitations in each approach. Potential advantages and disadvantages of point estimate calculations are summarized in Exhibit 1-6 and potential advantages and disadvantages of PRA are listed in Exhibit 1-7.

In general, compared to a point estimate risk assessment, a PRA based on the same state of knowledge may offer a more complete characterization of variability in risk, can provide a quantitative evaluation of uncertainty, and may provide a number of advantages in assessing if and how to proceed to higher levels of analysis. However, there are also some real and perceived disadvantages regarding additional effort on the part of both the risk assessor and the risk manager, and the potential to cause confusion if the effort is not clearly presented.

In general, the key question to consider in deciding whether a PRA should be performed is whether or not the PRA analysis is likely to provide information that will help in the risk management decision making. For some sites, the additional information provided by a PRA will not affect the decision that would have been made with a point estimate approach alone, and a PRA will not be useful. However, when the decision whether or not to take action is not completely clear, PRA may be a valuable tool. The tiered process for PRA (Chapter 2) introduces the concept of scientific management decision points (SMDPs) to guide the complexity of analysis that may be needed for decision making. An SMDP marks a point in the process in which the potential that another analysis may influence the risk management decision is evaluated based on the problem formulation, the information available to define input variables, the results of previous analyses, and the feasibility of a subsequent analysis.

☞ *A point estimate approach is conducted for every risk assessment; a probabilistic analysis may not always be needed.*

#### EXHIBIT 1-6

##### ADVANTAGES AND DISADVANTAGES OF POINT ESTIMATE APPROACH

###### Advantages

- Calculations are simple and do not require any advanced software.
- EPA has established default inputs and methods to help standardize point estimate calculations between sites.
- Useful as a screening method—may allow risk management decisions with no additional work.
- Central tendency and RME estimates of risk provide a semi-quantitative measure of variability.
- Method is easily described and communicated.
- Requires less time to complete; not as resource intensive.

###### Disadvantages

- Computational simplifications may result in deviations from target values.
- Results are often viewed as “the answer”; importance of uncertainty is sometimes lost.
- Information from sensitivity analysis is generally limited to dominant exposure pathways and chemicals of concern; may not highlight the key exposure variables and uncertain parameters.
- Does not provide a measure of the probability that risk exceeds a regulatory level of concern, or the level of confidence in a risk estimate.
- Provides fewer incentives for collecting better or more complete information.

**EXHIBIT 1-7**

**ADVANTAGES AND DISADVANTAGES OF PROBABILISTIC RISK ASSESSMENT**

**Advantages**

- Can make more complete use of available data when defining inputs to the risk equation.
- Can provide a more comprehensive characterization of variability in risk estimates.
- Can provide a more comprehensive characterization of uncertainty in inputs, which may support statements regarding confidence in risk estimates. Communication of uncertainty in the risk assessment can help to build trust among stakeholders.
- Sensitivity analysis can identify the exposure variables, probability models, and model parameters that influence the estimates of risk.
- Puts the risk assessment in a *Value-of-Information* framework (see Appendix D). Can identify data gaps for further evaluation/data collection and can use wider variety of site-specific information.
- Allows available site-specific information to inform the choice of high-end percentile from the risk distribution that corresponds with RME risk.

**Disadvantages**

- Concepts and approaches may be unfamiliar; there is often apprehension regarding added costs and potential for inadvertent error and/or intentional misrepresentation.
- Places more burden on risk assessors to ensure the PRA is done correctly and on managers to understand and make decisions within a range of alternatives.
- May require more time and resources to select and fit probability distributions, and may require greater effort to communicate methodology and results.
- May convey false sense of accuracy when data are sparse.
- Complexities of the PRA approaches may obscure important assumptions or errors in basic exposure or risk models.
- If communication of the more complex PRA is unsuccessful, then it may generate mistrust of the assessment and risk management decisions.

## 1.4 CONDUCTING AN ACCEPTABLE PRA

In 1997, EPA issued a memorandum which contained its policy statement on PRA (U.S. EPA, 1997g). The 1997 EPA Policy Statement is as follows:

It is the policy of the U.S. Environmental Protection Agency that such probabilistic analysis techniques as Monte Carlo analysis, given adequate supporting data and credible assumptions, can be viable statistical tools for analyzing variability and uncertainty in risk assessments. As such, and provided that the conditions described below are met, risk assessments using Monte Carlo analysis or other probabilistic techniques will be evaluated and utilized in a manner that is consistent with other risk assessments submitted to the Agency for review or consideration. It is not the intent of this policy to recommend that probabilistic analysis be conducted for all risk assessments supporting risk management decisions. Such analysis should be a part of a tiered approach to risk assessment that progresses from simpler (e.g., deterministic) to more complex (e.g., probabilistic) analyses as the risk management situation requires. Use of Monte Carlo or other such techniques in risk assessments shall not be cause, *per se*, for rejection of the risk assessment by the Agency. For human health risk assessments, the application of Monte Carlo and other probabilistic techniques has been limited to exposure assessments in the majority of cases. The current policy, Conditions for Acceptance and associated guiding principles are not intended to apply to dose response evaluations for human health risk assessment until this application of probabilistic analysis has been studied further. In the case of ecological risk assessment, however, this policy applies to all aspects including stressor and dose-response assessment.

In support of this policy statement, EPA has outlined eight *conditions for acceptance* (in italics below), and good scientific practice of PRA. A PRA that is submitted to the Agency for review and evaluation should generally comply with each condition in order to ensure that adequate supporting data and credible assumptions are used in the assessment. These conditions are as follows:

- (1) *The purpose and scope of the assessment should be clearly articulated in a "problem formulation" section that includes a full discussion of any highly exposed or highly susceptible subpopulations evaluated (e.g., children, the elderly). The questions the assessment attempts to answer are to be discussed and the assessment endpoints are to be well defined.*
- (2) *The methods used for the analysis (including all models used, all data upon which the assessment is based, and all assumptions that have a significant impact upon the results) are to be documented and easily located in the report. This documentation is to include a discussion of the degree to which the data used are representative of the population under study. Also, this documentation is to include the names of the models and software used to generate the analysis. Sufficient information is to be provided to allow the results of the analysis to be independently reproduced.*

Possible sources of bias inherent in the input distributions should be discussed along with the expected impacts on the resulting risk estimates. For example, if a site-specific study of fish consumption indicated consumption rates are five to ten times higher than other studies from similar

populations, this possible bias or inaccuracy should be discussed in the document. Computer programs should generally be described in sufficient detail to allow the reviewer to understand all aspects of the analysis. Computer code/spreadsheets should provide adequate documentation and annotation.

- (3) *The results of sensitivity analyses are to be presented and discussed in the report. Probabilistic techniques should be applied to the compounds, pathways, and factors of importance to the assessment, as determined by sensitivity analyses or other basic requirements of the assessment.*

Sensitivity analysis is a valuable tool in any tier of a PRA.

- (4) *The presence or absence of moderate to strong correlations or dependencies between the input variables is to be discussed and accounted for in the analysis, along with the effects these have on the output distribution.*
- (5) *Information for each input and output distribution is to be provided in the report. This includes tabular and graphical representations of the distributions (e.g., probability density function and cumulative distribution function plots) that indicate the location of any point estimates of interest (e.g., mean, median, 95<sup>th</sup> percentile). The selection of distributions is to be explained and justified. For both the input and output distributions, variability and uncertainty are to be differentiated where possible.*
- (6) *The numerical stability of the central tendency and the higher end (i.e., tail) of the output distributions are to be presented and discussed.*

As discussed in Section 1.2.5, numerical stability refers to the observed numerical changes in parameters of the output distribution (e.g., median, 95<sup>th</sup> percentile) from a Monte Carlo simulation as the number of iterations increases. Because most risk equations are linear and multiplicative, distributions of risk will generally be right-skewed, and approximate a lognormal distribution. Values in the tails of the distribution typically are less stable than the central tendency, and the rate of convergence for the tails will depend on the form of the risk model, the skewness of the probability distributions selected for input variables and the numerical methods used to simulate probability distributions. Provided that appropriate numerical methods are employed, numerical stability is generally not a concern for most 1-D MCA models, which can be run with a sufficient number iterations in minutes with modern high speed computers; however, it can be an important consideration for more complex simulations, such as with 2-D MCA models.

- (7) *Calculations of exposures and risks using deterministic (e.g., point estimate) methods are to be reported if possible. Providing these values will allow comparisons between the probabilistic analysis and past or screening level risk assessments. Further, deterministic estimates may be used to answer scenario specific questions and to facilitate risk communication. When comparisons are made, it is important to explain the similarities and differences in the underlying data, assumptions, and models.*

If results of PRA calculations differ substantially from point estimate calculations, a risk manager may benefit from understanding the reasons for the differences and the relative strengths of the different approaches. Sometimes, a closer look at uncertainties in the underlying data, assumptions, and

models will lead a risk assessor to revisit parts of the assessment in order to provide a more consistent basis for comparison.

- (8) *Since fixed exposure assumptions (e.g., exposure duration, body weight) are sometimes embedded in the toxicity metrics (e.g., Reference Doses, Reference Concentrations, Cancer risk factors), the exposure estimates from the probabilistic output distribution are to be aligned with the toxicity metric.*

#### **1.4.1 KEY POLICIES FOR APPLYING PRA AT SUPERFUND SITES**

EPA's recommended process for conducting an acceptable PRA generally follows the policy and guiding principles presented above. In addition, this section highlights four key policies for conducting acceptable PRAs at hazardous waste sites.

##### **(1) Follow the Tiered Approach to PRA**

In accordance with the *1997 EPA Policy Statement* (U.S. EPA, 1997g), this guidance recommends using a tiered approach when considering PRA to help with risk management decisions. A tiered approach begins with a relatively simple analysis and progresses stepwise to more complex analyses. The level of complexity should match the site-specific risk assessment objectives and the risk management goals. The tiered approach, with helpful suggestions on risk communication, is presented in Chapter 2. A brief introduction is given below.

The premise for recommending a tiered approach is that there is a balance between the benefits of conducting a more complex analysis, and the cost in terms of additional time, resources, and challenges for risk communication. PRA may require additional resources compared with the point estimate approach, and may not be used routinely for screening level assessment. At more complex hazardous waste sites, PRA may not be warranted if the investment of time and resources is unlikely to provide information on variability and uncertainty in risk that will affect the risk management decision.

This guidance recommends that a point estimate risk assessment be conducted in the first tier after completing the remedial investigation (RI) planning, site scoping, problem formulation, data collection, and the development of a site conceptual model. In general, when site decision making would benefit from additional analysis beyond the point estimate risk assessment, and when the risk manager needs more information to complete the RI/FS process, the risk manager would proceed to higher tiers. Sensitivity analysis should be conducted in each tier to guide decisions regarding data collection and the complexity of the analysis needed to characterize variability and/or uncertainty in risk. Sensitivity analysis can also play an important role in risk communication by supporting decisions to continue characterizing less influential variables with point estimates in higher tiers.

##### **(2) Select the RME Risk from the RME Risk Range (90<sup>th</sup> to 99.9<sup>th</sup> percentile)**

The RME is defined as the highest exposure that is reasonably expected to occur at a site. *Final Guidelines for Exposure Assessment* (EPA, 1992a) states that the "high-end" of exposure for a population occurs between the 90<sup>th</sup> and 99.9<sup>th</sup> percentiles, with the 99.9<sup>th</sup> percentile considered a bounding estimate. Using a point estimate approach, the calculation of the RME risk would be based on high-end input values in combination with average input values. For example, for estimation of risks from the ingestion

of groundwater, default exposure is based on a high-end water intake rate (2 L/day), a high-end exposure frequency and duration (350 days/year for 30 years), and an average body weight (70 kg).

With the probabilistic approach, the calculation of the RME risk would be based on a range of input values, or frequency distributions, including low, average, and high-end values for each of the input exposure factors. For example, for estimation of risks from ingestion of groundwater, exposure would be based on the combination of lognormal distributions for water intake rate, body weight, and exposure duration (each using a specified mean and standard deviation) and a triangular distribution for exposure frequency (using a specified minimum, most likely value, and maximum). As a result, the RME risk would become a probability distribution ranging from low- to high-end values based on varying a combination of input values. In PRA, a recommended starting point for risk management decisions regarding the RME is the 95<sup>th</sup> percentile of the risk distribution (see Chapter 7).

**(3) Use PRA for Dose-Response in Ecological Assessment, not in Human Health Assessment**

Approaches to characterizing variability and uncertainty in toxicological information should reflect both the latest developments in the science of hazard and dose-response evaluation and consistent application of EPA science policy. This statement is consistent with the *1997 EPA Policy Statement* presented in Section 1.4 above (U.S. EPA, 1997g). Probabilistic approaches to ecological dose-response assessment may be explored, as discussed and demonstrated in Chapter 4. This guidance does not develop or evaluate probabilistic approaches for dose-response in human health assessment and, further, *discourages undertaking such activities on a site-by-site basis*. Such activities require contaminant-specific national consensus development and national policy development. Parties wishing to undertake such activities should contact the OERR to explore ways in which they might contribute to a national process for the contaminant of interest to them.

**(4) Prepare a Workplan for EPA Review and Approval**

A workplan should be developed and submitted for review before commencement of a PRA. The workplan should document the combined decisions of the RPM and risk assessor involved in the risk assessment, and positions of the stakeholders. The workplan should address conditions and policies presented in this section of *RAGS Volume 3: Part A*, the software to be used, the exposure routes and models, and the input probability distributions and their basis, including appropriate literature references. The workplan is discussed in more detail in Chapter 2.

A checklist of some of the key considerations to assist in the review of a PRA is provided in Appendix F.

## **1.5 ORGANIZATION OF THE GUIDANCE**

Subsequent chapters of *RAGS Volume 3: Part A* focus on the following topics:

### ***Chapter 2 - The Tiered Approach to PRA***

Chapter 2 includes information regarding organizational issues that may need to be considered by the RPM in developing a PRA. Examples, include: workplans, involvement of the Community Involvement Coordinator (CIC), additional meetings with communities, and review of PRA documents.

Chapter 2 also presents the tiered approach in full detail. The approach begins with RI planning, scoping, problem formulation, and data collection. Tier 1 entails a point estimate risk assessment and sensitivity analysis. Tier 2 proceeds with additional data collection, a MCA to characterize variability and/or uncertainty, and a more in-depth sensitivity analysis. More advanced techniques are used in Tier 3 to simultaneously characterize variability and uncertainty. The endpoint of the tiered approach is to provide information that helps risk managers complete the RI/FS process.

### ***Chapter 3 - Probabilistic Human Health Risk Assessment***

Chapter 3 provides a discussion of how PRA approaches may be utilized in human health risk assessment. Probabilistic approaches focus on the exposure assessment, and an example is included to illustrate the application of the tiered approach to a human health risk assessment.

### ***Chapter 4 - Probabilistic Ecological Risk Assessment***

Chapter 4 provides a discussion of how PRA approaches may be utilized in ecological risk assessment. This includes a discussion of basic tactics, such as how to decide if, and when, a PRA is needed, along with technical discussions and examples of how to model variability and/or uncertainty in exposure, toxicity, and risk (characterized both as hazard quotients and responses) for different types of ecological receptors, both within and between species. The chapter also provides a discussion of how the results of an ecological PRA can be used in risk management decision making, and provides guidelines for planning and performing an ecological PRA.

### ***Chapter 5 - PRA and Preliminary Remediation Goals (PRGs)***

This chapter provides a discussion about issues associated with deriving PRGs from both point estimate risk assessment and PRA. Issues and limitations associated with back calculation are highlighted, along with an explanation and recommendation regarding the iterative forward calculations.

### ***Chapter 6 - Communicating Risks and Uncertainties in PRA***

Chapter 6 provides a basic overview of the current Superfund guidance on communicating with the public. With this as a basis, the chapter provides specific information regarding continuous involvement of stakeholders in the PRA process, various tools that may be useful in communicating the principles of PRA, organizational issues regarding planning of communication strategies, and examples of procedures that may be helpful at individual sites. This chapter also provides references to various documents on current approaches for communicating risk to the public.

### ***Chapter 7 - Role of PRA in Decision Making***

This chapter provides guidance on how to interpret the results of a PRA to determine if an unacceptable risk is present, and criteria to consider when moving from a risk-based PRG to a remedial goal.

### ***Appendix A - Sensitivity Analysis***

Important information from PRA includes the results of sensitivity analysis. This appendix outlines the methodology and interpretation of statistical methods used to conduct sensitivity analysis with point estimate and probabilistic models.

### ***Appendix B - Selecting and Fitting Distributions***

One of the more challenging aspects of PRA is choosing appropriate probability distributions to represent variability and uncertainty in the input variables. This appendix presents a process for selecting and fitting distributions to data, including hypothesizing families of distributions, parameter estimation techniques, and goodness-of-fit tests.

### ***Appendix C - Exposure Point Concentration (EPC)***

An important variable in most risk assessments is the concentration term. This appendix presents the basic principles of the EPC, and different methods for quantifying both variability and parameter uncertainty in the EPC.

### ***Appendix D - Advanced PRA Models***

Sometimes a more complex modeling approach can be used to improve the representativeness of the probabilistic risk estimates. These approaches are generally anticipated to be applied in Tier 3 of the tiered approach. Examples include the use of Microexposure Event modeling, geostatistics, and Bayesian Monte Carlo analysis.

### ***Appendix E - Definitions***

A list of definitions is provided at the beginning of each chapter. This appendix provides a compilation of all definitions presented in the guidance.

### ***Appendix F - Generic Checklist***

After a PRA has been submitted to the Agency, an efficient process is needed to evaluate the accuracy and clarity of the results. This appendix suggests a series of elements of the review process that can be adopted to structure the review of PRAs for both human health and ecological risk assessment.

### ***Appendix G - Frequently Asked Questions (FAQ) about PRA***

Risk assessors and risk managers who read *RAGS Volume 3: Part A* will find that probabilistic risk assessment covers a wide variety of topics ranging from statistical theory to practical applications and policy decisions. U.S. EPA OERR plans to maintain and periodically update a list of frequently asked questions and responses on an EPA Superfund web page at <http://www.epa.gov/superfund/index.htm>. This appendix provides a preliminary list of anticipated questions.

## *Appendix H - Index*

This index includes keywords and concepts used throughout this guidance document. They are listed alphabetically with numbers indicating the appropriate chapter and page number(s) within each chapter. Commas separate page numbers within a chapter or appendix, while semi-colons separate chapters and appendices. For example: probability density function, 1-5, 6-8; 4-3, 10-12; C-1, 8-10. This would indicate Chapter 1, page 5, and pages 6-8; Chapter 4, page 3, and pages 10-12; Appendix C, page 1 and pages 8-10.

### **1.6 NEXT STEPS FOR PRA IMPLEMENTATION**

This guidance has presented the current principles, including the tiered approach, and examples to aid in conducting acceptable PRAs at Superfund sites. Policies and practices will change over time as scientific advances continue in the future. The PRA Workgroup intends to keep current and provide new information on EPA Superfund web page at <http://www.epa.gov/superfund/index.htm>. EPA expects to make the following PRA support items available on-line in the near future:

- *RAGS Volume 3: Part B*: A workbook that serves as a companion to *RAGS Volume 3: Part A*; it will include case studies and examples in PRA.
- *Guidance on Probability Distributions*: Documents and/or spreadsheets to aid in selecting and fitting probability distributions for input variables.
- *Guidance on Data Representativeness*: A ranking methodology to evaluate data representativeness for various exposure scenarios.
- *Hands-On Training*: Basic MCA training materials, and limited computer hands-on training sessions available to Regional EPA and State staff.
- *Access to PRA Workgroup*: A workgroup to provide support on PRA to EPA regional risk assessors.
- *FAQs*: A list of Frequently Asked Questions (FAQs) about PRA and responses from the PRA Workgroup, maintained and periodically updated on-line.

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