

memorandum

DATE March 31, 1995

REPLY TO
ATTN OF Office of Environmental Policy and Assistance (EH-413): Bascietto:6-7919

SUBJECT Baseline Risk Assessment: Toxicity and Exposure Assessment and Risk Characterization

TO: Distribution

The purpose of this memorandum is to provide Department of Energy (DOE) Program Offices and Field Organizations with a copy of an environmental guidance document entitled: "*CERCLA Baseline Risk Assessment Manual for Toxicity and Exposure Assessment and Risk Characterization.*" This document is directed primarily to DOE and DOE contractor personnel responsible for planning, managing and communicating risk assessment information for environmental restoration projects performed under the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Notwithstanding, the attached document provides information to all personnel interested in gaining both-an understanding of selected baseline risk assessment topics and a perspective on the evolving nature of risk assessment guidance in the CERCLA program.

Over recent years the U.S. Environmental Protection Agency (EPA) has developed a considerable body of guidance about developing baseline risk assessments for uncontrolled hazardous waste sites. But the manner in which EPA's guidance is interpreted and applied can have a great impact on the risk estimates obtained and, in turn, on the remedial option selected to reduce those risks. In general, lower baseline risk estimates should necessitate less costly remedial options than will higher risks. This document was written to (1) guide project personnel through the process of interpreting EPA guidance and (2) help project personnel to discuss EPA guidance with regulators, decision makers, and stakeholder as it relates to conditions at a particular DOE environmental restoration site.

This environmental guidance document provides detailed insight into the science policy issues underlying the CERCLA baseline risk assessment process as it is implemented today by EPA, and serves as a continuing reference work that can be consulted for information on the baseline risk assessment process in the DOE environmental restoration program. To the extent possible, given the evolving nature of risk assessment guidance in general, the document attempts to summarize the Agency's up-to-date national guidance to EPA regional offices on selected CERCLA baseline risk assessment topics, and, through an historical perspective, examines how certain guidance has changed over time. This perspective facilitates a discussion of the pros, cons, weaknesses, uncertainties, and policy areas where more than one interpretation may be acceptable for each of the topics covered. Additionally, the document identifies reference materials for risk analysts who may desire a more in-depth understanding of a particular topic. A primary intent of this guidance is to assist in facilitating a thoughtful discourse on baseline risk assessment issues among the Department's environmental restoration project managers and their regulators.

A earlier draft of the attached document, entitled: "CERCLA Baseline Risk Assessment Issues" was circulated within DOE headquarters field elements for review and comment. EH-413 endeavored to ensure that the DOE perspective, and in particular the environmental restoration program CERCLA experience, has been accurately represented. To that end, the draft manual has been improved through the incorporation of the comments received from a select group of DOE headquarters and Field Organization representatives. The comments received by EH-413 reflected substantial DOE experience in planning, managing and communicating CERCLA baseline risk assessments.

Questions concerning the CERCLA baseline risk assessment guidance topics covered, or other comments on the information contained in the attached document, may be directed to John Bascietto of my staff by calling (202) 586-7917, fax to (202) 586-3915 and electronic mail at Internet address john.bascietto@hq.doe.gov.



Thomas T. Traceski
Director, RCRA/CERCLA Division
Office of Environmental Policy and Assistance

Attachment

CERCLA BASELINE RISK ASSESSMENT

Reference Manual

***for
Toxicity & Exposure Assessment and Risk Characterization***



MARCH 1995

Prepared by

**U.S. DEPARTMENT OF ENERGY
OFFICE OF ENVIRONMENTAL POLICY & ASSISTANCE
(formerly the Office of Environmental Guidance)
RCRA/CERCLA DIVISION
(EH-413)
Washington, D.C.**

Technical support by

**Energetic, Inc.
Columbia, MD**

ACKNOWLEDGEMENTS

This document was developed by the Department of Energy (DOE) Office of Environmental Policy and Assistance, RCRA/CERCLA Division (EH-413), with technical support provided by Energetic, Inc. Argonne National Laboratory provided a technical review of Chapter 6, "Radiation Risk Assessment." The following individuals provided technical review and invaluable perspectives on DOE experience with regulator oversight of CERCLA baseline risk assessments:

Steve Golian, Office of Environmental Activities, EM-22

Mildred Ierre, Environmental Restoration Div., Oak Ridge Operations Office

Kelly Kelkenberg, Regulatory Integration Div., EM-431

Steve Miller, Office of General Counsel, GC-51

Tish O'Connor, Office of Environmental Activities, EM-22

Melanie Pearson, Environmental Compliance Div., EH-411

Bruce Thatcher, Environmental Restoration Div., Rocky Flats Field Office

Wade Whittaker, Environmental Compliance Div., Savannah River Operations Office

Table of Contents

Chapter 1: Introduction	1-1
1.1 Background	1-1
1.2 Baseline Risk Assessment: an Overview	1-2
1.2.1 Introduction	1-2
1.2.2 Data Collection and Evaluation	1-2
1.2.3 Exposure Assessment	1-4
1.2.4 Toxicity Assessment	1-5
1.2.5 Risk Characterization	1-7
1.3 How to Use This Document	1-11
1.4 References	1-12
Chapter 2: Guide to Issue Discussions	2-1
2.1 Introduction	2-1
2.2 Issues Pertaining to Exposure Assessment	2-1
2.2.1 Exposure and Dose	2-3
Issue 1: Exposure/Dose Terminology	2-3
Issue 2: Exposure/Dose Calculations	2-4
Regulator Dialogue	2-4
2.2.2 Estimation of Average and Upper End Risk	2-4
Issue 1: Risk Descriptors	2-4
Issue 2: Professional Judgement	2-4
Regulator Dialogue	2-5
2.2.3 Radiation Risk Assessment	2-5
Issue 1: Exposure Calculations	2-5
Issue 2: Radionuclide Progeny	2-5
Regulator Dialogue	2-5
2.2.4 Institutional Controls	2-5
Issue 1: Evaluation of Institutional Controls	2-5
Issue 2: Exposure Scenario Development	2-6
Regulator Dialogue	2-6
2.2.5 Site-Specific Data Versus Default Factors	2-6



Issue 1: Use of Site-Specific Data	2-6
Issue 2: Use of Default Factors	2-6
Regulator Dialogue	2-6
2.2.6 Data Gaps, Uncertainty, and Professional Judgement	2-7
Issue 1: Sources of Uncertainty	2-7
Issue 2: Impact of Data Gaps on Risk Estimate	2-7
Issue 3: Means to Address Uncertainties	2-7
Regulator Dialogue	2-7
2.3 Issues Pertaining to Toxicity Assessment	2-7
2.3.1 Noncancer Health Endpoints	2-8
Issue 1: Alternative Toxicity Values	2-8
Issue 2: Alternative Toxicity Study Requirements	2-8
Regulator Dialogue	2-9
2.3.2 Data Gaps, Uncertainty, and Professional Judgement	2-9
Issue 1: Sources of Uncertainty	2-9
Issue 2: Impact of Uncertainty on Risk Estimates	2-9
Issue 3: Means to Address Uncertainty	2-9
Regulator Dialogue	2-9
2.4 Issues Pertaining to Risk Characterization	2-9
2.4.1 Chemical Mixtures	2-10
Issue 1: Dose Additivity	2-10
Issue 2: Impacts of Summing HQs and Slope Factors	2-10
Regulator Dialogue	2-11
2.4.2 Data Gaps, Uncertainty, and Professional Judgement	2-11
Issue 1: Sources of Uncertainty	2-11
Issue 2: Impact of Uncertainty on Risk Estimates	2-11
Issue 3: Means to Address Uncertainty	2-11
Regulator Dialogue	2-12
2.5 Conclusion	2-12
2.6 References	2-24
Chapter 3: Exposure and Dose	3-1
3.1 Introduction	3-1
3.2 Discussion of Exposure and Dose in Statutes, Regulations, and Guidelines	3-1



3.2.1 Statutes and Regulations	3-1
3.2.2 Guidelines	3-2
Guidelines for Estimating Exposures	3-2
Superfund Public Health Evaluation Manual (SPHEM)	3-2
Superfund Exposure Assessment Manual (SEAM)	3-3
The Exposure Factors Handbook (EFH)	3-3
EPA Region I Supplemental Guidance	3-3
Risk Assessment Guidance for Superfund, Volume I (RAGS)	3-3
Exposure Assessment Methods Handbook (EAMH)	3-4
Dermal Exposure Assessment: Principles and Applications (DEAPA)	3-5
Guidelines for Exposure Assessment	3-5
3.3 Issues and Regulator Dialogue	3-6
3.3.1 Exposure/Dose Issues	3-6
Semantic Ambiguities in Exposure/Dose Terminology	3-6
Inconsistent Exposure/Dose Calculations	3-7
3.3.2 Regulator Dialogue	3-8
3.4 References	3-9
Chapter 4: Estimation of Average and Upper-End Risk	4-1
4.1 Introduction	4-1
4.2 Discussion of Estimation of Average and Upper-End Risk in Statutes, Regulations, and Guidelines	4-2
4.2.1 Statutes and Regulations	4-2
Superfund Public Health Evaluation Manual (SPHEM)	4-2
Superfund Exposure Assessment Manual (SEAM)	4-3
4.2.3 Overcoming Initial Guidance Conceptual Framework Limitations	4-4
EPA Regional Guidance	4-5
EPA Headquarters Guidance	4-6
4.2.4 Further Concerns with Superfund Exposure Assessment Guideline Conceptual Framework	4-7
Creation of an EPA Risk Assessment Intra-Agency Group in March of 1990	4-7
Creation of EPA Superfund 30-Day Task Force	4-7
4.2.5 Addressing Exposure Assessment Guideline Conceptual Framework Concerns	4-7
Guidance for Risk Assessment	4-7



Supplemental Guidance to RAGS: Calculating the Concentration Term	4-8
Guidelines for Exposure Assessment	4-8
An SAB Report: Superfund Site Health Risk Assessment Guidelines	4-9
4.3 Issues and Regulator Dialogue	4-9
4.3.1 Average and Upper-End Risk Issues	4-9
Concept of Reasonableness	4-11
Use of Professional Judgement	4-12
4.3.2 Regulator Dialogue	4-12
4.4 References	4-13
Chapter 5: Chemical Mixtures	5-1
5.1 Introduction	5-1
5.2 Discussion of Chemical Mixtures in EPA Guidelines	5-2
5.2.1 Guidelines for the Health Risk Assessment of Chemical Mixtures	5-2
5.2.2 Guidelines for Estimating Exposures	5-3
5.2.3 Superfund Public Health Evaluation Manual (SPHEM)	5-3
5.2.4 Risk Assessment Guidance for Superfund, Volume I (RAGS)	5-4
5.2.5 Guidelines for Exposure Assessment	5-6
5.2.6 An SAB Report: Superfund Site Health Risk Assessment Guidelines	5-6
5.3 Issues and Regulator Dialogue	5-7
5.3.1 Chemical Mixture Issues	5-7
Dose Additivity Can Lead to Errors If Synergistic or Antagonistic Interactions Occur	
.....	5-8
Summing HQs Treats All RfDs Equally	5-9
Cancer-causing Substances are Treated Equally When Summing Slope Factors	
.....	5-10
Upper 95th Percentile Estimates of Potency Are Not Strictly Additive	5-10
5.3.2 Regulator Dialogue	5-10
5.4 References	5-11
Chapter 6: Radiation Risk Assessment	6-1
6.1 Introduction	6-1
6.2 Discussion of Radiation Risk Assessment in Statutes and Regulations	6-2
6.2.1 Statutory and Regulatory Radiation Risk Assessment Framework	6-2



6.3 Exposure	6-2
6.3.1 Exposure Pathways	6-2
6.3.2 Exposure Assessment	6-3
6.3.3 Radiation Dosimetry	6-3
6.4 Toxicity	6-4
6.4.1 Toxicity Assessment	6-4
6.4.2 Radiation Health Effects in Humans	6-6
6.5 Risk	6-6
6.5.1 Cancer Risks	6-6
6.5.2 Genetic Risks	6-6
6.5.3 Developmental Risks	6-7
6.5.4 Radiation Risk Calculation Methodology	6-7
Internal Exposure	6-7
External Exposure	6-8
6.6 Radiation Units Conversion	6-9
6.6.1 SI Units	6-9
6.6.2 Conversion Factors	6-9
6.7 Regulator Dialogue	6-10
6.8 References	6-10
Chapter 7: Noncancer Health Endpoints	7-1
7.1 Introduction	7-1
7.2 Discussion of Noncancer Health Endpoints in Statutes, Regulations, and Guidelines	7-1
7.2.1 Statutory and Regulatory Noncancer Toxicity Assessment Framework	7-1
7.2.2 General Guidance for Noncancer Toxicity Assessment	7-2
Superfund Public Health Evaluation Manual (SPHEM)	7-2
Risk Assessment Guidance for Superfund (RAGS), Volume 1: Human Health Evaluation Manual	7-2
7.2.3 Guidelines for Reproductive Toxicity Assessments	7-4
Proposed Guidelines for Assessing Female Reproductive Risk	7-5
Proposed Guidelines for Assessing Male Reproductive Risk	7-6
7.2.4 Guidelines for Developmental Toxicity Assessments	7-7
Guidelines for the Health Assessment of Suspect Developmental Toxicants	7-7
Guidelines for Developmental Toxicity Risk Assessment	7-8



7.3 Issues and Regulator Dialogue	7-10
7.3.1 Noncancer Health Endpoint Issues	7-10
Alternative Toxicity Values Can Be Presented in the Risk Assessment	7-11
Appropriate Study Design	7-11
Selection and Interpretation of Toxicity Endpoints	7-12
7.3.2 Regulator Dialogue	7-12
7.4 References	7-13
Chapter 8: Institutional Controls in Baseline Risk Assessments	8-1
8.1 Introduction	8-1
8.2 Discussion of Institutional Controls in Statutes, Regulations, and Guidelines	8-1
8.2.1 Statutes	8-1
8.2.2 Regulations	8-1
8.2.3 Guidelines	8-2
8.3 Issues and Regulator Dialogue	8-3
8.3.1 Institutional Controls Issues	8-3
Evaluation of Institutional Controls	8-3
Institutional Controls in Exposure Scenario Development	8-3
Institutional Controls in Land Use Determination	8-4
8.3.2 Regulator Dialogue	8-5
8.4 References	8-5
Chapter 9: Site-Specific Data Versus Default Factors	9-1
9.1 Introduction	9-1
9.2 Discussion of Site-Specific Data Versus Default Factors in Statutes, Regulations, and Guidelines	9-1
9.2.1 Statutes and Regulations	9-1
9.2.2 Guidelines	9-1
Guidelines for Estimating Exposures	9-1
Superfund Public Health Evaluation Manual (SPHEM)	9-2
Superfund Exposure Assessment Manual (SEAM)	9-3
Risk Assessment Guidance for Superfund, Volume I (RAGS)	9-3
The Exposure Factors Handbook (EFH)	9-4
Research to Improve Health Risk Assessments (RIHRA)	9-4



Supplemental Guidance to RAGS: EPA Region I Guidance	9-5
Supplemental Guidance to RAGS: Standard Default Exposure Factors	9-5
EPA Superfund 30-Day Task Force	9-5
Exposure Assessment Methods Handbook (EAMH)	9-6
An SAB Report: Superfund Site Health Risk Assessment Guidelines	9-6
9.3 Issues and Regulator Dialogue	9-6
9.3.1 Site-Specific Data versus Default Factors Issues	9-6
Limited Site-Specific Data Warrants the Use of Conservative Default Factors	9-7
Site-Specific Data are Preferred to Standard Default Factors	9-8
9.3.2 Regulator Dialogue	9-8
9.4 References	9-9
Chapter 10: Data Gaps, Uncertainty, and Professional Judgement	10-1
10.1 Introduction	10-1
10.2 Discussion of Data Gaps, Uncertainty, and Professional Judgement in Statutes, Regulations and Guidelines	10-2
10.2.1 Statutes and Regulations	10-2
10.2.2 Guidelines	10-2
Guidelines for Estimating Exposures	10-2
Superfund Public Health Evaluation Manual (SPHEM)	10-3
Superfund Exposure Assessment Manual (SEAM)	10-3
EPA Region I Supplemental Guidance	10-4
The Exposure Factors Handbook (EFH)	10-4
Risk Assessment Guidance for Superfund, Volume I (RAGS)	10-5
Guidance for Data Useability in Risk Assessment (GDURA)	10-6
Supplemental Guidance to RAGS: Standard Default Exposure Factors	10-7
Exposure Assessment Methods Handbook (EAMH)	10-7
Guidance for Risk Assessment	10-8
Supplemental Guidance to RAGS: Calculating the Concentration Term	10-8
Guidelines for Exposure Assessment	10-9
10.3 Issues and Regulator Dialogue	10-10
10.3.1 Data Gaps, Uncertainty, and Professional Judgement Issues	10-10
Exposure Assumptions and Toxicity Values are Great Sources of Uncertainty	10-10
Uncertainties Tend to Overestimate Risk	10-11

Limited Prescribed Protocols to Address Uncertainty 10-13
Use of Professional Judgement 10-13
10.3.2 Regulator Dialogue 10-13
10.4 References 10-14

Appendix A: Annotated Bibliography

Appendix B: Land Use in the CERCLA Remedy Selection Process

Appendix C: EPA Risk Characterization Program



List of Figures

Figure 1.1:	RI/FS Process	1-3
Figure 2.1:	Correspondence Between BRA Components and Chapters in This Guidance	2-2
Figure 2.2:	Issues Pertaining to Exposure Assessment	2-3
Figure 2.3:	Issues Pertaining to Toxicity Assessment	2-8
Figure 2.4:	Issues Pertaining to Risk Characterization	2-10
Figure 7.1	Benchmark Dose Approach	7-10



List of Tables

Table 1.1:	EPA Weight-of-Evidence Classification System for Carcinogenicity	1-7
Table 2.1:	Guide to Issues and Source Documents	2-13
Table 10.1:	Typical Sources of Uncertainty in CERCLA Risk Assessments	10-11



Chapter 1: Introduction

1.1 Background

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA, 1980) (CERCLA or Superfund) was enacted to provide a program for identifying and responding to releases of hazardous substances into the environment. The Superfund Amendments and Reauthorization Act (SARA, 1986) was enacted to strengthen CERCLA by requiring that site clean-ups be permanent, and that they use treatments that significantly reduce the volume, toxicity, or mobility of hazardous pollutants. The National Oil and Hazardous Substances Pollution Contingency Plan (NCP) (USEPA, 1985; USEPA, 1990) implements the CERCLA statute, presenting a process for (1) identifying and prioritizing sites requiring remediation and (2) assessing the extent of remedial action required at each site. The process includes performing two studies: a Remedial Investigation (RI) to evaluate the nature, extent, and expected consequences of site contamination, and a Feasibility Study (FS) to select an appropriate remedial alternative adequate to reduce such risks to acceptable levels. An integral part of the RI is the evaluation of human health risks posed by hazardous substance releases. This risk evaluation serves a number of purposes within the overall context of the RI/FS process, the most essential of which is to provide an understanding of “baseline” risks posed by a given site. Baseline risks are those risks that would exist if no remediation or institutional controls are applied at a site. Thus, the baseline risk assessment (BRA) provides the foundation from which DOE risk assessors can determine the most appropriate options for remediation.

Over recent years the U.S. Environmental Protection Agency (EPA) has developed a considerable body of guidance about developing baseline risk assessments for uncontrolled hazardous waste sites. But the manner in which EPA’s BRA guidance is interpreted and applied can have a great impact on the risk estimates obtained and, in turn, on the remedial option selected to reduce those risks. In general, lower baseline risk estimates should necessitate less costly remedial options than will higher risks. This document was written to (1) guide risk assessors through the process of interpreting EPA BRA policy and (2) help risk assessors to discuss EPA policy with regulators, decision makers, and Stakeholders as it relates to conditions at a particular DOE site.

This guidance provides detailed insight into the science policy issues underlying the CERCLA baseline risk assessment process as it is implemented today by EPA. It also provides the current EPA position on each issue and, through the historical perspective, explains how/why this position has changed over time. This guidance outlines the pros, cons, weaknesses uncertainties, and policy areas where more than one interpretation may be acceptable for each science policy issue. It identifies reference materials for each issue to provide risk analysts with further understanding of these issues, enabling them to both analyze their relevance and to intelligently discuss them with regulators.

The following discussion presents an overview of the CERCLA baseline risk assessment process. Introduction of the analytical components of a risk assessment will provide the framework for subsequent discussion of relevant issues. The risk assessment section will be followed by a discussion of the statutory and regulatory requirements for and key guidance related to the baseline risk assessment process. The final section of this chapter explains the structure of the remainder of this guidance document.



1.2 Baseline Risk Assessment: an Overview

1.2.1 Introduction

Figure 1.1 broadly outlines the major elements of a site assessment and remediation process and shows how these elements relate to each other. Site information development activities are conducted to make an initial evaluation of the severity of contamination at the site and to guide subsequent activities, including data gathering for the baseline risk assessment. The four steps of a baseline risk assessment are data collection and evaluation, exposure assessment, toxicity assessment and risk characterization. The results of the baseline risk assessment provide a basis for selecting an appropriate remedial option for subsequent implementation at the site. Each component of the overall process is interdependent on the others in that, if information is lacking or of poor quality in one of the components, then the entire process will suffer and produce results with higher uncertainty.

This document assumes that data collection and evaluation have already been performed, and issues related to that topic are not included herein (for completeness in this overview, however, a brief summary of the data collection and evaluation process is provided below). Subsequent chapters of this guidance focus on the three remaining components of the BRA process: exposure assessment, toxicity assessment, and risk characterization. The information for this section was obtained from the Risk Assessment Guidance for Superfund (RAGS) (USEPA, 1989).

1.2.2 Data Collection and Evaluation

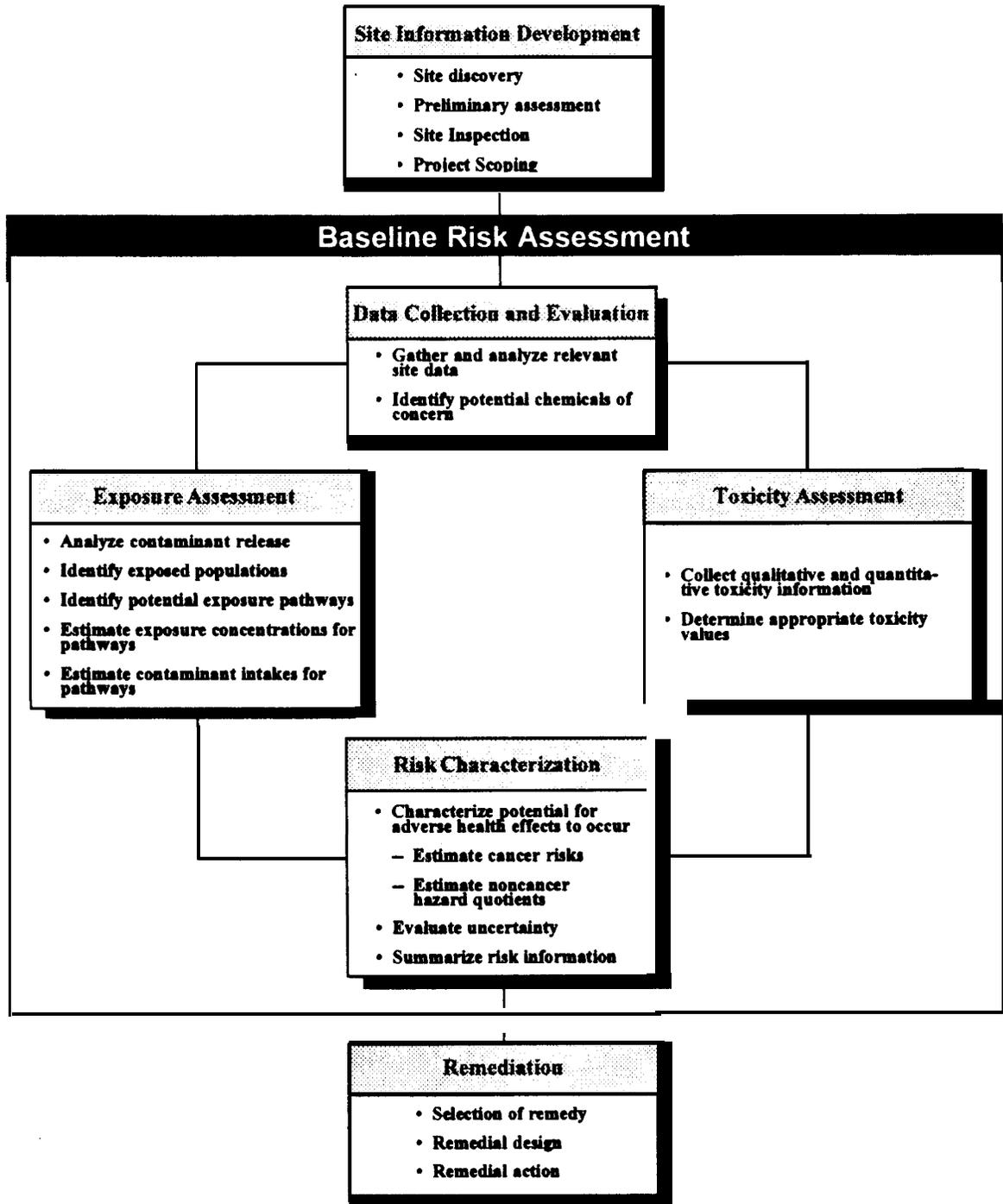
Data collection and evaluation, the first component of a baseline risk assessment consists of gathering and analyzing relevant site data and identifying potential chemicals of concern. The types of data essential for the baseline risk assessment are (USEPA, 1989) as follows

- contaminant identities,
- contaminant concentrations in the key sources and media of interest;
- characteristics of sources, especially information related to release potential; and
- characteristics of the environmental setting that may affect the fate, transport, and persistence of the contaminants.

The risk assessor must identify data needs early in the RI/FS process so that the appropriate samples can be incorporated into a sampling and analysis plan. To assess their data needs, risk assessors must have a preliminary understanding of the current and future contaminant sources, fate, and exposure routes. The risk assessor **must** also have a preliminary idea as to what predictive model(s) may be used in the risk assessment. Model parameters that require site-specific data should be addressed in the sampling and analysis plan. The sampling and analysis plan must also include the appropriate number and placement of background samples, along with blank samples.



Figure 1.1
RIFS Process



Source: Adapted from USEPA (1989)



Once collected, site data should be separated by medium (e.g., soil, water, air) and then evaluated. The evaluation should include analysis of the sampling and analytical method(s) employed and the quality of the data with respect to quantification limits, QA/QC measures, etc. After the above steps have been completed a tentative list of compounds upon which subsequent evaluations will focus can be established, and a corresponding data set can be chosen to be used in the risk assessment.

1.2.3 Exposure Assessment

Exposure assessment is the second component of a baseline risk assessment. The objective of the exposure assessment is to estimate the type and magnitude of human exposures to the chemicals of potential concern that are present at or migrating from a site. The exposure assessment process begins after the chemical concentration and location data have been collected and validated and the chemicals of potential concern have been selected. The results of the exposure assessment are combined with chemical-specific toxicity information to characterize potential risks.

Exposure, as currently in use, is defined as the contact of a chemical or biological agent with the outer boundary of an organism (USEPA, 1992). The magnitude of exposure is determined by measuring or estimating the amount of an agent available at the visible exterior of a person (i.e., the skin, mouth, nostrils) during a specified time period. Exposure assessment is the determination or estimation (qualitative or quantitative) of the route, frequency, duration, and magnitude of exposure. Exposure assessments may consider past, present, and future exposures, using varying assessment techniques. Generally, Superfund exposure assessments are concerned with current and future exposures.

The exposure assessment process consists primarily of three steps: characterizing exposure setting, identifying exposure pathways, and quantifying exposure. These three steps are described below.

Step 1: Characterization of exposure setting. Important elements of the exposure setting include the physical features of the site and pertinent aspects of the populations on and near the site. More specifically, exposure setting characteristics include climate and weather conditions, vegetation, ground-water hydrology, surface water identification, soil characteristics and population characteristics such as location relative to the site, human activity patterns, and the location of any sensitive subpopulations.

Step 2: Identification of exposure pathways. Exposure pathways are based on the types and location of chemicals present at the site, the sources and release mechanisms of these chemicals, the likely environmental transport and fate of these chemicals, and the location and activities of populations that may be exposed. For each exposure pathway, exposure points and routes of exposure are identified.

Step 3: Quantification of exposure concentrations. This step involves three stages. During the first stage, the exposure assessor determines the concentration of chemicals that will be contacted, the frequency of the contacts, and the duration of each contact. Monitoring data combined with chemical fate and transport models are used to estimate the exposure concentrations. Both current and future exposure concentrations are estimated. The assessor also calculates chemical intakes,



or “exposure estimates.” This done for each exposure pathway identified in Step 2. Chemical intakes are expressed in terms of the mass of the contaminant in contact with the body per unit body weight per unit time. After intakes have been estimated, they are organized by grouping all applicable exposure pathways for each exposed population. Sources of uncertainty in the exposure estimates must be evaluated because this may affect decisions regarding the degree of remediation necessary at the site. Actions at Superfund sites should be based on the level of exposure reasonably expected to occur under both current and future land use conditions.

1.2.4 Toxicity Assessment

Toxicity assessment is the third component of a baseline risk assessment. During a toxicity assessment, risk assessors establish whether a substance can potentially produce an adverse effect (“hazard identification”), and quantify the dose/response relationship (“dose/response evaluation”). Hazard identification establishes whether exposure to an agent can cause an increase in the incidence of a particular adverse health-effect (e.g., cancer, birth defects) and whether the adverse health effect is likely to occur in humans. During the dose/response evaluation, assessors evaluate the toxicity information and quantitatively characterize the relationship between the dose of the contaminant or amount of exposure received by people or animals and the incidence of adverse health effects in the exposed population. Toxicity values are derived from the dose/response evaluation and are used in the next step (risk characterization) to estimate risks at different exposure levels.

The first part of the hazard identification process involves the collection of toxicological information. Assessors collect data from a variety of sources, including epidemiologic studies, clinical studies, and animal experiments. Information may also be available from supporting studies such as *in vitro* experiments. The most convincing evidence of human risk derives from epidemiological studies showing an association between an agent and a disease. Human toxicity studies are given first priority in the dose-response assessment if they are available, and animal studies are used as supportive evidence. Adequate human studies are usually not available; therefore, animal studies are most often used.

Metabolic and pharmacokinetic studies, cell cultures, and structure-activity relationship studies are used to support conclusions about the likelihood of occurrence of adverse health effects in humans. Metabolic and pharmacokinetic studies may provide insights into the mechanism of action of a particular compound exhibiting a toxic effect. Studies using cell cultures or microorganisms may be used to estimate a compound’s potential for biological activity. Structure-activity studies may predict toxicologic activity based on analysis of chemical structure.

EPA recommends that risk assessors use the Integrated Risk Information System (IRIS) as the primary source for toxicity data. IRIS contains only those reference doses (RfDs) and cancer slope factors that have been verified by EPA experts. The Health Effects Assessment Summary Table (HEAST) (USEPA, 1994) presents toxicity information and values for which Health Effects Assessments (HEAs), Health and Environmental Effects Profiles (HEEPs), Health Assessment Documents (HADs), or Ambient Air Quality Criteria Documents (AAQCDs) have been prepared. HEAST summarizes interim and verified RfDs and slope factors, and refers risk assessors to the most current sources of supporting toxicity information. HEAST is a good source to supplement IRIS.



EPA developed the reference dose to express, within an order of magnitude, daily exposure levels for specific noncarcinogenic chemical substances (carcinogenic substances are handled differently, as described below). Three types of RfDs have been developed: chronic, subchronic, and developmental. Chronic RfDs are developed for exposures between seven years and a lifetime, subchronic RfDs for exposures between two weeks and seven years, and developmental RfDs for single exposures during gestation. EPA believes that for chronic RfDs daily exposures below the RfD are unlikely to cause “appreciable risk of deleterious effects during a Lifetime” (USEPA, 1989).

The experimental study used to calculate the RfD is called the critical study. It is chosen by ascertaining either the test species that is the most relevant to humans based on a biological rationale or the species that demonstrates a toxic effect at the lowest dose. After dosimetric conversions are made to the animal data to adjust for species differences, the critical toxic effect is chosen. This is done by determining the dose that results in the lowest-observed- adverse-effect-level (LOAEL) for any noncancer adverse effect. Next, the highest experimental dose level that does not produce an adverse effect is determined from the critical study. This value is called the no-observed-adverse-effect-level (NOAEL), and it is the key data point used to calculate the RfD. If the NOAEL is not available, then the LOAEL can be used to calculate the RfD. *{Note: RfDs are calculated for oral exposures. Reference concentrations (RfCs) are calculated for inhalation exposures. They are both derived in the same manner.}*

The RfD is calculated by dividing the NOAEL (or LOAEL) for the critical toxic effect by uncertainty factors and a modifying factor. Each uncertainty factor represents a specific area of uncertainty inherent in extrapolating data from experiments to expected real-life scenarios. The modifying factor reflects a qualitative, professional assessment of additional uncertainties in the entire data base for the chemical not explicitly addressed by the uncertainty factors. In general, the modifying factor (MF) reflects the overall confidence that the EPA experts have in the experimental data.

As already mentioned, carcinogens are handled differently. Scientists believe that a small number of certain molecular events can cause cellular changes that may lead to carcinogenesis. According to EPA, exposure to any amount of chemical or agent that is capable of producing these effects has a finite probability, however small, to initiate this process. Therefore, there is no exposure level that is considered to be totally risk free, and a threshold cannot be estimated for carcinogens.

EPA uses a two-part process to evaluate carcinogens. The first part is to assign a “weight of evidence” to the data to determine the likelihood that the substance is actually a human carcinogen. The weight of evidence places the chemical or agent into one of five groups as shown in Table 1.1 (USEPA, 1989). The second part is to calculate a chemical-specific slope factor. Cancer slope factors determine the potential risk levels associated with exposure to carcinogens. First, the assessor chooses an appropriate dose/response data set from either animal or human data. Then, a high-to-low dose extrapolation model is applied to the data set(s). The model is used to extrapolate from the high doses utilized in experiments to the low doses expected to be found in the environment (i.e., exposure levels). The slope factor is calculated by taking the upper 95th percent confidence limit of the slope of the line from the model fitted to the dose/response curve. This value represents a 95-percent probability of a response per unit intake of a chemical over a lifetime. In other words, there is only a 5-percent chance that the probability of the response will be higher.



Table 1.1: EPA Weight-of-Evidence Classification System for Carcinogenicity

Group	Description
A	Human carcinogen
B1 or B2	Probable human carcinogen <i>B1 indicates that limited human data are available</i> <i>B2 indicates sufficient evidence in animals and inadequate or no evidence in humans</i>
C	Possible human carcinogen
D	Not classifiable as to human carcinogenicity
E	Evidence of noncarcinogenicity for humans

1.2.5 Risk Characterization

Risk characterization, the final component of the baseline risk assessment, combines the toxicity and exposure assessments into quantitative and qualitative expressions of risk. There are six major steps in risk characterization (USEPA, 1989), as described below:

Step 1: Organize outputs of exposure and toxicity assessments

Step 2: Quantify pathway risks

Step 3: Combine risks across pathways that affect the same individuals over the same time periods

Step 4: Assess and present uncertainty

Step 5: Consider site-specific health or exposure studies

Step 6: Summarize results of the baseline risk assessment

Activities carried out in each of these steps are briefly described in the following sections,

1. Organize Outputs of Exposure and Toxicity Assessments



Before the final risk calculations are begun the assessor should verify that all necessary exposure and toxicity information has been collected and organized for each exposure pathway and land use evaluated. The exposure periods (e.g., short-term, chronic) for the toxicity and exposure values must be the same. For example, cancer risks should always be expressed as average lifetime exposure. Less-than-lifetime exposure values should be converted to average lifetime exposure. Chronic RfDs should only be compared with long-term (i.e., greater than 7 years) exposures. Subchronic noncarcinogenic exposures can not be converted to chronic exposures. Subchronic exposures should only be compared with subchronic RfDs.

Exposure routes should be properly matched for the toxicity and exposure values (e.g., oral to oral, inhalation to inhalation). Toxicity values for localized effects (e.g., dermal) should not be compared to systemic exposures (e.g., oral, inhalation). Conversion of values from one exposure route to another (e.g., oral to inhalation) should only be done after consulting with EPA's Environmental Criteria and Assessment Office (ECAO). The units used to express toxicity and exposure values for the inhalation exposure route should be checked to make sure that they are identical. Inhalation values can be expressed either as mg/m^3 or as $\text{mg}/\text{kg}\text{-day}$.

Finally, both the toxicity value and exposure estimate should be expressed either as absorbed dose or intake (i. e., administered dose). Except for dermal exposures, the preferred method is to express these values as intakes. Dermal values must take into account absorption through the skin. If strong evidence is available for absorption efficiencies for the oral and inhalation routes, then the toxicity and exposure values may be appropriately modified.

2. Quantify Pathway Risks

A. Calculate Risks for Individual Substances

The first step in assessing composite risks is to calculate risk for individual substances. "For carcinogens, risks are estimated as the incremental probability of an individual developing cancer over a lifetime as a result of exposure to the potential carcinogen" (USEPA, 1989). Because chemical intakes at Superfund sites are relatively low compared to doses given to experimental animals, it is assumed that these intakes lie in the linear portion of the low-dose, multistage dose-response model. This assumption results in the slope factor being a constant, and therefore the risk is directly related to the exposure intake. The carcinogenic risk equation is (USEPA, 1989):

$$\text{Risk} = \text{CDI} \times \text{SF}$$

Where:

Risk = a unitless probability (e.g., 2×10^{-5}) of an individual developing cancer

CDI = chronic daily intake averaged over 70 years ($\text{mg}/\text{kg}\text{-y}$)

SF = slope factor, expressed in $(\text{mg}/\text{kg}\text{-day})^{-1}$

Currently, EPA does not use probabilistic approaches to estimate the potential for noncarcinogenic health effects. Instead, a noncancer hazard quotient (HQ) is calculated for noncancer health effects:



$$\text{Noncancer Hazard Quotient} = E/\text{RfD}$$

Where:

E = exposure level (or chemical intake)

RfD = reference dose for same exposure pathway as E

This ratio does not represent a statistical probability of an adverse effect occurring. The hazard quotient assumes that for noncancer health effects a threshold dose exists below which adverse health effects are unlikely to occur, even for sensitive populations. If the hazard quotient is less than unity there is less concern for adverse health effects. The higher the hazard quotient is above unity, the greater the concern.

B. Aggregate Risks for Multiple Substances

The second step in assessing risks for each pathway is to calculate risk for multiple chemicals or chemical mixtures. When little or no quantitative information is available on the potential interaction among the components in a chemical mixture, EPA recommends dose additivity (USEPA, 1989; USEPA, 1992). For carcinogens, assessors assume a linear dose-response curve; therefore, they calculate total carcinogenic risk by adding the estimated carcinogenic risk for each substance of concern. For carcinogens, addition of individual risks assumes three things: that the various carcinogens in the mixture act independently, that intakes of the individual substances are small, and that all of the substances produce the same effect. Summed cancer risk estimates should be expressed using only one significant figure.

Risks from mixtures of noncarcinogens are assessed differently. For these, assessors calculate a hazard index (HI) for each exposure pathway. This is done by adding the individual HQs for that pathway. HQs should only be summed for those chemicals that produce the same toxic effect (that is, those chemicals that affect the same target organ) and that do so by the same ‘mechanism of action and for the same exposure period (chronic, subchronic, and shorter-term exposures). “This approach assumes that simultaneous subthreshold exposures to several chemicals could result in an adverse health effect” (USEPA, 1989). It also assumes that the magnitude of the adverse effect will be proportional to the sum of the hazard quotient ratios and that 100 percent of the contaminant is absorbed for each exposure pathway.

3. Combine Risks Across Exposure Pathways

The final step in the risk estimate is to sum the risks across exposure pathways, if appropriate. Some individuals might be exposed to a substance or combination of substances through several pathways. By following the steps below, assessors ensure that the estimate for the total site risk is appropriate.

- First, assessors identify the reasonable exposure pathway combinations. For each pathway, cancer risks and HIs are developed for particular exposure areas and time periods. If two pathways do not affect the same individual or subpopulation, neither pathway’s individual cancer risk estimate or HI affects the other, and they should not be combined.



- Second, assessors examine the likelihood that the same individuals would face the reasonable maximum exposure (RME) by more than one pathway. Because contaminant concentrations vary over time and space, one individual may not experience the RME for more than one pathway over a certain period of time. Therefore, assessors may combine the RME risks for more than one pathway if they can explain why the key RME assumptions for these pathways apply to the same individual or subpopulation.

4. Assess and Present Uncertainty

Highly quantitative, statistical uncertainty analysis is usually not necessary for Superfund risk assessments. It is more important to identify the site-related variables and assumptions that contribute to the uncertainty rather than to precisely quantify the degree of uncertainty in the risk assessment. The categories of uncertainties associated with risk assessments include the following:

- initial selection of substances,
- toxicity values for each substance, and
- exposure assessment for individual substances and individual exposures.

5. Consider Site-Specific Health or Exposure Studies

The results of the BRA should be compared with the results of the Agency for Toxic Substances Disease Registry (ATSDR) health assessment. This is a separate assessment conducted by the ATSDR. It is more qualitative in nature, and focuses on sensitive populations, toxic mechanisms, and possible public health impacts associated with exposures at a site. It is a source of additional information for the risk assessor. If there are any differences between these studies the reasons for these differences should be explained in the BRA. The assessor should also check with local health agencies and ATSDR to determine if any site-specific epidemiological studies have been performed. Any existing studies should be reviewed carefully by a trained epidemiologist to check for confounding factors not associated with the site. The results of the BRA and any reliable site-specific study should be compared and explained in the risk characterization section of the BRA.

6. Summarize and Present the Baseline Risk Assessment Results

Presentation of the risk assessment should address the following (USEPA, 1989):

- a discussion of the degree of confidence that the key site-related contaminants were identified, and their concentrations relative to background determined;
- a description of the various types of health endpoints (i.e., cancer, noncancer) present at the site, and a discussion distinguishing between those effects known to occur in humans and those that are predicted to occur based on animal experiments,



- a discussion of the level of confidence in the quantitative toxicity information, and a discussion of qualitative toxicity information on the substances not included in the quantitative assessment;
- a discussion of the level of confidence in the exposure assessment
- a comparison of the site cancer risk and noncancer hazard index values to the Superfund site remediation goals in the NCP (e.g., the cancer risk range of 10^{-4} to 10^{-7} and noncancer hazard index of 1.0);
- a discussion identifying the major factors driving the site risks (e.g., substances, pathways, and pathway combinations);
- a discussion of the major factors contributing to the uncertainty in the risk assessment (e.g., adding risks over several substances and pathways);
- a characterization of the exposed population; and
- a comparison of the site BRA results with ATSDR site-specific health studies, when available.

A tabular summary of the estimated cancer and noncancer risks should be prepared for all exposure pathways and land uses analyzed and for all substances carried through the risk assessment.

1.3 How to Use This Document

Detailed discussions of baseline risk assessment issues related to eight key policy topics are provided in Chapters 3 through 10. The topics addressed in those chapters are as follows

- Exposure and Dose - Chapter 3,
- Estimation of Average and Upper-End Risk - Chapter 4,
- Chemical Mixtures - Chapter 5,
- Radiation Risk Assessment - Chapter 6,
- Noncancer Health Endpoints - Chapter 7,
- Institutional Controls in Baseline Risk Assessments - Chapter 8,
- Site Specific Data vs. Default Values - Chapter 9, and



- Data Gaps, Uncertainty, and Professional Judgement - Chapter 10.

Each chapter begins with an introduction that explains how the topic/issues fit into the overall analytical framework of the baseline risk assessment process. Next, an historical perspective on how the topic has evolved is provided. The statutory and regulatory origins of the topic are detailed, and relevant guidance that has been developed addressing the topic are identified and reviewed. It is within these discussions that specific issues pertaining to the topic are identified and analyzed. The evolution of each issue will be presented chronologically. The major development, changes, etc. in the issue, its underlying science policy, and/or its application to the baseline risk assessment process will be highlighted. The current status of and position on each issue will be detailed, along with the issue's pros, cons, and uncertainties. The potential impacts on the outcome of risk assessments and the basis for negotiation will be clearly presented. In addition, each chapter will outline conclusions as to how those issues affect the interpretation of estimated baseline risks, and how they may provide a basis for negotiation with EPA. Finally, each chapter concludes with a listing of the reference materials cited in that chapter's text.

Discussion of the statutory history of each topic, its evolution, etc., is presented fully within each chapter. Thus, readers interested in only a specific topic can turn to the appropriate chapter and find a full discussion of pertinent information relating to that topic without having to cross-refer to other chapters. Readers of this entire document will observe, however, that in order to treat the subject matter in each chapter completely, a certain amount of unavoidable repetition of information that pertains to multiple topics exists from chapter to chapter.

Chapter 2 is structured differently from the other chapters in that it directs the reader to detailed information relating to specific risk assessment issues to be found in Chapters 3 through 10. The introduction to Chapter 2 illustrates the correspondence between each chapter and the specific component of the risk assessment process to which it pertains. Subsequent sections of Chapter 2 provide an overview of the specific issues to be evaluated under the risk assessment topics addressed in Chapters 3 through 10. Finally, the chapter concludes with an index of key risk assessment terms.

Appendix A, which follows Chapter 10, contains a brief summary of each of the source documents used in developing this guidance. It is intended to constitute a resource for identifying sources of information necessary for those who are responsible for developing or evaluating baseline risk assessments.

1.4 References

CERCLA. 1980. Comprehensive Environmental Response, Compensation, and Liability Act. PL 96-510.

SARA. 1986. Superfund Amendments and Reauthorization Act. PL 99-499.

USEPA. 1985. National Oil and Hazardous Substances Pollution Contingency Plan. U.S. Environmental Protection Agency. [50 FR 47912].

USEPA. 1989. Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual (Part A) (RAGS). U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D. C.; EPA 540/1-89/002.



USEPA. 1990. National Oil and Hazardous Substances Pollution Contingency Plan. U.S. Environmental Protection Agency. [55 FR 8666].

USEPA. 1992. Guidelines for Exposure Assessment. U.S. Environmental Protection Agency, Office of Health and Environmental Assessment. Washington, D.C. [57 FR 22888].

USEPA. 1994. Health Effects Assessment Summary Tables. U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. Washington, D.C. EPA 540/R-94/020.



Chapter 2: Guide to Issue Discussions

2.1 Introduction

As addressed in Chapter 1, the scope of this document covers three critical components of the overall site assessment and remediation process—exposure assessment, toxicity assessment and risk characterization. When combined with site data collection and evaluation these analytical elements constitute the baseline risk assessment. This chapter serves as a guide to the information presented in the body of this report. It will help the reader identify specific information pertaining to those components of the BRA that should be discussed with regulators prior to finalizing project-specific baseline risk assessment methodologies.

Figure 2.1 outlines which baseline risk assessment components are discussed in each chapter. As shown in this figure, the majority of chapters deal with the exposure assessment component. This is because most potentially negotiable analytical issues apply to that segment of the BRA process. Considerably more resources may be required to negotiate toxicity assessment issues than issues associated with either the exposure assessment or risk characterization. That is because these negotiations will require the assistance of an experienced toxicologist.

This chapter is divided into four sections. The first three sections outline the issues related to the following components of the baseline risk assessment process—exposure assessment, toxicity assessment, and risk characterization. These sections also outline the chapter in which each issue is discussed. The final section of this chapter lists key words that are associated with each of the issues, and points the reader to the specific section(s) of the document that discuss that keyword. The organization of this section assures that readers of this document rapidly can locate a given subject of interest either by the subject heading or by pertinent keywords.

2.2 Issues Pertaining to Exposure Assessment

Many of the controversial issues in risk assessments are associated with exposure assessment, and it is recommended that attempts at risk assessment methodology negotiation begin with this component. Figure 2.2 outlines the issues that apply to exposure assessments and the chapters in which these issues are discussed. Following is an overview of each issue. Please refer to the appropriate chapter for a more comprehensive discussion of these issues.



Figure 2.1 Correspondence Between BRA Components And Chapters in This Guidance

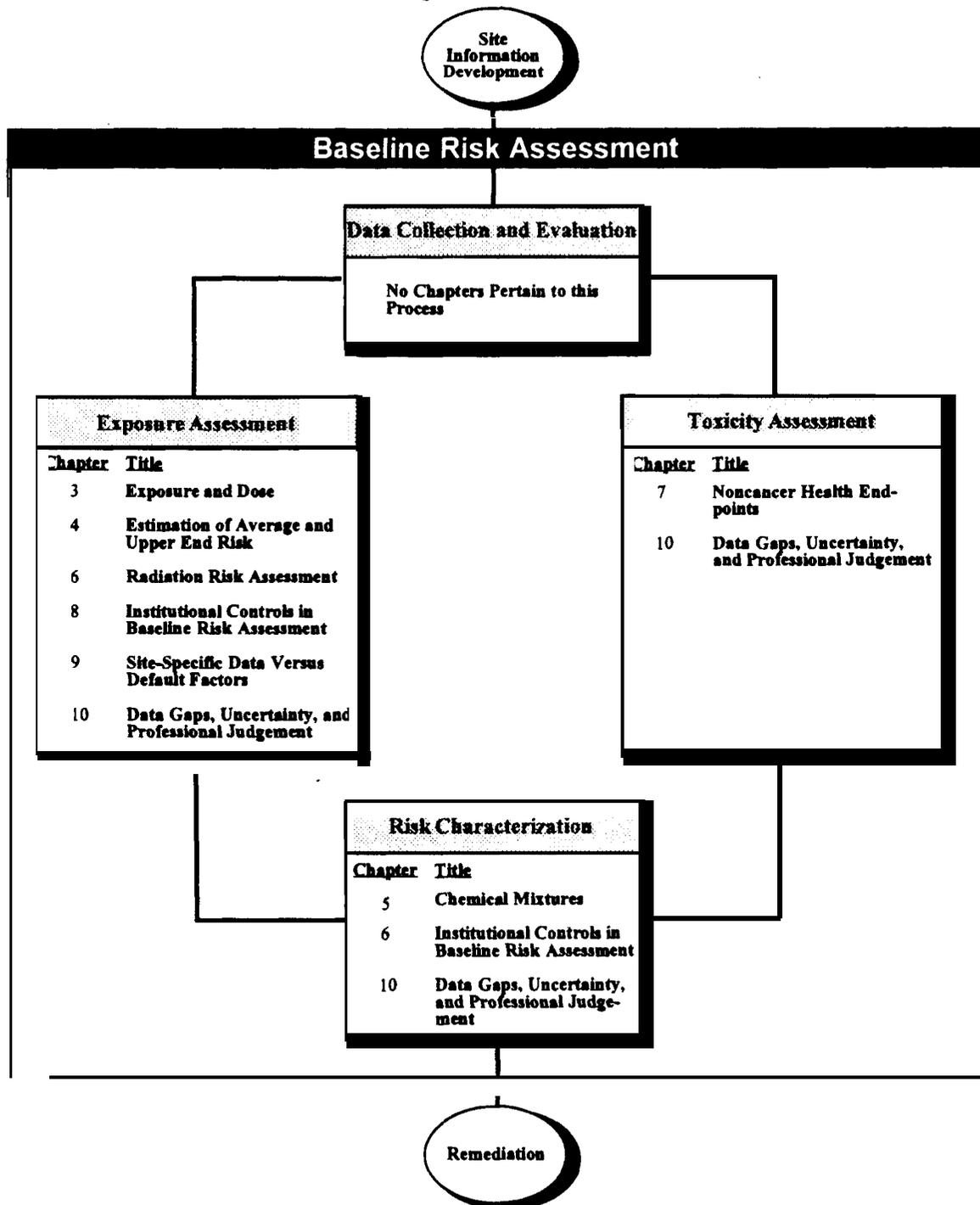


Figure 2.2: Issues Pertaining to Exposure Assessment

Chapter 3: Exposure and Dose	
Issue 1:	Exposure/Dose Terminology
Issue 2:	Exposure/Dose Calculations
Chapter 4: Estimation of Average and Upper End Risk	
Issue 1:	Risk Descriptors (e.g., RME)
Issue 2:	Professional Judgement
Chapter 6: Radiation Risk Assessment	
Issue 1:	Exposure Calculations
Issue 2:	Radionuclide Progeny
Chapter 8: Institutional Controls	
Issue 1:	Evaluation of Institutional Controls
Issue 2:	Exposure Scenario Development
Chapter 9 Site Specific Data vs. Default Factors	
Issue 1:	Use of Site Specific Data
Issue 2:	Use of Default Factors
Chapter 10: Data Gaps, Uncertainty, and Professional Judgement	
Issue 1:	Sources of Uncertainty
Issue 2:	Impact of Data Gaps on Risk Estimate
Issue 3:	Means to Address Uncertainty

2.2.1 Exposure and Dose

Issue 1: Exposure/Dose Terminology

Exposure and dose terminology are discussed in Chapter 3. These definitions have changed over the years. Originally, exposure was quantified by measuring or estimating the amount of a chemical at the exchange boundaries (i.e., lungs, gut, skin) during some specified time period. The current concept of exposure and dose is delineated in the [Guidelines for Exposure Assessment](#) (USEPA 1992a). Exposure is defined as contact of a chemical, physical, or biological agent with the outer boundary of an organism:



that is, the skin, mouth, or nostrils. There are six different terms used for close: administered, potential, applied, absorbed, internal, and delivered. See Chapter 3 for a definition on each of these terms.

Issue 2: Exposure/Dose Calculations

The change in definitions has resulted in some confusion in how exposures and dose are calculated. In the original definition, exposure was equivalent to the administered doses given in animal experiments (i.e., the exposure equation included the intake rate for inhalation or ingestion). The current concept of exposure, however, is the concentration of the substance in the medium (e.g., soil, air, water) integrated over the time duration of the contact. The exposure must be multiplied by the intake rate to calculate the amount of substance at the exchange boundaries (i.e., gut lung and skin). This calculation is performed so that exposures become equivalent to the administered dose given in animal experiments. Dermal exposure estimates have always included the amount of substance absorbed through the skin because it is known that dermal and internal absorption (i.e., gut and lung) occur at different rates, and the skin acts as both an outer boundary and an exchange boundary.

Regulator Dialogue

It is vital that DOE and the regulator fully understand the assumptions inherent in these definitions as those assumptions affect the way exposure is calculated.

2.2.2 Estimation of Average and Upper End Risk

Issue 1: Risk Descriptors

As guidance for conducting risk assessments has evolved over the years, various loosely defined descriptors (such as reasonable worst case, worst case, and maximum exposed individual [MEI]) have been used to describe the upper-end exposure scenario. Chapter 4 describes the development of these risk descriptors. Often these risk descriptor terms were poorly defined in the guidance documents, and guidance was often unclear as to how exposure should be calculated under these various exposure conditions. The current risk descriptor used is reasonable maximum exposure (RME).

Issue 2: Professional Judgement

Because the risk descriptor terms were loosely defined, it was left to the “professional judgement” of the assessor to choose how to calculate upper-end exposure. When site-specific information was not available, the risk assessor used professional judgement to choose the various default factors used in calculating the RME. For example, the RME is now calculated by combining 95% upper confidence limit values with 50th and 90th percentile values for some of the default values, but specific guidance was never given as to which values should be 50th or 90th percentile.



Regulator Dialogue

The professional judgement used by DOE, so long as it is reasonable and defensible, should be acceptable to the regulatory personnel. Assessors may negotiate which default factors and chemical concentration values are to be used. The Science Advisory Board (SAB) is recommending the use of frequency distributions to calculate the variables used in the exposure equations. Assessors may also negotiate the use of such techniques (e.g., Monte Carlo simulation) with EPA.

2.2.3 Radiation Risk Assessment

Issue 1: Exposure Calculations

Chapter 6 discusses two aspects of radiation risk that must be considered in the exposure assessment. The first aspect to consider is what type of radiation risk (alpha, beta, or gamma) is being calculated. Gamma radiation is important both internally and externally. Because gamma radiation is an external penetrating source, this type of exposure must also be considered with gamma emitters. Alpha and beta emitters are only important for internal exposures. Alpha or beta radionuclide must be absorbed into the body before they can exert their deleterious effects. This is also true for dermal exposures. The alpha or beta emitter must be absorbed through the skin before this exposure scenario can be considered.

Issue 2: Radionuclide Progeny

The second aspect to consider in exposure assessments with radiation risk is radionuclide progeny. Radionuclide decay to produce other radionuclides that will have different half lives, and possibly different types of radiation. Some of the progeny may have long half lives, while others may have very short half lives, on the order of days or hours. Exposure to all of the progeny must be considered in the risk assessment.

Regulator Dialogue

Radiation exposures behave as a continuum. As the parent radionuclide decays the progeny can change to a different type of emitter (i.e., alpha, beta, or gamma), and therefore the exposure route of concern may also change. Because some of the radionuclides have a long half life, the parent compound along with its progeny can exist at a site at the same time. DOE and regulatory personnel must be aware of which radionuclides are involved at the site at present, what type of radiation they emit, what their half lives are, and how this will change over time.

2.2.4 Institutional Controls

Issue 1: Evaluation of Institutional Controls

Institutional controls in risk assessments are discussed in Chapter 8. It is clear from NCP and the various risk assessment guidelines that institutional controls cannot be considered as part of the baseline



risk assessment- The risk-reduction implications of existing institutional controls only can be considered as part of the remedial action plan.

Issue 2: Exposure Scenario Development

A related topic discussed in Chapter 8 is land-use development. The default land-use scenario for risk assessments is residential. The guidelines state that if another land use is reasonable, then that land use can be used.

Regulator Dialogue

If DOE is going to retain control of a site, then industrial land use can reasonably be assumed in assessing exposure in the baseline risk assessment. Industrial land-use scenarios can usually reduce the risks in the risk assessment as compared with residential scenarios.

2.2.5 Site-Specific Data Versus Default Factors

Issue 1: Use of Site-Specific Data

Baseline risk assessments are conducted using both site-specific data and default factors. Chapter 9 discusses this issue. All of the exposure guidelines state that site-specific data are preferable to default factors, but complete site-specific data are never available, particularly with respect to environmental fate, transport, and human behavior patterns.

Issue 2: Use of Default Factors

Professional judgement is used to determine which default factors and exposure models are the most appropriate for a particular site. Typically, the standard default factors are conservative, and the overall exposure assessment potentially can become overly conservative when the default factors are compounded together.

Regulator Dialogue

Assessors can negotiate which factors and models are the most appropriate to use in the assessment. It is to DOE's advantage to gain as much site-specific information as possible. More site-specific information results in less conservative default factors and models being used in the risk assessment. This will also reduce the amount of negotiation needed with respect to the use of default factors and models.



2.2.6 Data Gaps, Uncertainty, and Professional Judgement

Issue 1: Sources of Uncertainty

All risk assessments involve some data gaps, which must be resolved through professional judgement. This, however, may result in greater uncertainties being introduced into the assessment. Chapter 10 discusses how data gaps, uncertainty, and professional judgement affect the various components of the risk assessment. As stated above, typically some site-specific information is missing from any exposure assessment. The gaps are filled with models and default factors chosen by the assessor using professional judgement, but there is always uncertainty attached to such data and models. In fact, there are six basic sources of uncertainty in exposure assessment measurement errors, indirect empirical or generic data, variability of natural systems, environmental modeling, sampling errors, and professional judgement.

Issue 2: Impact of Data Gaps on Risk Estimate

As stated above, data gaps are filled with models and default factors. Chapter 10 points out that these models and default factors are usually conservative, and therefore they normally overestimate the risk. Minimizing the use of models and default factors will help to minimize the overestimation of the risk.

Issue 3: Means to Address Uncertainties

There are various means to address the uncertainty inherent in risk assessments. More site-specific data can be collected to reduce data gaps. Also, as the science of exposure assessment is improved, better models will be produced thereby reducing uncertainty.

Regulator Dialogue

Both the models and default factors used can be negotiated with EPA.

2.3 Issues Pertaining to Toxicity Assessment

The fewest and most resource-intensive negotiable issues are associated with the toxicity assessment. The toxicity values used in the risk assessment come from peer-reviewed sources. It will require the assistance of an experienced toxicologist to challenge these peer-reviewed values. It is recommended that the toxicity assessment be the last component of the baseline risk assessment that is negotiated. Figure 2.3 illustrates the chapters and the issues addressed herein that apply to toxicity assessments. This section will give a brief discussion of each issue. The reader is referred to the appropriate chapter to gain a full understanding of these issues.



Figure 2.3: Issues Pertaining to Toxicity Assessment

Chapter 7: Noncancer Health Endpoints	
Issue 1:	Alternative Toxicity Values
Issue 2:	Alternative Toxicity Study Requirements
Chapter 10: Data Gaps, Uncertainty and Professional Judgement	
Issue 1:	Sources of Uncertainty
Issue 2:	Impact of Uncertainty on Risk Estimates
Issue 3:	Means to Address Uncertainty

2.3.1 Noncancer Health Endpoints

Issue 1: Alternative Toxicity Values

Alternative toxicity values and the types of studies that can be used to generate these values are discussed in Chapter 7. Both the regulations (USEPA, 1990a) and the guidelines (USEPA 1989a) indicate that alternative toxicity values may be considered by EPA. There are generally three reasons to present new toxicity values:

- if there are no existing value(s) in the Integrated Risk Information System (IRIS),
- if the value in IRIS is assigned a low confidence, or
- to evaluate the estimation of risk using existing values in IRIS (according to EPA, “other information, such as additional toxicity information, may be evaluated to determine whether the risks are likely to have been under- or overestimated” [USEPA, 1989a]).

Issue 2: Alternative Toxicity Study Requirements

There are several requirements that any new study must meet for EPA to seriously consider the new study. The study must have a better design than the previously accepted investigation. This may include a more relevant animal model backed by the appropriate biological and/or pharmacokinetic data, a dosing regime that follows prescribed protocols, and a route of administration that is appropriate for the expected human exposure. In general, the new research must produce a higher level of confidence in the data than the previously accepted study. It is also important for the new study to provide a clearer interpretation of the results. If the new investigation does not produce any more lucid results, then EPA will probably not accept the new results.



Regulator Dialogue

As stated in Sections 2.1 and 2.3.1, the toxicity assessment will be the most difficult component to negotiate. It is recommended that negotiations on toxicity values not be attempted unless DOE has compelling evidence to change a value.

2.3.2 Data Gaps, Uncertainty, and Professional Judgement

Issue 1: Sources of Uncertainty

As discussed in Section 2.2.7, data gaps and uncertainty are a natural part of all risk assessments, including the toxicity assessment component. Sources of uncertainty include the animal experiments and their associated uncertainties in the choice of the animal model, study design, interpretation of the results, and extrapolating from high to low doses and from animals to humans.

Issue 2: Impact of Uncertainty on Risk Estimates

The assumptions used in toxicity experiments and data extrapolation normally produces overestimation in the risk.

Issue 3: Means to Address Uncertainty

The uncertainties can be reduced by choosing better animal models, using human epidemiological data if available, and applying better extrapolation models.

Regulator Dialogue

Both the models and default factors used can be negotiated with EPA.

2.4 Issues Pertaining to Risk Characterization

Risk characterization is the step where information from the exposure and toxicity assessments are combined to project the potential risk posed by a hazardous waste site. There are issues related to combining these two steps to produce the risk calculation, which are outlined in Figure 2.4. This section will give a brief discussion of each issue. Please refer to the appropriate chapter to gain a more comprehensive understanding of each issue.



Figure 2.4 Issues Pertaining to Risk Characterization

Chapter 5: Chemical Mixtures	
Issue 1:	Dose Additivity
Issue 2:	Impact of Summing HQs
Chapter 10: Data Gaps, Uncertainty, and Professional Judgement	
Issue 1:	Sources of Uncertainty
Issue 2:	Impact of Uncertainty on Risk Estimates
Issue 3:	Means to Address Uncertainty

2.4.1 Chemical Mixtures

Chemical mixtures are defined as any combination of two or more chemical substances. The mixture may be purposely formulated (such as gasoline or pesticides), or the chemicals may have been combined inadvertently through improper disposal. Chapter 5 discusses how risks are calculated for chemical mixtures.

Issue 1: Dose Additivity

Although the guidelines recommend that toxicological information on the specific chemical mixture of interest be used to calculate risks, toxicological information on chemical mixtures is rarely available. Therefore, EPA recommends using dose additivity in the absence of specific data. Dose additivity assumes that the chemicals have the same mode of action and elicit the same effects, an assumption that may not reflect reality. The dose additivity assumption also ignores antagonistic or synergistic interactions. If the chemicals act synergistically, then the calculated risk will underestimate the actual risk; if the chemicals act antagonistically, then the calculated risk will overestimate the actual risk.

Issue 2: Impacts of Summing HQs and Slope Factors

For noncarcinogens, an estimation of risk is determined by calculating Hazard Quotients (HQs) and the Hazard Index (HI) for each chemical. Chapters 1 and 5 discuss these calculations in more detail. The HI is calculated by summing the individual chemical HQs. Summing the HQs has the same limitations as stated above for dose additivity. Summing the HQs also treats all RfDs equally. The HQs are calculated from RfDs, which are derived from a single point on the dose/response curve. This calculation ignores the shape of the dose/response curve. The RfDs for each chemical are derived from animal experiments that contain a spectrum of toxic endpoints and disparate levels of confidence. There is a great deal of uncertainty attached to this estimation of risk for noncarcinogens.



Summing the slope factors for carcinogens has many of the same limitations previously stated. Summing the slope factors treats all carcinogens equally, regardless of their carcinogenicity classification. Known carcinogens, Class A, can be summed with probable (Class B) or possible (Class C) carcinogens. Slope factors are derived from the upper 95th percentile of the high to low dose extrapolation model. Upper 95th percentiles are not strictly additive. Summing slope factors can result in compounding conservatism, and it also increases uncertainty in the risk calculation.

Regulator Dialogue

The best method to use to avoid such uncertainties is to obtain toxicological information of the chemical mixture of interest. If this information cannot be obtained then the next solution is to concentrate on the noncarcinogens. As outlined in Risk Assessment Guidance for Superfund (RAGS) (USEPA 1989a), HQs for noncarcinogens should only be summed for those chemicals that affect the same target organ by the same mode of action. For carcinogens, there is no level of exposure that is considered safe; therefore, negotiations for carcinogens may be more difficult. An attempt should be made to sum slope factors for each individual carcinogen classification. That is, Class A carcinogens should only be summed with other Class A carcinogens, Class B with Class B, and Class C with Class C. Presently, acceptable risk levels for carcinogens range from 10^{-4} to 10^{-6} probability of developing cancer. Because Class C carcinogens are labeled as only possible carcinogens, it may be possible to negotiate an acceptable risk level for Class C carcinogens at 10^{-4} , whereas Class A carcinogens (i.e., known human carcinogens) and Class B carcinogens (i.e., probable human carcinogens) may have to be negotiated at a higher risk (e.g., 10^{-6} for Class A and 10^{-5} for Class B). Summing all of the classes together will probably result in having to negotiate at a higher risk level because the Class A and B carcinogens will be mixed in with the Class C compounds.

2.4.2 Data Gaps, Uncertainty, and Professional Judgement

Issue 1: Sources of Uncertainty

The sources of uncertainty for the risk characterization include those discussed above in Section 2.4.2. Data gaps in either the exposure or toxicity assessment impact the risk characterization because both of those components feed information into the final risk calculation.

Issue 2: Impact of Uncertainty on Risk Estimates

Missing information results in an incomplete risk assessment, which creates uncertainty in the overall findings of the assessment.

Issue 3: Means to Address Uncertainty

Filling the data gaps with reliable information can remove a great deal of the uncertainty in the risk assessment. Upgrading the models used in all steps of the assessment will also reduce the uncertainty in the risk calculation. The risk characterization component of the risk assessment is the section of the assessment where uncertainty is discussed.



Regulator Dialogue

A full and thorough analysis of uncertainty should be discussed so that the risk managers can make an informed decision.

2.5 Conclusion

The previous sections briefly discussed the issues involved with baseline risk assessments. The remaining chapters in this document will fully discuss each of these issues. Table 2.1 lists the issues and associated keywords to which they pertain, identifies the section of the document that discusses the particular issue, and identifies the EPA source documents where these issues are discussed. “



Table 2.1: Guide to Issues and Source Documents

ISSUE	KEYWORDS	DOE GUIDANCE SECTION	SOURCE DOCUMENT
Alternative Toxicity Values	Acceptable Daily Intake (ADI)	7.2.2	USEPA 1989a
	Benchmark Dose	7.2.4	USEPA 1991a
	Lowest-Observed-Adverse-Effect-Level (LOAEL)	7.2.2, 7.2.3, 7.2.4	USEPA 1988a; USEPA 1988b; USEPA 1989a; USEPA 1991a
	No-Observed-Adverse-Effect-Level (NOAEL)	7.2.2, 7.2.3, 7.2.4, 7.3.1	USEPA 1988a; USEPA 1988b; USEPA 1989a; USEPA 1991a
	Reference Concentration (RfC)	7.1, 7.2.4	USEPA 1989a; USEPA 1991a
	Reference Dose (RfD)	7.1, 7.2.2, 7.2.3, 7.2.4, 7.3.1	USEPA 1986a; USEPA 1988a; USEPA 1988b; USEPA 1989a; USEPA 1991a
	Study Design	7.2.2, 7.2.3, 7.2.4, 7.3.1, 7.3.2	USEPA 1986b; USEPA 1988a; USEPA 1988b; USEPA 1989a; USEPA 1991a
	Threshold	7.2.4	USEPA 1991a
Default Factors vs. Site-Specific Data	Default Factors/Values	9.1, 9.2.2, 9.3.1, 9.3.2	USEPA 1989b; USEPA 1989c; USEPA 1991b; USEPA 1991c
	Site-Specific	9.1, 9.2.2, 9.3.1, 9.3.2	USEPA 1986a; USEPA 1988c; USEPA 1989a; USEPA 1989b; USEPA 1989c; USEPA 1991b; USEPA 1992b



Table 2.1: Guide to Issues and Source Documents (continued)

ISSUE	KEYWORDS	DOE GUIDANCE SECTION	SOURCE DOCUMENT
Dose Additivity	Antagonism (antagonistic)	5.2.1, 5.2.3, 5.2.4, 5.3.1	USEPA 1986a; USEPA 1986c; USEPA 1989a; USEPA 1993
	Dose Additivity	5.1, 5.2.1, 5.2.3, 5.2.4, 5.2.6, 5.2.7, 5.3.1, 5.3.2	USEPA 1986a; USEPA 1986c; USEPA 1989a; USEPA 1993
	Hazard Index (HI)	5.1, 5.2.1, 5.2.3, 5.2.4, 5.2.7, 5.3.1, 5.3.2	USEPA 1986a; USEPA 1986c; USEPA 1989a; USEPA 1993
	Hazard Quotient (HQ)	5.1, 5.2.4, 5.2.7, 5.3.1, 5.3.2	USEPA 1989a; USEPA 1993
	Lowest-Observed-Adverse-Effect-Level (LOAEL)	5.1, 5.2.5, 5.3.1	USEPA 1989a; USEPA 1993
	No-Observed-Adverse-Effect-Level (NOAEL)	5.1, 5.2.7, 5.3.1	USEPA 1989a; USEPA 1993
	Non-Threshold	5.1, 5.2.5	USEPA 1989a; USEPA 1991d
	Reference Concentration (RfC)	5.2.5	USEPA 1989a; USEPA 1991d; USEPA 1993
	Reference Dose (RfD)	5.1, 5.2.1, 5.2.4, 5.2.5, 5.2.7, 5.3.1, 5.3.2	USEPA 1986c; USEPA 1989a; USEPA 1991d; USEPA 1993



Table 2.1: Guide to Issues and Source Documents (continued)

ISSUE	KEYWORDS	DOE GUIDANCE SECTION	SOURCE DOCUMENT
Dose Additivity (continued)	Slope Factor	5.1, 5.2.4, 5.3.1, 5.3.2	USEPA, 1989a
	Synergism (synergistic)	5.2.1, 5.2.2, 5.2.3, 5.2.4, 5.3.1	USEPA 1986a, USEPA 1986c; USEPA 1986d; USEPA 1989a; USEPA 1993
	Threshold	5.1, 5.2.3, 5.2.4, 5.2.7	USEPA, 1986a, USEPA, 1989a; USEPA, 1993
Exposure Assessment Risk Descriptors	Absolute Worst Case	4.2.3, 4.3.1	USEPA 1989b
	Arithmetic Average	4.2.3, 4.2.5, 4.3.1	USEPA 1989c; USEPA 1992d; USEPA 1993
	Average Case	4.2.3, 4.3.1	USEPA 1989c
	Best Estimate	4.2.2, 4.2.3, 4.3.1	USEPA, 1986a; USEPA, 1989d
	Central Tendency	4.2.5, 4.3.1	USEPA, 1991d
	Confidence Limit	4.2.2, 4.3.1	USEPA, 1988c
	Equivalent Exposure Populations (EEP)	4.2.3, 4.3.1	USEPA 1988d
	Geometric Mean	4.2.5	USEPA, 1993
	High End	4.2.5, 4.3.1	USEPA 1991d
	Highest Individual Exposure	4.2.2, 4.3.1	USEPA 1986a



Table 2.1: Guide to Issues and Source Documents (continued)

ISSUE	KEYWORDS	DOE GUIDANCE SECTION	SOURCE DOCUMENT
Exposure Assessment Risk Descriptors (continued)	Maximally Impacted Residence	4.2.3, 4.3.1	USEPA 1988d
	Maximum Exposed Individual (MEI)	4.2.3, 4.2.5, 4.3.1	USEPA 1988d; USEPA 1992a
	Maximum Exposure Range	4.2.5, 4.3.1	USEPA 1992a
	Mid-Range	4.2.1, 4.3.1	USEPA 1990a
	Most Reasonable	4.2.5, 4.3.1, 4.3.2	USEPA 1993
	Overly Worst Case	4.2.3	USEPA 1989b
	Reasonable Maximum Exposure (RME)	4.1, 4.2.1, 4.2.3, 4.2.4, 4.2.5, 4.3.1, 4.3.2,	USEPA 1988e; USEPA 1989a; USEPA 1990a; USEPA 1991b; USEPA 1992d, USEPA 1993
	Reasonable Worst Case	4.1, 4.2.2, 4.2.3, 4.2.5, 4.3.1	USEPA 1986a; USEPA 1989b; USEPA 1989c; USEPA 1992a
	Standard Deviation	4.2.2, 4.3.1	USEPA 1988c
	Theoretical Upper Bounding Estimate (TUBE)	4.2.5, 4.3.1	USEPA 1992a
Upper Confidence Limit	4.2.5, 4.3.1, 4.3.2	USEPA 1992a; USEPA 1993	



Table 2.1: Guide to Issues and Source Documents (continued)

ISSUE	KEYWORDS	DOE GUIDANCE SECTION	SOURCE DOCUMENT
Exposure Assessment Risk Descriptors (continued)	Upper-Bound	4.2.1, 4.2.2, 4.2.3, 4.3.1	USEPA 1986a; USEPA 1989c; USEPA 1989d; USEPA 1990a
	Worst Case	4.1, 4.2.5, 4.3.1	USEPA 1992a
Exposure/Dose Calculation	Dose	3.2.2, 3.3.1, 3.3.2	USEPA 1992c
	Exchange Boundary	3.2.2, 3.3.1	USEPA 1989a; USEPA 1989b; USEPA 1991c; USEPA 1992a; USEPA 1992c
	Exposure	3.2.2, 3.3.1, 3.3.2	USEPA 1988c; USEPA 1989a; USEPA 1989b; USEPA 1991c; USEPA 1992a; USEPA 1992c
Exposure/Dose Terminology	Absorbed Dose	3.2.2	USEPA 1986d; USEPA 1989a; USEPA 1991c; USEPA 1992a; USEPA 1992c
	Administered Dose	3.2.2	USEPA 1989a; USEPA 1989b; USEPA 1989c; USEPA 1991c; USEPA 1992a; USEPA 1992c
	Applied Dose	3.2.2, 3.3.1, 3.3.2	USEPA 1989a; USEPA 1992a
	Delivered Dose	3.2.2	USEPA 1992a
	Dose	3.2.2, 3.3.1, 3.3.2	USEPA 1986a; USEPA 1989a; USEPA 1992a



Table 2.1: Guide to Issues and **Source Documents (continued)**

ISSUE	KEYWORDS	DOE GUIDANCE SECTION	SOURCE DOCUMENT
Exposure/Dose Terminology (continued)	Exchange Boundary	3.2.2, 3.3.1, 3.3.2	USEPA 1986d; USEPA 1989a; USEPA 1989b; USEPA 1991c; USEPA 1992a
	Exposure	3.2.2, 3.3.1, 3.3.2	USEPA 1986a; USEPA 1986d; USEPA 1988c; USEPA 1989a; USEPA 1989b; USEPA 1989c; USEPA 1991c; USEPA 1992a; USEPA 1992c
	Exposure Dose	3.2.2	USEPA 1989c
	Exposure Point Concentration	3.2.2	USEPA 1989c
	Intake	3.2.2, 3.3.1, 3.3.2	USEPA 1986a; USEPA 1986d; USEPA 1989a; USEPA 1992a
	Internal Dose	3.2.2	USEPA 1992a
	Point of Contact	3.1, 3.3.1, 3.3.2	USEPA 1986d; USEPA 1989a; USEPA 1992a
	Potential Dose	3.2.2, 3.3.2	USEPA 1992a
Exposure Scenario Development	Land Use	8.2.3, 8.3.1, 8.3.2	USEPA 1989a; USEPA 1990a; USEPA 1991e
Impact of Summing HQs and Slope Factors	Antagonism (antagonistic)	5.2.1, 5.2.4, 5.2.7, 5.3.1	USEPA 1986c; USEPA 1989a; USEPA 1993



Table 2.1: Guide to Issues and Source Documents (continued)

ISSUE	KEYWORDS	DOE GUIDANCE SECTION	SOURCE DOCUMENT
Impact of Summing HQs and Slope Factors (continued)	Dose Additivity	5.2.1, 5.2.4, 5.2.7, 5.3.1	USEPA 1986c; USEPA 1989a; USEPA 1993
	Hazard Index (HI)	5.2.1, 5.2.4, 5.2.7, 5.3.1	USEPA 1986c; USEPA 1989a; USEPA 1993
	Hazard Quotient (HQ)	5.2.4, 5.2.7, 5.3.1	USEPA 1989a; USEPA 1993
	Lowest-Observed-Adverse-Effect-Level (LOAEL)	5.2.4, 5.3.1, 5.3.2	USEPA 1989a
	No-Observed-Adverse-Effect-Level (NOAEL)	5.2.4, 5.2.7, 5.3.1	USEPA 1989a; USEPA 1993
	Reference Dose (RfD)	5.2.1, 5.2.4, 5.2.7, 5.3.1	USEPA 1986c; USEPA 1989a; USEPA 1993
	Slope Factor	5.2.4, 5.3.1, 5.3.2	USEPA 1989a
	Synergism (synergistic)	5.2.1, 5.2.4, 5.2.7, 5.3.1	USEPA 1986c; USEPA 1989a; USEPA 1993
	Threshold	5.2.4, 5.2.7, 5.3.1	USEPA 1989a; USEPA 1993
Professional Judgement	Absolute Worst Case	4.2.3	USEPA 1989b
	Best Estimate	4.2.2	USEPA 1986a; USEPA, 1988c



Table 2.1: Guide to Issues and Source Documents (continued)

ISSUE	KEYWORDS	DOE GUIDANCE SECTION	SOURCE DOCUMENT
Professional Judgement (continued)	Data Gaps	10.2.2, 10.3.1, 10.3.2	USEPA 1989a; USEPA 1992a
	Exposure	8.3.1, 10.2.2	USEPA 1986a; USEPA 1989a; USEPA 1991b; USEPA 1992a
	Hazard Index (HI)	5.3.2	USEPA 1986a
	Highest Individual Exposure	4.2.2	USEPA 1986a
	Land Use	8.3.1, 10.2.2	USEPA 1989a
	Overly Worst Case	4.2.3	USEPA 1989b
	Reasonable Maximum Exposure (RME)	4.2.3, 4.2.4, 4.3.1, 9.2.2	USEPA 1989a; USEPA 1991b
	Reasonable Worst Case	4.2.2, 4.2.3	USEPA 1986a; USEPA 1989b
	Reference Dose (RfD)	7.2.2, 7.3.1	USEPA 1989a
	Study Design	7.2.2	USEPA 1989a
Radiation Calculations	Alpha Emitters/Particles/Radiation	6.3.1, 6.5.1, 6.6.2, 6.7	USEPA 1994a; USEPA 1994b
	Becquerel (Bq)	6.6.1, 6.6.2	NAS, 1990
	Beta Emitters/Particles/Radiation	6.3.1, 6.5.1, 6.7	USEPA 1994b



Table 2.1: Guide to Issues and Source Documents (continued)

ISSUE	KEYWORDS	DOE GUIDANCE SECTION	SOURCE DOCUMENT
Radiation Calculations (continued)	Curie (Ci, pCi)	6.5.4, 6.6.1, 6.6.2	NAS, 1990; USEPA 1989a; USEPA 1989e
	Gamma Emitters/Particles/Radiation	6.3.1, 6.5.1, 6.5.3, 6.7	USEPA 1989a; USEPA 1989e; USEPA 1994b
	Gray (Gy)	6.6.1, 6.6.2	NAS, 1990
	High LET	6.5.1, 6.5.2	NAS, 1990; USEPA 1994b
	Linear Energy Transfer (LET)	6.4.1, 6.5.1	USEPA 1994b
	Low LET	6.4.1, 6.5.1, 6.5.2, 6.5.3	NAS, 1990; USEPA 1994b
	Nonstochastic	6.1, 6.4.1	USEPA 1994b
	Progeny	6.3.2, 6.5.4, 6.7	USEPA 1989a; USEPA 1989e
	Rad	6.5.1, 6.5.2, 6.6.1, 6.6.2	NAS, 1990; USEPA 1994b
	Rem	6.4.1, 6.5.2, 6.5.4, 6.6.1, 6.6.2	NAS, 1990; USEPA 1989a; USEPA 1989e; USEPA 1994b
Sievert (Sv)	6.6.1, 6.6.2	NAS, 1990	



Table 2.1: Guide to Issues and Source Documents (continued)

ISSUE	KEYWORDS	DOE GUIDANCE SECTION	SOURCE DOCUMENT
Uncertainty	Communicating Uncertainty	4.2.2, 4.2.3, 4.3.2, 5.3.2, 7.2.1, 9.2.2, 9.3.1, 10.2.1, 10.2.2, 10.3.2	USEPA 1986a; USEPA 1988c; USEPA 1988d; USEPA 1989a; USEPA 1989c; USEPA 1990a; USEPA 1991c; USEPA 1992a
	Impact of Uncertainty	10.2.2, 10.3.1	USEPA 1989a; USEPA 1990b; USEPA 1991c
	Means to Address Uncertainty	5.3.2, 7.3.1, 9.1, 9.2.2, 10.2.2, 10.3.1	USEPA 1989a; USEPA 1990a; USEPA 1990b; USEPA 1991c; USEPA 1991fi USEPA 1992a
	Sources of Uncertainty	3.3.2, 4.2.3, 5.2.1, 5.3.1, 5.3.2, 7.3.1, 9.2.2, 9.3.1, 10.1, 10.2.2, 10.3.1	USEPA 1986d; USEPA 1989a; USEPA 1989b; USEPA 1989c; USEPA 1989d; USEPA 1990b; USEPA 1991c



Table 2.1: Guide to Issues and Source Documents (continued)

ISSUE	KEYWORDS	DOE GUIDANCE SECTION	SOURCE DOCUMENT
Uncertainty	Communicating Uncertainty	4.2.2, 4.2.3, 4.3.2, 5.3.2, 7.2.1, 9.2.2, 9.3.1, 10.2.1, 10.2.2, 10.3.2	USEPA 19863; USEPA 1988c; USEPA 1988d; USEPA 1989a; USEPA 1989c; USEPA 1990a; USEPA 1991c; USEPA 1992a
	Impact of Uncertainty	10.2.2, 10.3.1	USEPA 1989a; USEPA 1990b; USEPA 1991c
	Means to Address Uncertainty	5.3.2, 7.3.1, 9.1, 9.2.2, 10.2.2, 10.3.1	USEPA 1989a; USEPA 1990a; USEPA 1990b; USEPA 1991c; USEPA 1991f; USEPA 1992a
	Sources of Uncertainty	3.3.2, 4.2.3, 5.2.1, 5.3.1, 5.3.2, 7.3.1, 9.2.2, 9.3.1, 10.1, 10.2.2, 10.3.1	USEPA 1986d; USEPA 1989a; USEPA 1989b; USEPA 1989c; USEPA, 1989d; USEPA 1990b; USEPA 1991c



2.6 References

NAS. 1990. Health Effects of Exposure to Low Levels of Ionizing Radiation. (National Research Council, Committee of the Biological Effects of Ionizing Radiation, BEIR V), National Academy of Sciences. NAS Press, Washington D.C.

USEPA. 1986a. Superfund Public Health Evaluation Manual (SPHEM). U.S. Environmental Protection Agency. Office of Emergency and Remedial Response. Washington, D. C.; EPA 540/1-86/060.

USEPA. 1986b. Guidelines for the Health Assessment of Suspect Developmental Toxicants. U.S. Environmental Protection Agency. Office of Health and Environmental Assessment, Washington, D. C.; 51 FR 34028.

USEPA. 1986c. Guidelines for the Health Risk Assessment of Chemical Mixtures. U.S. Environmental Protection Agency. [51 FR 34014].

USEPA. 1986d. Guidelines for Estimating Exposures. U.S. Environmental Protection Agency. U.S. Environmental Protection Agency. [51 FR 34042].

USEPA. 1988a. Reposed Guidelines for Assessing Female Reproductive Risk U.S. Environmental Protection Agency. Office of Health and Environmental Assessment, Washington, D.C. 53 FR 24834.

USEPA. 1988b. Proposed Guidelines for Assessing Male Reproductive Risk. U.S. Environmental Protection Agency. Office of Health and Environmental Assessment, Washington, D.C. 53 FR 24850.

USEPA. 1988c. Superfund Exposure Assessment Manual (SEAM). U.S. Environmental Protection Agency. Office of Remedial Response, Washington, D.C. EPA 540/1-88/001.

USEPA. 1988d. Recommended Procedures for Implementation of Superfund Risk Assessment Guidelines. U.S. EPA Region IX. In. Exposure Assessment at Superfund Sites. U.S. Environmental Protection Agency, Environmental Monitoring Systems Laboratory. Las Vegas, NV. EPA 600/X-89/381. December 1989.

USEPA. 1988e. Guidance for Conducting Remedial Investigations and Feasibility Studies Under CERCLA U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. OSWER Directive 9355.34)1.

USEPA. 1989a. Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual (Part A) (RAGS). U.S. Environmental Protection Agency. Office of Emergency and Remedial Response, Washington, D.C.; EPA 540/1-89/002.

USEPA. 1989b. Exposure Factors Handbook. U.S. Environmental Protection Agency. Office of Health and Environmental Assessment, Washington, D.C. EPA 600/8-89/043.



USEPA. 1989c. Supplemental Manual to Risk Assessment Guidance for the Superfund Program. U.S. Environmental Protection Agency. U.S. EPA Region I. EPA 901/5-89401.

USEPA. 1989d. Exposure Assessment at Superfund Sites. U.S. Environmental Protection Agency, Environmental Monitoring Systems Laboratory, Las Vegas, NV. EPA 600/X-89/381.

USEPA. 1989e. "Background Information Document-Environmental Impact Statement for NESHAPs Radionuclide. Volume 1. Risk Assessment Methodology," U.S. Environmental Protection Agency. EPA/520/1-89-005.

USEPA. 1990a. National Oil and Hazardous Substances Pollution Contingency Plan. U.S. Environmental Protection Agency. [55 FR 8666].

USEPA. 1990b. Guidance for Data Useability in Risk Assessment Interim Final. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/G-90/008, October 1990.

USEPA. 1991a. Guidelines for Developmental Toxicity Risk Assessment. Final. U.S. Environmental Protection Agency. Office of Health and Environmental Assessment, Washington, D.C. 56 FR 63798.

USEPA. 1991b. Supplemental Guidance to RAGS: Standard Default Exposure Factors. U.S. Environmental Protection Agency. Office of Emergency and Remedial Response, Washington, D. C.; OSWER Directive: 9285.6-03.

USEPA. 1991c. Exposure Assessment Methods Handbook. Exposure Assessment Group. U.S. Environmental Protection Agency. Office of Health and Environmental Assessment, Washington, D.C. EPA 600/2-91

USEPA. 1991d. Guidance for Risk Assessment. In: Guidance on Risk Characterization for Risk Managers and Risk Assessors. Memorandum from F. Henry Habicht II to Assistant and Regional Administrators, U.S. Environmental Protection Agency, Office of The Administrator, Washington, D. C.; (February 26, 1992).

USEPA. 1991e. Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual (Part B, Development of Risk-based Preliminary Remediation Goals). U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D. C.. OSWER Directive 9285.7-01B, December 1991.

USEPA. 1991f. Accelerating Superfund Cleanups and Evaluating Risk at Superfund Sites. In: Superfund 30-Day Task Force Report. U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. Washington, D. C..

USEPA. 1992a. Guidelines for Exposure Assessment, U.S. Environmental Protection Agency. [57 FR 22888].



Chapter 3: Exposure and Dose

3.1 Introduction

To characterize risk assessors compare exposure intakes with toxicity values. Historically, these calculations have relied on divergent definitions of exposure and dose (USEPA, 1986a; 1992a). CERCLA guidance documents have consistently defined exposure as contact with a chemical or physical agent (e.g., USEPA, 1986b, 1989a, 1992a). However, the terminology used in defining the point of contact where exposure takes place is inconsistent and has led to ambiguity in the use of terms and units for estimating the magnitude of exposure. This has resulted in calculational disparities of risk levels. This chapter provides an overview of the evolution and use of the terms exposure and dose, the issues associated with calculating exposure and dose according to these changing definitions, and approaches that DOE assessors could take when engaging regulators in a dialogue on calculating exposure and dose as outlined in EPA guidelines.

3.2 Discussion of Exposure and Dose in Statutes, Regulations, and Guidelines

3.2.1 Statutes and Regulations

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) of 1980, the Superfund Amendments and Reauthorization Act (SARA) of 1986, and the National Oil and Hazardous Substances Pollution Contingency Plan (NCP) of 1985 and its revisions in 1990 (USEPA, 1985a; 1990) are the statutes and regulations that establish the broadly defined goal of reducing and mitigating human exposures to hazardous wastes. The statutes and regulations are implemented by guidelines published in Guidance on Remedial Investigations Under CERCLA (RI) (USEPA, 1985b) and Guidance on Feasibility Studies Under CERCLA (FS) (USEPA, 1985c), later consolidated as Guidance for Conducting Remedial Investigations and Feasibility Studies Under CERCLA (RI/FS) (USEPA, 1988a) to reflect the SARA amendments made to CERCLA in 1986.

CERCLA, SARA, NCP, and the RI/FS documents do not provide specific guidance on how to conduct baseline risk assessments and, as such, do not define exposure or dose. The documents provide general directives regarding risk assessments:

- CERCLA was amended by SARA to “assure, to the maximum extent feasible, that the system accurately assesses the relative degree of risk to human health.”
- The NCP of 1985 indicated that CERCLA investigations should consider “the assessment of the population at risk, the routes of exposure, and the amount, concentration, hazardous properties, and environmental fate and transport of the substances present.”



- The NCP of 1990 states that exposure assessments be conducted “to identify the magnitude of actual or potential human or environmental exposures, the frequency and duration of those exposures, and the routes by which receptors are exposed.”

3.2.2 Guidelines

The risk assessment guidance documents that were developed to support the RI/FS process discuss exposure and dose issues in detail. This section focuses on the evolution of the definition of exposure and dose through these guidelines. Guidance on how to conduct CERCLA risk assessments was initially provided in the Superfund Public Health Evaluation Manual (SPHEM) (USEPA, 1986b). Later, SPHEM was revised and published as Risk Assessment Guidance for Superfund (USEPA, 1989a). In addition to SPHEM and RAGS, EPA developed further guidance supporting CERCLA risk assessments, such as the Superfund Exposure Assessment Manual (SEAM) (USEPA, 1988b), the Exposures Factors Handbook (EFH) (USEPA, 1989b), and exposure assessment guidelines (USEPA, 1986a; 1992a). In between these important guidelines have been other documents in which exposure and dose are addressed. Following is an overview of these EPA documents and guidelines, which are listed in chronological order.

Guidelines for Estimating Exposures

The Federal Register of September 24, 1986, [51 FR 34042] published the final EPA Guidelines for Estimating Exposures, as well as the responses to comments by the public and the EPA Scientific Advisory Board (SAB) on the guidelines. The guidelines, which provide a framework for performing exposure assessments, defined exposure as “the contact with a chemical or physical agent” (USEPA, 1986a). The agency defended this definition as the definition used by the Committee E-47, Biological Effects and Environmental Fate of the American Society for Testing and Materials (ASTM). According to EPA, the magnitude of exposure should be determined by measuring or estimating the amount of an agent at the exchange boundaries (i.e., lungs, gut, skin) during some specified time. EPA also stated in the guidelines that “contact between the subject of concern and the agent may lead to the intake of some of the agent,” and that “if absorption occurs, this constitutes an uptake (or an absorbed dose).”

Superfund Public Health Evaluation Manual (SPHEM)

SPHEM provided detailed guidance on how to conduct a public health evaluation at a CERCLA site (USEPA, 1986b). SPHEM indicated that its exposure assessment procedures were the result of earlier draft guidelines which also provided additional scientific background. Exposure assessment is defined in SPHEM as “an estimation of the probable dose of a substance to a target population.” Exposure is expressed as “intake,” defined as the “amount of substance taken into the body per unit body weight per unit time.” Intake is used instead of dose because the information required to estimate dose is often unavailable: “To estimate dose, information indicating the amount of a chemical that may be absorbed (e.g., across lung or GI tract lining or through the skin) and subsequently distributed to target organs or tissues would be needed.”



Superfund Exposure Assessment Manual (SEAM)

SEAM (USEPA, 1988b) provided specific methodologies for estimating contaminant release, environmental fate and transport, and human exposure to contaminants emanating from hazardous waste sites. Developed to give consistency in conducting exposure assessments at CERCLA sites within the framework provided by SPHEM, SEAM compiled and integrated a host of medium- and setting-specific techniques published by EPA and others. SEAM was the first document to present a fully integrated body of specific estimation methods that, as a whole, addresses the range of possible exposure settings that may need to be evaluated at an uncontrolled hazardous waste site.

SEAM defines exposure as “the amount of pollutant contacting body boundaries (skin, lungs, or intestinal tract).” Estimates of exposure are expressed in mass of contaminant per unit of body mass per day.

The Exposure Factors Handbook (EFH)

The EPA’s guidelines for estimating exposures, as delineated in SEAM, were expanded and improved in the Exposure Factors Handbook (USEPA, 1989b). The handbook, intended to serve as a support document to the 1986 EPA's Guidelines for Estimating Exposures, provides basic equations for estimating exposure for various exposure scenarios. Exposure is defined in EFH as “the contact with a chemical or physical agent.” The magnitude of the exposure is calculated as “the amount of the agent available at human exchange boundaries (skin, lungs, gut) during some specified time.”

EFH indicates that exposure may also be referred to as “administered dose.” Since the dose/response curve is derived from animal toxicological studies on the basis of the administered dose, EFH recommends that exposure should be expressed on a comparable basis.

EPA Region I Supplemental Guidance

EPA Region I (Connecticut Maine, Massachusetts, New Hampshire, Rhode Island, Vermont) released the Region I Supplemental Manual to Risk Assessment Guidance for the Superfund Program (USEPA, 1989c). EPA Region I guidance differentiates “exposure point concentration,” which is “the amount of chemical in an environmental medium to which one may be exposed and “exposure dose,” which is “a term used to describe the resulting exposure from a particular concentration.” Exposure dose was also noted in the EPA Region I guidance as being “similar to the administered dose of a laboratory experiment from which cancer potency factors and reference doses are usually derived.”

Risk Assessment Guidance for Superfund, Volume I (RAGS)

RAGS (USEPA, 1989a) constitutes the present conceptual framework for CERCLA risk assessments. The exposure assessment process and the quantification of exposures is delineated in RAGS as follows “The exposure assessor calculates chemical-specific exposures for each exposure pathway. Exposure estimates are expressed in terms of the mass of substance in contact with the body per unit body



weight per unit time. These exposure estimates are termed intakes and represent the normalized exposure rate (equivalent to intake).”

RAGS contains several definitions associated with exposure and dose. Following is a list of these definitions.

- Absorbed Dose: The amount of a substance crossing the exchange boundaries (e.g., gut, lung, skin) after contact. It is calculated from the intake and the absorption efficiency for that particular chemical. The absorbed dose is equivalent to intake’ multiplied by the absorption factor.
- Administered Dose: The mass of a substance purposely given to a test organism that is in contact with an exchange boundary (e.g., gut) per unit body weight per unit time. Administered dose is equivalent to intake.
- Applied Dose: The amount of a substance purposely given to a test organism for dermal toxicity experiments.
- Exposure: Contact of an organism with a chemical or physical agent at the exchange boundaries of the organism (e.g., skin, lungs, gut) and available for absorption. It is quantified as the amount of substance at the exchange boundary.
- Intake: This is termed the normalized exposure rate, and is expressed as the mass of a substance in contact with the exchange boundary per unit body weight per unit time (e.g., mg chemical per kg body weight per day). It is also equivalent to administered and applied dose.

Exposure Assessment Methods Handbook (EAMH)

The Exposure Assessment Methods Handbook (USEPA, 1991) was published to provide guidance to exposure assessors on methodologies to estimate concentrations of chemicals in the environment. EAMH also provides an overview of the exposure assessment process, where it defines exposure and dose in a manner consistent with the EFH. Both documents abide by the definitions set forth in the 1986 exposure guidelines, where exposure is defined as “contact with a chemical or physical agent,” and the magnitude of exposure is defined as “the amount available at the exchange boundaries (skin, lungs, gut)” (USEPA, 1986a).

EAMH equates the term “exposure” with the term “administered dose”: “For most exposure assessments, the dose is estimated based on external exposure because the human/animal toxicological data used in combination with exposure data to calculate risk are most frequently based on administered dose or ambient exposure rather than internal dose.” However, the EAMH recommends that when calculating exposure estimates incurred from different exposure routes, “the absorbed dose is the desired common denominator for different routes.” EAMH refers to absorbed dose as “a function of the degree of



penetration through and chemical transfer across barriers (e.g., skin) and membranes (e.g., the lining of the lung) that the chemical contacts.”

Dermal Exposure Assessment: Principles and Applications (DEAPA)

Dermal Exposure Assessment: Principles and Applications (USEPA, 1992b) addressed the quantification of human risks due to dermal exposures. This document defines exposure as “the contact between a contaminant and the external boundary of an organism.” However, this document states that dermal exposure assessments are defined as “including the estimation of absorbed doses from contaminants contacting the skin.”

DEAPA indicates that dose estimates are needed in dermal exposure assessments because ‘oral dose-response relationships and toxicity reference values are based on the “potential (i.e., administered) dose,” whereas the dermal dose estimates are based on the absorbed dose. This document also remarks that the cancer slope factors and RfDs used in CERCLA risk assessments are based on toxicological studies of ingestion or inhalation exposure, not dermal exposure.

Guidelines for Exposure Assessment

These guidelines (USEPA, 1992a), published in response to recommendations from EPA's SAB and the general public, superseded and replaced the Guidelines for Estimating Exposures (USEPA, 1986a) and Proposed Guidelines for Exposure-Related Measurements (USEPA, 1988c). The guidelines convey the principles of exposure assessments and constitute the current theoretical framework to be used in the Superfund program. The goal of the document is to outline a method of calculating human exposures to contaminants from hazardous waste sites that is “a more realistic approach to exposure determination.”

EPA acknowledged that the terminology in previous exposure guidelines raised concerns regarding inconsistencies in defining the point at which exposure occurs on the body. As a result of the review by the public and SAB, EPA revised both the definition and usage of these terms in order to be in accordance with definitions “suggested by the National Academy of Sciences.” Definitions of the following terms are included in the document:

- Exposure: Contact of a chemical, physical, or biological agent with the outer boundary of an organism. Exposure is quantified as the concentration of the agent in the medium in contact with the organism integrated over the time duration of the contact. Exposure is calculated using monitoring data and models.
- Dose: The amount of a substance available for interaction with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism. Administered Dose is the amount of a substance given to a test subject (human or animal) through ingestion or inhalation to determine dose-response relationships. In exposure assessment, because exposure to chemicals is usually inadvertent, this quantity is called potential dose. Potential Dose is the amount of a chemical contained in material ingested, air breathed, or bulk material applied to the skin. Applied Dose is the amount of a



substance in contact with the primary absorption boundaries of an organism (e.g., skin, lung, gastrointestinal tract) and available for absorption (although not necessarily having yet crossed the outer boundary of the organism). Absorbed Dose is the amount of a substance crossing a specific absorption barrier (e.g., the exchange boundaries of the skin, lung, and digestive tract) through uptake processes. Internal Dose is the amount of a substance penetrating across the absorption barriers (the exchange boundaries) of an organism, via either physical or biological processes, without respect to specific absorption barriers or exchange boundaries. This term is synonymous with absorbed dose. The amount of the chemical available for interaction by any particular organ or cell is termed the Delivered Dose for that organ or cell. The administered, potential, and applied doses incorporate intake rate into their values for oral and inhalation exposures. Dermal doses are calculated differently as explained in Section 3.3.2.

3.3 Issues and Regulator Dialogue

3.3.1 Exposure/Dose Issues

Because of the uncertainties inherent to the sciences supporting the risk assessment process, the relationship between exposure and dose is sometimes unclear. The following issues are illustrative.

Semantic Ambiguities in Exposure/Dose Terminology

Review of CERCLA guidance documents revealed that exposure has always been defined in CERCLA exposure assessments as contact with the chemical or agent (e.g., USEPA, 1986a, 1989a, 1992a). However, the terminology used in defining the point of contact where exposure takes place is inconsistent and has led to ambiguity in the use of terms and units for estimating the magnitude of exposure. Specifically, exposure can be conceptualized as occurring:

Scheme (1): at the exchange boundaries (skin, lungs, gastrointestinal tract), or

Scheme (2): at the visible exterior of a person (skin, mouth, nostrils).

If an exposure assessor follows Scheme (1), ingestion of water is considered an exposure under the old definition; following Scheme (2), that same water ingestion is considered an exposure under the current definition. The choice of either scheme implies that different units be used under the old definition exposure is expressed as the mass of the chemical times the intake rate (e.g., milligrams of chemical/liters of water x liters of water ingested/day x days exposed); under the present definition, exposure is expressed as a concentration of chemical per unit of time (e.g., milligrams of chemical/liters of water x minutes of contact). The old definition of exposure, Scheme (1), is now considered to equate with administered, potential, and applied dose.

The exposure assessment guidelines published in 1992 changed EPA's definition of exposure from "contact with the exchange boundaries (skin, lungs, gastrointestinal tract)" to "contact with the visible exterior of a person (skin, mouth, nostrils)" (USEPA, 1992a). EPA decided to define exposure as contact



with the visible exterior of the person based on comments received from the general public and the scientific community on previous guidelines. The chosen definition is in contrast with the previous view of exposure as “contact with exchange boundaries where contaminants are actually absorbed (skin, lungs, gastrointestinal tract)” (USEPA, 1986a).

Inconsistent Exposure/Dose Calculations

Inconsistencies in conceptualizing exposure and dose are not just restricted to semantic ambiguities; they are intrinsic to how exposure and dose are calculated. According to the 1992 exposure assessment guidelines, defining exposure as contact with the visible exterior improves consistency in quantitative risk assessments. The toxicity values are often derived from dose-response relationships generated in toxicological studies where the chemical under study is administered to animals. That is, toxicity values incorporate intake rate into the value. According to USEPA (1992a) “estimates of doses should be expressed in a manner that can be compared with available dose-response data.” The comparison can be made for oral and inhalation exposures after the exposures have been adjusted by the intake rate for that chemical. This adjustment by intake rate is the calculation used to convert oral and inhalation exposures to potential or applied doses. Skin exposure comparisons are discussed in the next section. RAGS recommends the following consistency checks:

1. Averaging period of exposure: Estimated exposure duration should be similar to duration of the toxicological study from which a chemical-specific risk value is derived (i.e., use of subchronic toxicity values to evaluate short-term exposures).
2. Exposure route: Toxicity values used for each pathway should be consistent with exposure route (e.g., oral toxicity values should be consistent with ingestion, inhalation values with respiratory exposures, etc.).
3. Absorption adjustments: Toxicity values and exposure estimates should be expressed as either absorbed doses or as exposure intakes. Except for dermal exposures, exposures are expressed as intakes.

The EPA IRIS database contains the currently available toxicological values to be used in CERCLA risk assessments. Because the IRIS database lacks comprehensive toxicological information for various chemicals (or mixtures of chemicals), often the risk characterization cannot follow the three consistency checks delineated in RAGS. For example, regarding the first check, less-than-lifetime exposures are converted to equivalent lifetime exposures for cancer risk, and chronic RfDs are used in the absence of short-term toxicity values. In relation to the second check, in the absence of inhalation toxicity values the recommendation is to extrapolate from oral toxicity values. Regarding the final check many oral RfDs and slope factors assume ingestion in water, even when toxicity values were derived from studies employing administration in oil by gavage or in feed. Most CERCLA risk assessments encounter various toxicological data gaps requiring extrapolations that may result in inconsistent calculations of dose or exposure.



3.3.2 Regulator Dialogue

EPA has acknowledged that the terms “exposure” and “dose” were defined inconsistently in various agency documents and guidelines. This raised concerns regarding inconsistencies in defining the point at which exposure occurs on the body (USEPA 1992a). The current acceptable terminology in CERCLA risk assessments is delineated in Guidelines for Exposure Assessment (USEPA 1992a):

- Dose: The amount of a substance available for interaction with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism.
- Exposure: Contact of a chemical, physical, or biological agent with the outer boundary of an organism.

As explained above, intake rates are used to calculate potential or applied doses for inhalation or oral exposures. The risk assessor uses professional judgement to determine which intake rates to use in calculating doses. Any intake rate can be negotiated so long as it can clearly be defended as appropriate for use at that site. Some default intake rates used are overly conservative. For example, the drinking water intake rate of 2 L/day is based on the U.S. Army rate for soldiers in the field. This scenario is generally not applicable for Superfund sites. EFH (USEPA, 1989b) states “the Agency believes that a water consumption rate of 2 L per day is an overestimate for most people.”

Exposures are estimated using monitoring data and models. The choice of models, and the variables used in the models are determined by the risk assessor. As with intake rates, any model or variable can be negotiated with EPA so long as it can clearly be defended as appropriate for use at that site. The models given in EPA guidance documents are examples of models that can be used, but the risk assessor is not required to use those particular models and/or model variables. EAMH (USEPA, 1991) states that the document “should help improve the consistency with which exposure assessments are conducted across the Agency, but still allow different approaches that may be appropriate based on considerations of policy, precedent, or other factors.” The effect that conservative default values have on the risk assessment is discussed in detail in Chapter 9.

The chemicals of concern in CERCLA sites are usually contained in air, ground water, surface water, soils, and/or sediments. Exposure concentration is calculated as the concentration of the chemical of concern at the point of contact, over a period of time. The guidelines suggest meaningful comparisons between exposure calculations and toxicological values. But while the advice for consistent comparisons is warranted as a precautionary matter, the limitations of the available toxicity data can still hinder the characterization of risk. For example, dermal risk levels in CERCLA risk assessments frequently are calculated using oral-derived toxicity values because the reference doses derived from dermal exposure experiments are often unavailable. The resulting trans-pathway calculation introduces additional uncertainty into the risk assessment.

To calculate an exposure intake and compare it to toxicity values, exposure assessors use the term “potential dose,” which is defined as the amount of the chemical ingested, inhaled, or applied to the skin (USEPA, 1992b). Although potential dose simplifies the conceptualization of dose, there are implications



to its use, particularly in dermal exposures where absorption is an uptake across the outer boundary. Potential dose in dermal exposures includes the amount of the chemical in the total amount of the medium contacting the skin. This differs from applied dose, which is the amount of the chemical in the layer actually touching the skin. The exposure guidelines warn that calculations of potential or applied dose may not be useful where there is immersion in a fluid such as water.

Consider two dermal exposure (immersion) situations in which the subject is exposed to contaminated surface water. In the first scenario, the subject is exposed while taking a bath in water obtained from a contaminated river. In this case, the assessor may conservatively assume that the individual may be exposed to all of the mass of contaminant in the tub full of bath water, and both the contaminant concentration as well as the total amount of water potentially contacting the body (i.e., the total number of gallons in the tub) can be quantified with confidence. In the second scenario, however, the subject is exposed while swimming in a lake. Although the contaminant concentration is the same in both cases, the maximum amount of water to which the individual may be exposed while swimming is unknown. It seems logical to assume that the swimmer is exposed to a constantly replaced film of contaminated water, but the total mass of the contaminant available for exposure cannot be defined as the total mass of the contaminant in the lake because it is unlikely that the swimmer would contact all the contaminant in the lake.

The problem cited above traditionally was resolved by defining exposure differently for the two scenarios. In the first case, the assessor would conservatively assume that the total mass of contaminant in the bath water is available for exposure, and calculate the magnitude of exposure as a potential dose, (i.e., as a function of contaminant concentration and amount of water applied to the skin). In the second case, the scenario cannot be described as a potential dose (because the swimmer did not contact all the contaminant in the lake), or as an applied dose (because the boundary layer is being constantly renewed). Instead, the scenario is conceptualized as a flux of a contaminant across the skin. Thus, exposure became a function not of concentration and water mass, but of concentration and exposure time. That approach frequently was frustrated by a lack of chemical-specific absorption factors, however, and the absorption rate of pure water was often used as a default value.

The calculation of dermal exposures differs from oral and respiratory exposures because the skin is considered both an exchange boundary and an outer boundary. As indicated in the hypothetical situations described above, the calculation of risks from dermal exposures is dependent on how the exposure scenarios are crafted. When addressing dermal exposure routes, Dermal Exposure Assessment: Principles and Applications (USEPA, 1992a) should be consulted as it contains information pertinent to developing exposure scenarios, and recent information on chemical-specific absorption factors. Overly conservative default absorption factors, such as 50 percent or 100 percent, should not be used in BRAs unless it is shown that the chemical in question actually is absorbed at such high rates.

3.4 References

USEPA. 1985a. National Oil and Hazardous Substances Pollution Contingency Plan. U.S. Environmental Protection Agency. [50 FR 47912].



- USEPA. 1985b. Guidance on Remedial Investigations Under CERCLA. U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. Washington, D.C. EPA 540/G-85/002.
- USEPA. 1985c. Guidance on Feasibility Studies Under CERCLA. U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. Washington, D.C. EPA 540/G-85/003.
- USEPA. 1986a. Guidelines for Estimating Exposures. U.S. Environmental Protection Agency. [51 FR 34042].
- USEPA. 1986b. Superfund Public Health Evaluation Manual. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/1-86/060.
- USEPA. 1988a. Guidance for Conducting Remedial Investigations and Feasibility Studies Under CERCLA. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. OSWER Directive 9355.3-01.
- USEPA. 1988b. Superfund Exposure Assessment Manual. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response, Washington, D.C. EPA 540/1-88/001.
- USEPA. 1988c. Proposed Guidelines for Exposure-Related Measurements. U.S. Environmental Protection Agency. Washington, D.C. [53 FR 48830].
- USEPA. 1989a. Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual “ (Part A) (RAGS). U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/1-89/002.
- USEPA. 1989b. Exposure Factors Handbook. U.S. Environmental Protection Agency, Office of Health and Environmental Assessment. Washington, D.C. EPA 600/8-89/043.
- USEPA. 1989c. Supplemental Manual to Risk Assessment Guidance for the Superfund Program. U.S. Environmental Protection Agency, Region I. EPA 901/5-89-001.
- USEPA. 1990. National Oil and Hazardous Substances Pollution Contingency Plan. U.S. Environmental Protection Agency. Washington, D.C. [55 FR 8666].
- USEPA. 1991. Exposure Assessment Methods Handbook. U.S. Environmental Protection Agency, Exposure Assessment Group, Office of Health and Environmental Assessment. Washington, D.C. EPA 600/2-91.
- USEPA. 1992a. Guidelines for Exposure Assessment. U.S. Environmental Protection Agency. [57 FR 22888].



USEPA. 1992b. Dermal Exposure Assessment Principles and Applications. U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Office of Research and Development Washington, D.C. EPA-600/8-91/011F.



Chapter 4: Estimation of Average and Upper-End Risk

4.1 Introduction

Exposure assessments evaluate scenarios that are a combination of facts, data, assumptions, inferences, and professional judgments about environmental settings, contaminant characterization exposure pathways, population characterization, and contaminant intake rates. The contaminant concentration, the intake rate, and the duration of exposure are the primary variables in quantitative exposure assessments. The general exposure intake equation is delineated as follows:

$$\text{Exposure Intake} = \frac{C \times IR \times EF \times ED}{BW \times AT}$$

where:

C = Contaminant Concentration

IR = Intake/Contact Rate

EF = Exposure Frequency

ED = Exposure Duration

BW = Body Weight

AT = Averaging Time

Human health risk assessments conducted under the EPA Superfund program have historically made conservative exposure assumptions when assigning numerical values to these key variables in order to be protective of public health (CEQ, 1985; USEPA, 1986a). The calculation of conservative estimates of risk reflects the complexities of natural systems and the limitations of science in characterizing risk. The evolution of CERCLA public health risk assessments has been driven by the recognition that uncertainties are inherent in the estimation of human health risks and by the incremental gain of knowledge and experience on how exposure assumptions affect the timely completion of the CERCLA process.

EPA recognized that there needed to be a full characterization of risk for risk assessments to be perceived as a reliable tool for informative decisionmaking, and thus heighten their credibility. This meant that assessors would need to associate numerical estimates with a discussion of the level of confidence in the exposure estimates for key exposure pathways and related assumptions (USEPA, 1992a). Over the years CERCLA guidance began to use the following loosely defined terms to describe risks and exposure scenarios

- reasonable maximum exposure (RME),



- reasonable worst case,
- worst case, and
- maximum exposed individual (MEI)

This section provides an overview of the use and evolution of these terms and the associated statutes and regulations from which they derived.

4.2 Discussion of Estimation of Average and Upper-End Risk in Statutes, Regulations, and Guidelines

4.2.1 Statutes and Regulations

CERCLA, SARA, and the 1985 NCP (USEPA, 1985a) did not define or discuss any of the above terms. The 1990 revisions to the NCP (USEPA, 1990) directed that Superfund cleanup decisions be based on RME estimates, which are based on “likely scenarios for those individuals near a site that would receive the greatest exposure.” According to the 1990 NCP, the goal of the RME concept is to combine upper-bound and mid-range exposure factors so that the resulting exposure scenario is “protective and reasonable, not the worst possible case.” The NCP did not discuss which values should be average or 95th percentile, or how to mix them.

4.2.2 Initial CERCLA Exposure Assessment Guideline Conceptual Framework

As mentioned previously, guidance on how to conduct CERCLA risk assessments was initially provided in the Superfund Public Health Evaluation Manual (SPHEM) (USEPA, 1986a) and the Superfund Exposure Assessment Manual (SEAM) (USEPA, 1988a). These two supporting documents provided the initial exposure assessment conceptual framework for CERCLA activities.

Superfund Public Health Evaluation Manual (SPHEM)

SPHEM provides detailed guidance on how to conduct a public health evaluation at a Superfund site. Exposure assessment is defined as an estimation of the probable dose of a substance to a target population. Because the actual dose received by actual people is generally uncertain, the exposure assessment requires the use of complex exposure models that are based on incomplete knowledge of how hazardous substances are transported and undergo transformation in the environment and how they affect human health. SPHEM indicates that the most appropriate models for Superfund sites are “simple environmental fate models using conservative (i.e., reasonable worst case) assumptions.” No definition is given to what is meant by “reasonable worst case.”

SPHEM states that “the Superfund risk assessment process is based on concern’ for both individual risk and risk to exposed populations” and recommends that “an exposure point that should be evaluated for an exposure pathway is the geographic point of highest individual exposure.” While SPHEM does not define or specifically show how to estimate a “highest individual exposure,” it recognizes the following approaches during the calculation of exposure points:



- one approach would calculate a single conservative measure of risk (“use a conservative, not necessarily worst-case, approach in making the assumptions”);
- another approach would require two measures of risk described as “best estimates and conservative upper bound estimates”; and yet,
- another approach, “more complex and time consuming than a deterministic approach” would be to “model the important variables determining chemical concentration and risk stochastically” and provide an “estimation of a risk distribution, from which median and 90th percentile (or other upperbound) values can be determined.”

Exposure assessments performed under SPHEM were directed toward using the second approach (i.e., estimating a range of exposure scenarios a “best estimate” and an “upper-bound” scenario). The best estimate was quantified using the average concentration of the detected contaminant concentrations and conservative default values and exposure assumptions. The upper-bound estimate was quantified using the maximum detected contaminant level in a specific medium at a site and the most conservative default values and exposure assumptions related to a hypothetical highest individual exposure. According to SPHEM, this approach would provide “not only an estimate of the risk magnitude but also a good indication of the overall uncertainty of the analysis” (USEPA, 1986a).

Superfund Exposure Assessment Manual (SEAM)

SEAM provided guidance for assessing contaminant release, environmental fate and transport, and human exposure to contaminants emanating from hazardous waste sites. SEAM was developed to support consistency in conducting exposure assessments at Superfund sites. It compiled and integrated various methodological approaches published by EPA and others.

SEAM recognizes that the approach to conducting exposure assessments is conservative: “While it is traditional in exposure assessments to make conservative assumptions in the absence of data, such assumptions must be reasonable.” However, it warns of the possibility that multiple conservative assumptions may result in extreme and unrealistic assessment “Use of reasonably conservative assumptions at each step may produce cumulative assessment results that are overly conservative and thus unreasonable.”

On communicating the uncertainty associated with the estimated level of risk, SEAM recommends including a standard deviation or the 95% confidence limit. As indicated in the earlier Guidelines for Estimating Exposures, SEAM also suggested that further research was needed on the use of a distributional approach to characterize exposure uncertainty.

Both SPHEM and SEAM employ terms such as “reasonable” and “best estimate,” but they do not practically define those terms other than suggesting the use of professional judgement in choosing the various exposure variables and in warning of cumulative effects of using conservative values. Although SPHEM and SEAM were published with the intention of performing more consistent Superfund risk assessments, the use of undefined subjective terms created contradictory interpretations among risk assessment personnel and across EPA programs and regions. For example, responding to public comments



expressing concerns that worst-case estimates would be used when data are limited or absent, the EPA stated in Guidelines for Estimating Exposures (USEPA, 1986b) that “The Guidelines do not encourage the use of worst-case assessments, but rather the development of realistic assessments based on the best data available. However, the Agency will err on the side of public health when evaluating uncertainties when data are limited or nonexistent.”

The 16th Annual Report of the Council on Environmental Quality (CEQ, 1985) described EPA's overall strategy as “inefficient and unable to solve environmental problems.” The report argues that the cause originates in part in the “uncertainty of the scientific basis for action.” The CEQ also observes that policymaking at EPA was dominated by cancer control “not only because it is dreaded and widespread, but because a peculiarity of risk assessment, the inability to set a threshold dosage for carcinogens, insures that when some exposure is found, some risk can be calculated.”

4.2.3 Overcoming Initial Guidance Conceptual Framework Limitations

SARA promulgated amendments to CERCLA'S hazard ranking system in effect since September of 1984 to “assure, to the maximum extent feasible, that the system accurately assesses the relative degree of risk to human health.” SARA'S push for more accurate human health risk assessments is reflected in the establishment of various EPA programs, in the revision of the RI and FS program, and in the publication of Risk Assessment Guidance for Superfund, Volume I (RAGS) (USEPA, 1989a) and the Exposure Factors Handbook (EFH) (USEPA, 1989b).

In 1988, the RI/FS document, which reflected amendments made to CERCLA in 1986, stated the following about exposure assessments:

[An exposure assessment] should include not only identification of current exposures but also exposures that may occur in the future if no action is taken at the site... The purpose of this analysis is to provide the decisionmakers with an undemanding of both the current risks and potential future risks if no action is taken. Therefore, as part of this evaluation, a reasonable maximum exposure (RME) scenario should be developed, which reflects the type(s) and extent of exposures that could occur based on the likely or expected use of the site (or surrounding areas) in the future.

Although the RI/FS document was the first document to use the term “reasonable maximum exposure (RME),” guidance for developing an RME scenario was provided later in RAGS.

One of the programs established by EPA was labeled Research to Improve Health Risk Assessments (RIHRA). The program'S primary objective was to identify the factors that produced the variability and uncertainty in Superfund exposure assessments. RIHRA published a report entitled Exposure Assessment at Superfund Sites (USEPA, 1989c). The report observed that “most Regional risk assessment personnel are relying almost exclusively on the SPHEM and SEAM for use in preparing CERCLA risk assessments. Deficiencies in the guidance documents were supplemented by the EPA regions with open scientific literature, communications with EPA headquarters, contractors, etc. In addition, the RIHRA report identified supplemental guidance documents prepared by EPA Regions I and



IX. One of the recommendations in RIHRA is that further guidance was needed on procedures to calculate best estimate and upper-bound concentrations.

EPA Regional Guidance

Responsibility for determining and explaining the guidance rationale for the exposure assumptions fell on the various EPA regional administrators. For instance, EPA Region I (Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont) formed a Risk Assessment Group that released the “Region I Supplemental Manual to Risk Assessment Guidance for the Superfund Program” (USEPA, 1989d). This guidance stated that each selected exposure pathway required the estimation of a range of conditions characterized as the “average case” and “reasonable worst case” scenarios.

- In the average case scenario the exposures would “reasonably occur”; however, Region I recognized that the actual level of upper-bound risk was likely to be higher than the average value reported. The quantification of exposures under this scenario would require combining the arithmetic average values of the detected contaminant concentrations with “reasonably conservative exposure parameters.”
- The reasonable worst case scenario was intended to provide an upper-bound of the possible risk posed by a contaminated site. Region I guidance in this scenario directed analysts to combine maximum detected contaminant concentrations in each medium with “reasonably conservative exposure parameters.”

As with SPHEM and SEAM, the EPA Region I guidance provided for a reportable range of exposure values, but it also called for a greater imperative to communicate and substantiate exposure assumptions and choice of exposure parameters. While no attempt was made to clarify terms such as “reasonable”, Region I guidance provided for a set of default exposure parameters, and recommended more communication with EPA remediation project managers.

Region IX (Arizona, California, Hawaii, Nevada, Commonwealth of the Northern Mariana Islands, Republic of Palau, Federated States of Micronesia, The Republic of the Marshall Islands) developed and published a document entitled Recommended Procedures for Implementation of Superfund Risk Assessment Guidelines (USEPA, 1988b) wherein it recommended that risk estimates be “presented and discussed with language describing the uncertainty.” Region IX also required the calculation of risk levels for three potential exposures

- Maximally Exposed Individual (MEI), defined as the “site of highest potential exposure (regardless of whether this site is inhabited).”
- Maximally Impacted Residence (MIR), defined as “habitation site experiencing the highest estimated potential exposure.”



- Equivalent Exposure Populations (EEP), defined as “populations experiencing roughly equivalent potential risks.” The risks are expressed at order-of-magnitude levels (e.g., 10^{-4} , 10^{-6} , etc.).

Region IX states that the MEI and the worst-case scenario may be useful for screening purposes, not for justifying remediation or setting cleanup levels. Region IX guidelines did not show how to develop the exposure scenarios.

EPA Headquarters Guidance

The Exposure Factors Handbook (EFH). The EPA's guidelines for estimating exposures, as delineated in SEAM, were expanded and improved in the EFH (USEPA, 1989b). The guidelines were developed to promote consistency among the various exposure assessment activities and to standardize exposure assessment calculations. The handbook demonstrates how to apply standard default factors to specific exposure scenarios when site-specific data are not available, and for each scenario, it provides

- basic equations for estimating exposure;
- recommended default values for each parameter in the exposure equations (the default values are presented as averages [intended to represent typical values], ranges [derived from distributions, where possible, basing the lower end on the 50th percentile and the upper end on the 90-95th percentile], and frequency distributions); and
- justification for each recommended value.

The handbook indicates that the recommended default values should be selected to represent a range of scenarios from typical to reasonable worst case, but it recognizes that “EPA does not have an official position on how to define a reasonable” worst case scenario, ...reasonable is a largely subjective term.” EFH recommends using the best scientific judgment when combining lower and upper values to “reduce the possibility of creating an ‘overly worst case’.” Calculating an “absolute worst case” would be useful, however, for the purpose of demonstrating that site risk levels were of no concern.

Risk Assessment Guidance for Superfund. Volume I (RAGS). RAGS (USEPA, 1989a) provides guidance on using the “reasonable maximum exposure” (RME) conceptual framework. RAGS defines RME as the “highest exposure that could reasonably be expected to occur for a given exposure pathway.” RAGS specifically states that the selection of exposure factors in CERCLA exposure assessments should result in “an estimate of the reasonable maximum exposure.” RAGS also indicates that “a determination of “reasonable” cannot be based solely on quantitative information, but also requires the use of professional judgment.”



4.2.4 Further Concerns with Superfund Exposure Assessment Guideline Conceptual Framework

Creation of an EPA Risk Assessment Intra-Agency Group in March of 1990

An EPA intra-agency group was formed in March of 1990 “to address concerns regarding inconsistencies among exposure assumptions in Superfund risk assessments” and released an interim final document entitled Supplemental Guidance to RAGS: Standard Default Exposure Factors (USEPA, 1991a). According to the EPA intra-agency group, the principal reasons for the inconsistencies were as follows:

- factors derived from site-specific data,
- professional judgment when choosing values for key variables, and
- assumptions based on limited data.

The document provides further guidance on which default exposure factors to use when site-specific data are unavailable. The standard set of default values follows the 1990 NCP directive for quantification of exposures under RME scenarios. This supplemental guidance argues that “further guidance is needed on how to calculate a reasonable maximum exposure, because the RME methodology “has been subject to a variety of interpretations.”

Creation of EPA Superfund 30-Day Task Force

A 30-Day Task Force, created as part of a program to improve the effectiveness of the Superfund program, published the report Accelerating Superfund Cleanups and Evaluating Risk at Superfund Sites (USEPA, 1991b). Continuing concerns raised about the Superfund program’s exposure assumptions resulted in a Task Force recommendation for the review of the Superfund risk assessment guidance and policies. The Task Force indicated the need for the exposure assumptions to be reviewed by EPA’s Office of Research and Development the Risk Assessment Council, and the Science Advisory Board, as well as by industry and environmental groups. Review of the Superfund risk assessment guidance and policies has resulted to date in the following publications Guidance for Risk Assessment (USEPA, 1991c); Supplemental Guidance to RAGS: Calculating the Concentration Term (USEPA, 1992b); Guidelines for Exposure Assessment (USEPA, 1992a); and An SAB Report: Superfund Site Health Risk Assessment Guidelines (USEPA, 1993).

4.2.5 Addressing Exposure Assessment Guideline Conceptual Framework Concerns

Guidance for Risk Assessment

This document (USEPA, 1991c) was released as part of a memorandum from EPA Deputy Administrator Henry Habicht. The document directs EPA risk assessments to include the central tendency and the high-end portions of the risk distribution when describing individual risk. “High end” was defined as a risk level “conceptually above the 90th percentile of the actual (measured or estimated) distribution, but not higher than the individual in the population who has the highest risk.” The high-end scenario was to be perceived as an estimation of the exposure level in an actual population, not a bounding estimate



to be perceived as an estimation of the exposure level in an actual population, not a bounding estimate or worst-case scenario. Guidance for Risk Assessment defines bounding estimates of risk as “purposely overestimating the exposure level in order to develop a statement like ‘not greater than...’.” The “worst-case” scenario was defined as a “combination of conditions producing the highest conceivable risk” This guidance recommends that when complete distributions are not available (most cases) the high-end exposure can be estimated by the following:

- Monte Carlo simulation of distributions if there is sufficient information about the variability of factors, or
- by using maximum, or near maximum, values for some variables, and leaving others at their mean values if there is limited information on the distribution of the exposure.

The document did not indicate which variables should be at their maximum or average values. The choice of the actual values was left to the discretion of the risk assessor.

Supplemental Guidance to RAGS: Calculating the Concentration Term

This supplemental guidance (USEPA, 1992b) was designed to help explain how the concentration term in the RME equation is calculated. It defines RME as the “highest exposure that could reasonably be expected to occur for a given exposure pathway.” The concentration term is the result of the calculation of the 95% upper confidence limit (UCL) on the arithmetic average (mean). The 95% UCL is used as an alternative to the maximum detected contaminant value; however, if the sample population size is small (less than 10) the UCL calculation results in a value greater than the maximum detected contaminant concentration. Usually more samples are recommended. If that is not possible, the concentration term defaults to the maximum detected value.

Guidelines for Exposure Assessment

These guidelines, published in response to recommendations from EPA’s SAB and the general public (USEPA, 1992a), superseded and replaced the Guidelines for Estimating Exposures (USEPA, 1986b) and Proposed Guidelines for Exposure-Related Measurements (USEPA, 1988d). The guidelines convey the principles of exposure assessments and constitute the current theoretical principles to be used in the Superfund program. The central theme of the document is to move “toward a more realistic approach to exposure determination.” Explanations of the following terms are included in the document:

- High-end risk: Risks above the 90th percentile of the population distribution, but not higher than the individual in the population who has the highest risk.
- Maximum Exposed Individual (MEI): The individual with the highest exposure in a given population.



- **Maximum Exposure Range:** This refers to the uppermost portion of the exposure distribution; this range falls above the 98th percentile of the distribution, but not higher than the individual with the highest exposure (MEI).
- **Theoretical upper bounding estimate (TUBE):** TUBE was designed to estimate exposure, dose, and risk levels that are expected to exceed the levels experienced by all individuals in the actual distribution. TUBE is calculated by assuming limits for all the factors used to calculate exposure that will provide the highest possible levels of risk (highest concentration, lowest body weight, etc.).
- **Worst case:** This term refers to the maximum possible exposure, dose, or risk conceivable.

The guidelines mentioned that, historically, the MEI and the reasonable worst case scenario have been equated with the worst case or bounding estimate.

An SAB Report: Superfund Site Health Risk Assessment Guidelines

This SAB report was published as a result of an SAB meeting on April 7-8, 1992, in Bethesda, Maryland. The meeting was organized to review key issues related to RAGS. One of these issues was the definition and calculation of the RME. The SAB supports the RME conceptual framework as a better alternative to the use of the MEI scenario previously used. SAB also agrees with EPA on the reasonableness of using the arithmetic mean, as opposed to the geometric mean, for calculating the concentration term in the exposure equations. However, the SAB is recommending Monte Carlo techniques (i.e., probabilistic approach) as an alternative to the UCL estimate on the mean (i.e., develop frequency distributions for each of the variables needed to calculate exposures).

The SAB report of February 1993 indicates that calculating an RME based on the UCL presents conceptual and practical difficulties. The report maintains that the UCL on the arithmetic average concentration at a site may not be equated with a reasonable maximum exposure. The UCL approach works under the assumption that the site is well characterized, and that samples taken are representative of the possible exposures likely to occur. But because of the spatial distribution of contamination (i.e., existence of hot spots) as it relates to the frequency of exposures, assessors may question the reasonableness of the RME scenario. Also, it is difficult to interpret the exposure value after combining the 95% UCL on the arithmetic average concentration at a site with the 50th and 90th percentile for some of the default values. The SAB report of February 1993 recommends that in the absence of further guidance regarding the quantification of exposures at Superfund sites, some type of “most reasonable” estimate of exposure also be calculated along with the RME.

4.3 Issues and Regulator Dialogue

4.3.1 Average and Upper-End Risk Issues

Review of the documents mentioned in the preceding section indicates that the conceptualization of exposure scenarios has required the use of terms that due to their subjective nature, have been



employed under different interpretations. The use of subjective terms to communicate levels of risk to human health from CERCLA sites, and the uncertainty inherent in the estimation of those levels of risk have necessitated the development of supporting guidelines. Specifically, the concept and use of the term RME to frame an exposure scenario indicative of an individual high-end exposure evolved from earlier CERCLA exposure assessment descriptors (i.e., upper bound, MEI, worst case, etc).

Below is a brief summary of how these terms were first used. Section 2 of this chapter describes these documents and the evolution of these terms in more detail.

- SPHEM (USEPA, 1986a): Environmental fate models should use “reasonable worst case” assumptions. Exposure points should use the geographic point of “highest individual exposure.” Exposure assessments should estimate a range of exposure scenarios using an “upper-bound and a “best estimate” scenario.
- SEAM (USEPA, 1988a): The uncertainty associated with the estimated level of risk should include a “standard deviation” or the “95% confidence limit”
- Region IX Guidance (USEPA, 1988b): This guidance required the calculation of risk levels for three potential exposures, “maximally exposed individual”, “maximally impacted residence,” and “equivalent exposure populations.”
- RI/FS (USEPA, 1988c): “Reasonable maximum exposure” was introduced, but guidance on its use did not come until RAGS was published in 1989.
- RAGS (USEPA, 1989a): This was the first document to give specific guidance on the use of the term “reasonable maximum exposure”. RME was defined as the “highest exposure that could reasonably be expected to occur for a given exposure pathway.”
- Exposure Factors Handbook (USEPA, 1989b): Default values are presented as “averages,” “ranges” and “distributions. “ An “absolute worst case” calculation would be useful for demonstrating that the site risk levels were of no concern.
- Region I Guidance (USEPA, 1989d): Each selected exposure pathway required the estimation of a range of conditions characterized as “average case” and “reasonable worst case.” The reasonable worst case scenario was intended to provide an “upper bound of the possible risk.
- NCP (USEPA, 1990): The goal of the RME concept is to combine “upper-bound” and “mid-range” exposure factors so that the resulting exposure scenario is “protective and reasonable, not the worst possible case.”
- Guidance for Risk Assessment (USEPA, 1991c): Directs EPA risk assessments to include the “central tendency” and the “high end portions of the risk distribution. The “worst-



case” scenario was defined as a “combination of conditions producing the highest conceivable risk”

- Guidelines for Exposure Assessment (USEPA, 1992a): Six terms were defined in this document: “high-end risk,” “maximum exposed individual,” “maximum exposure range,” “reasonable worst case,” “theoretical upper bounding estimate,” and “worst case.” High-end risk is defined as being above the 90th percentile of the population distribution, but not higher than the individual with the highest risk. MEI is defined as the individual with the highest exposure in a given population. Maximum exposure range is defined as being above the 98th percentile of the population distribution, but not higher than the individual with the highest risk. Reasonable worst case is defined as covering the 90th to 98th percentile of the distribution. TUBE is designed to estimate exposure, dose, and risk levels that are expected to exceed levels experienced by all individuals in the actual distribution. Worst case refers to the maximum possible exposure, dose, or risk that can conceivably occur, whether or not it actually occurs.
- Supplemental Guidance to RAGS: Calculating the Concentration Term (USEPA, 1992b): Calculating the RME should utilize the “95% upper confidence limit” on the “arithmetic average.”
- Superfund Site Health Risk Assessment Guidelines (USEPA, 1993): The “upper confidence limit” on the “arithmetic average” concentration at a site may not be equated with a “reasonable maximum exposure.” The document recommends that some type of “most reasonable” estimate of exposure also be calculated along with the RME.

The following issues have been identified relating to the conceptual use of the term RME:

Concept of Reasonableness

Although the concept of “reasonableness” was first introduced as a framework to provide more realistic descriptions of risk estimates, it has resulted in conflicting views among various societal groups. The National Resources Defense Council and the Environmental Defense Fund have declared in the popular press that assumptions contained in Supplemental Guidance to RAGS: Standard Default Exposure Factors result in “abandoning the reasonable worst-case scenario” and provides “less protection to the public” (BNA, 1991). However, the Chemical Manufacturers Association indicated that a “30-year exposure duration is a more reasonable assumption than 70 years,” and views the guidance as a “step in the right direction, moving toward a more realistic worst-case assumption” (BNA, 1991). The EPA rationale for the new default values to be used when site-specific information is lacking was designed “to facilitate more consistent evaluation of the risks posed by the Superfund sites,” and the, guidance “attempts to reduce unwarranted variability” (USEPA, 1991a).



Use of Professional Judgement

Associated with the thematic evolution of the RME, and underlying the quantification of exposures, is the use of professional scientific judgement. Indeed, in the absence of site-specific information (e.g., contaminant characterization, exposed population data, etc.), the best choice for the description of the actual exposure and risk outcome is determined by a *combination of factors chosen by the risk assessor*. The improvement of basic research in the various science branches and its application in the environmental field will inevitably lead to the reduction of uncertainty in risk estimates.

4.3.2 Regulator Dialogue

The need at EPA for greater consistency and comparability among various sites has led to the development and evolution of guidance documents that provide agency-wide standard default factors and procedures to be used in the absence of site-specific factors. RME constitutes the current conceptual framework for how exposure assessments are performed under CERCLA risk assessments.

The current RME definition and applicable policies are found in Guidelines for Exposure Assessment (USEPA, 1992a). The “Supplemental Guidance to RAGS: Calculation of the Concentration Term” (USEPA, 1992a). The “Supplemental Guidance to RAGS: Standard Default Exposure Factors” (USEPA, 1991a) may also provide a better understanding of practical issues in the RME. The first document shows how the concentration term in the RME equation is calculated using the 95% UCL on the mean, explains the significance of the RME, and discusses the basic concepts concerning the concentration term. USEPA (1992b) provides the standard default exposure factors to be used in the Superfund program. The exposure factors in this guidance are considered the most appropriate and are intended to be used under the RME scenario.

The representation of risks posed by contaminants in CERCLA sites will continue to evolve to better represent the scientific, as well as the regulatory, consensus. Whether the EPA accepts the representation of risk as a range of exposure value estimates (Habitch’s memo) or as a single value (RME) will be determined by what information the risk manager provides to EPA. The exposure guidelines call for an increased effort to communicate the uncertainty associated with the calculation of risk levels. In discussing the role of exposure characterization, the guidelines state that “risk managers should be given some sense of how exposure is distributed over the population and how variability in population activities influences this distribution” (USEPA, 1992b). The SAB report of February 1993 also recommends that in the absence of further guidance regarding the quantification of exposures at Superfund sites, some type of “most reasonable” estimate of exposure can also be calculated along with the RME.

There have been recommendations for CERCLA risk assessments to consider the use of frequency distributions for the various exposure parameters (probabilistic approach) as an alternative to the use of choosing a single exposure point value for the exposure parameters (deterministic approach). Various key guidance documents, including SPHEM, RAGS, SEAM, and EFH indicated that the probabilistic concept could be a potential alternative; however, EPA has not yet published formal exposure assessment guidance reflecting those recommendations.



Even though EPA has not issued guidance on how to use probabilistic approaches in risk assessments, this does not prevent DOE from using this approach and presenting the results along with the results from the RME scenario. If the probabilistic approach can be shown to be “reasonable,” then these results should be presented as a viable alternative to the RME approach. The uncertainties involved with the probabilistic approach should be clearly discussed in the uncertainties section of the BRA. The negotiation tactics discussed in Section 3.3.2 of this document also apply to the RME scenario presented in this chapter.

4.4 References

BNA. 1991. Environment Reporter. The Bureau of National Affairs Inc., Washington, D.C. pp. 258, May 31, 1991.

CEQ. 1985. Environmental Quality. 16th Annual Report of the Council on Environmental Quality. Washington, D.C.

USEPA. 1985. National Oil and Hazardous Substances Pollution Contingency Plan (NCP). U.S. Environmental Protection Agency. [50 FR 47912].

USEPA. 1986a. Superfund Public Health Exposure Manual. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/1-86/060.

USEPA. 1986b. Guidelines for Estimating Exposures. U.S. Environmental Protection Agency. [51 FR 34042].

USEPA. 1988a. Superfund Exposure Assessment Manual. U.S. Environmental Protection Agency, Office of Remedial Response. Washington, D.C. EPA 540/1-88/001.

USEPA. 1988b. Recommended Procedures for Implementation of Superfund Risk Assessment Guidelines. U.S. EPA Region IX. In: Exposure Assessment at Superfund Sites. U.S. Environmental Protection Agency, Environmental Monitoring Systems Laboratory. Las Vegas, NV. EPA 600/X-89/381. December 1989.

USEPA. 1988c. Guidance for Conducting Remedial Investigations and Feasibility Studies Under CERCLA. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. OSWER Directive 9355.3-01.

USEPA. 1988d. Proposed Guidelines for Exposure-Related Measurements. U.S. Environmental Protection Agency. Washington, D.C. [53 FR 48830].

USEPA. 1989a. Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual (Part A). U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/1-89/002.



USEPA. 1989b. Exposure Factors Handbook. U.S. Environmental Protection Agency, Office of Health and Environmental Assessment- Washington, D.C. EPA 600/8-89/043.

USEPA. 1989c. Exposure Assessment at Superfund Sites. U.S. Environmental Protection Agency, Environmental Monitoring Systems Laboratory, Las Vegas, NV. EPA 600/X-89/381.

USEPA. 1989d. Supplemental Manual to Risk Assessment Guidance for the Superfund Program. U.S. Environmental Protection Agency Region 1. EPA 901/5-89-001.

USEPA. 1990. National Oil and Hazardous Substances Pollution Contingency Plan. U.S. Environmental Protection Agency. [55 FR 8666].

USEPA. 1991a. Supplemental Guidance to RAGS: Standard Default Exposure Factors. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. OSWER Directive: 9285.6-03.

USEPA. 1991b. Accelerating Superfund Cleanups and Evaluating Risk at Superfund Sites. In: Superfund 30-Day Task Force Report- U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. Washington, D.C.

USEPA. 1991c. Guidance for Risk Assessment. In: Guidance on Risk Characterization for Risk Managers and Risk Assessors. Memorandum from F. Henry Habicht II (dated February 26, 1992) to Assistant and Regional Administrators, U.S. Environmental Protection Agency, Office of the Administrator. Washington, D.C.

USEPA. 1992a. Guidelines for Exposure Assessment, U.S. Environmental Protection Agency. [57 FR 22888].

USEPA. 1992b. Supplemental Guidance to RAGS: Calculating the Concentration Term. U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. Washington, D.C. Publication 9285.7-08 1

USEPA. 1993. An SAB Report: Superfund Site Health Risk Assessment Guidelines. Review of the Office of Solid Waste and Emergency Responses Draft Risk Assessment Guidance for Superfund Human Health Evaluation Manual by the Environmental Health Committee. U.S. Environmental Protection Agency, Office of the Administrator, Science Advisory Board Washington, D.C. EPA-SAB-EHC-93-007.



Chapter 5: Chemical Mixtures

5.1 Introduction

The first step in characterizing risk posed by CERCLA sites is to compare estimated exposure intakes with toxicity values for each chemical of potential concern. This determines the likelihood of adverse effects in potentially exposed populations. Risk characterization is done separately for carcinogenic and noncarcinogenic effects because organisms respond differently to exposure from carcinogenic and noncarcinogenic agents (USEPA, 1989; 1990).

For carcinogens, a non-threshold dose-response model is used to calculate a cancer slope factor (the slope of the dose-response curve) for each chemical. EPA uses the linearized, multistage dose-response model in deriving the slope estimates. This model assumes that the dose-response relationship is linear in the low end of the curve (i.e., that the slope factor is a constant and risk is directly proportional to exposure intake).

For noncarcinogens, toxicologists recognize the existence of a threshold of exposure below which there is likely to be no appreciable risk of adverse health impacts. CERCLA guidance documents recommend comparing the estimated exposure intake to the reference dose (RfD) of each chemical of concern (USEPA, 1986a; 1986b; 1989). The RfD is defined as an estimate (with uncertainty spanning an order of magnitude or more) of a daily exposure level for human populations, including sensitive sub-populations, that is likely to be without an appreciable risk of adverse effect over the period of exposure (USEPA, 1989). RfDs are derived in toxicological studies from no-observable-adverse-effects levels (NOAELs) or from lowest-observable-adverse-effects levels (LOAELs), and the application of uncertainty and modifying factors (USEPA, 1989). The ratio exposure intake/RfD is termed the “hazard quotient” (HQ). Unlike the cancer slope factor, the hazard quotient is not a probabilistic measure of risk, but an indicator of the potential for adverse health effects.

Statistical studies performed by the EPA revealed that CERCLA sites contain hundreds of chemicals of potential concern in various media (USEPA, 1990). During a CERCLA risk characterization, assessors base the level of risk to human health from exposure to a multitude of chemicals on the toxic or carcinogenic properties of the individual components in the mixture. This is done because available toxicological data are not sufficient to derive RfDs for the chemical mixtures as a whole (USEPA, 1986a).

When little or no quantitative information is available on the potential interaction among the components in a chemical mixture, EPA recommends dose additivity (USEPA, 1986a; 1989; 1992). For carcinogens, the assumption of a linear dose-response relationship results in the calculation of a total carcinogenic risk by simply adding the estimated carcinogenic risk for each substance of concern. For noncarcinogens, the assumption that there is an identifiable exposure threshold below which there are no observable adverse effects results in the calculation of a hazard index (HI) by adding the hazard quotients of the substances that produce similar toxicological effects. Various concerns have been expressed about this methodology (Murphy, 1983; USEPA, 1992).



This chapter provides an overview of the use and evolution of the chemical mixtures methodology, the associated statutes and regulations from which this methodology derives, and issues associated with this methodology that are open to interpretation.

5.2 Discussion of Chemical Mixtures in EPA Guidelines

5.2.1 Guidelines for the Health Risk Assessment of Chemical Mixtures

The Guidelines for the Health Risk Assessment of Chemical Mixtures (USEPA, 1986a) were published to guide analysis of information relating to health effects data on chemical mixtures. The guidelines reflect the work initiated in January 1984, peer-reviewed by industry, environmental, and university groups, and published for public comment on January 9, 1985, [50 FR 1170] under the title Proposed Guidelines for the Health Risk Assessment of Chemical Mixtures.

The guidelines define “mixtures” as “any combination of two or more chemical substances regardless of source or of spatial or temporal proximity.” The examples given for mixtures include by-products from a single source or process (e.g., coke oven emissions, diesel exhaust), commercial products (e.g., PCBs, gasoline, pesticide formulations), and substances that come in contact after disposal or storage in the same area. The guidelines single out the final group of substances because (1) most instances of environmental contamination involve concurrent or sequential exposures to a mixture of compounds that may induce similar or dissimilar effects over exposure periods ranging from short-term to lifetime, and (2) there are uncertainties inherent in predicting the magnitude and nature of toxicant interactions, therefore no single approach can be recommended for application to risk assessments involving multiple chemical exposures.

The guidelines recommended that assessment of chemical mixtures is best conducted using toxicologic data on the specific mixture of concern or a reasonably similar mixture. However, if no data are available on the mixture of concern (a common situation), the risk assessment may be based on the toxic or carcinogenic properties of the individual components in the mixture. For systemic toxicants, the guidelines state that the methodology used by the EPA results in the derivation of a hazard index (HI) based on an exposure level that is not anticipated to cause significant adverse effects. The exposure levels are expressed as acceptable daily intakes (ADIs) or as reference doses (RfDs). For carcinogens, whenever linearity of the individual dose-response curves has been assumed, the increase in risk caused by an exposure is related to the carcinogenic potency.

The guidelines remark that the assumption of dose addition only applies to compounds that induce the same effect by similar modes of action, and that a separate HI should be generated for each end point of concern. For carcinogens, addition of individual risks assumes independence of action by the various carcinogens in the mixture. The guidelines note that most risk assessments are based on an assumption of dose additivity, as long as the components elicit similar effects, and that the methodologies used do not incorporate any form of synergistic or antagonistic interaction. If the compounds in a mixture do not have the same mode of toxicologic action, the guidelines recognize that dose additivity is not “the most biologically plausible approach,” and “can lead to substantial errors in risk estimates if synergistic or antagonistic interactions occur.”



5.2.2 Guidelines for Estimating Exposures

The Federal Register of September 24, 1986, published the EPA Guidelines for Estimating Exposures (USEPA, 1986b), as well as the responses to comments by the public and the EPA Scientific Advisory Board (SAB) on the guidelines. The guidelines provide EPA with a framework for performing exposure assessments. Before the guidelines became final, some commentors thought more discussion was necessary on the effect of chemical mixtures and potential synergistic effects on exposure. EPA answered by recognizing the need for further research in the area of exposure to chemical mixtures.

5.2.3 Superfund Public Health Evaluation Manual (SPHEM)

SPHEM (USEPA, 1986c) provided detailed guidance on how to conduct a public health evaluation at a Superfund site. Regarding chemical mixtures, SPHEM noted that for noncarcinogens, assessors compare estimated exposure intakes (E) to toxicological reference levels (RL). A hazard index (HI) is then calculated and is expressed as:

$$HI = \frac{E_1}{RL_1} + \frac{E_2}{RL_2} + \frac{E_i}{RL_i}$$

SPHEM indicated that the HI approach developed to assess the overall potential for noncarcinogenic effects posed by multiple chemicals assumes the following:

- multiple exposures to chemicals below their thresholds could result in an adverse effect, and
- the magnitude of the adverse effect will be proportional to the HI.

In addition, SPHEM required that assessors determine a subchronic HI and a chronic HI and that they evaluate the possible effects of multimedia exposure, which is estimated by summing the HIs for inhalation and oral exposures at each exposure point.

For carcinogens, assessors calculate risk by combining estimated exposure intakes with carcinogenic potency factors. SPHEM indicated that for carcinogens, risks are estimated as probabilities. Because “relatively low intakes are most likely from environmental exposures, it can be assumed that the dose-response relationship will be in the linear portion of the dose-response curve.” SPHEM remarks that the carcinogenic risk estimate will generally be an upper-bound estimate. Cancer risk additivity is based on the following assumptions delineated in SPHEM:

- The compounds involved act independently (i.e., there is no synergism or antagonism).
- Intakes of the individual carcinogens are small.



5.2.4 Risk Assessment Guidance for Superfund, Volume I [RAGS]

RAGS (USEPA, 1989) constitutes the present conceptual framework for CERCLA risk assessments. This guidance provides the current definitions for the following terms:

- Slope Factor: A upper-bound estimate of the probability of developing cancer per unit intake of a chemical over a lifetime. This value represents a 95-percent probability of developing cancer.
- Hazard Quotient (I-IQ): The ratio of a single substance exposure level to a reference dose for that substance. The exposure level and reference dose should have similar exposure periods (e.g., subchronic).
- Hazard Index (HI): The sum of the HQs for multiple substances and/or multiple exposure pathways. It is calculated separately for chronic, subchronic, and short-term exposures.

RAGS requires CERCLA risk assessments to evaluate the total risks to human health posed by a CERCLA site. The evaluation involves quantification of risks for each exposure pathway and quantification of site risks. The first step is accomplished by quantifying the cancer risk and hazard quotient for each substance of concern, and then summing the results to get the total cancer risk and hazard index for each exposure pathway. The second step involves combining risks across exposure pathways that affect the same individual over the same period of time. This is accomplished by summing the cancer risks and the hazard indexes.

The first step, quantification of risks for each exposure pathway, is delineated in RAGS under the section “Aggregate Risks for Multiple Substances.” Although the calculation procedures differ for carcinogenic and noncarcinogenic effects, both sets of procedures assume dose additivity in the absence of information on specific mixtures. Calculating a total cancer risk for each exposure pathway involves summation of carcinogenic effects, which, according to RAGS, involves the following assumptions:

- Intakes of the individual carcinogens are small.
- The substances involved act independently (i.e., there are no synergistic or antagonistic chemical interactions).
- All substances produce the same effect (i.e., cancer),

RAGS recognizes that there are several limitations in the approach. The implications of these limitations will be discussed in the summary and conclusions section.

- Total cancer risk estimates might become “artificially more conservative” because cancer slope factors are upper 95th percentile estimates of potency, which are not strictly additive.



- The risk equation for multiple substances sums all carcinogens equally, giving as much weight to Class B or C as to class A carcinogens. Slope factors derived from animal data will be given the same weight as slope factors derived from human data.
- Two different carcinogens might not act independently,

To assess the overall potential for noncarcinogenic effects posed by more than one chemical, the hazard index approach assumes the following:

- Simultaneous exposures to several chemicals below their RfDs could result in an adverse health effect.
- The magnitude of the adverse effect will be proportional to the sum of the HQs.

RAGS also recognizes several limitations with this approach:

- RfDs are derived from a single point on the dose/response curve, and they do not take into account the shape of that curve, resulting in RfDs not exhibiting equal accuracy or precision and not being based on the same severity of effect. Therefore, the level of concern does not increase linearly as the reference dose is approached or exceeded.
- RfDs are based on critical effects of varying toxicological significance. That is, two chemicals may cause liver damage, but one chemical may produce liver damage that is irreversible while the other does not. RfDs are also based on varying levels of confidence that include different uncertainty adjustments and modifying factors.
- Assumption of dose additivity is most properly applied to compounds that induce the same effect by the same mechanism of action. If the HI is greater than unity as a consequence of summing several HQs of similar value, it maybe appropriate to segregate the compounds by effect and by mechanism of action. Segregation of HIs requires identification of the major effects of each chemical, including those seen at doses higher than that causing the critical effect. Major effect categories include neurotoxicity, developmental toxicity, reproductive toxicity, immunotoxicity, and adverse effects by target organ (i.e., hepatic, renal, respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, and dermal/ocular effects). ATSDR Toxicological Profiles are well suited in format and content to allow a rapid determination of additional health effects that may occur at exposure levels higher than those that produce the critical effect.

The final step, quantification of site risks, is delineated in RAGS under the section “Combining Risks Across Exposure Pathways.” RAGS states that “the total exposure to various chemicals will equal the sum of the exposures by all pathways.” According to RAGS, the following steps assure the appropriateness of combining cancer risks or HIs to get the total site risk



1. Identify reasonable exposure pathway combinations. For each pathway, cancer risks and HIs are developed for particular exposure areas and time periods. If two pathways do not affect the same individual or subpopulation, neither pathway's individual cancer risk estimate or HI affects the other, and they should not be combined.
2. Examine of the likelihood that the same individuals would face the RME by more than one pathway. Because contaminant concentrations vary over time and space, the same individual may not experience the RME for more than one pathway over a certain period of time. Combining the RME risks for more than one pathway may be done if it is explained why the key RME assumptions for more than one pathway apply to the same individual or subpopulation.

5.2.5 Guidelines for Exposure Assessment

These guidelines (USEPA, 1992), published in response to recommendations from EPA's SAB and the general public, superseded and replaced the Guidelines for Estimating Exposures (USEPA, 1986b) and Proposed Guidelines for Exposure-Related Measurements (USEPA, 1988). The guidelines convey the principles of exposure assessments and constitute the current theoretical principles to be used in the Superfund program. The central theme of the document is to find "a more realistic approach to exposure determination." The guidelines suggest that "since risks resulting from exposures to complex mixtures of chemicals with the same mode of toxic action are generally treated as additive in a risk assessment, failure to evaluate one or more of the constituents would neglect its contribution to the total exposure of risk."

5.2.6 An SAB Report: Superfund Site Health Risk Assessment Guidelines

This SAB report (USEPA, 1993) was published as a result of an SAB meeting held on April 7-8, 1992, in Bethesda, Maryland. The meeting was organized to review key issues related to RAGS. One of these issues was how to assess and deal with exposures to multiple chemicals using the hazard index (HI)/hazard quotient (HQ).

The SAB committee was asked the following specific questions:

1. Is it appropriate to add risk estimates for multiple contaminant exposures (i.e., to calculate HI for noncarcinogenic chemicals with similar toxic endpoints, and simple additivity of cancer risks)?
2. Is it appropriate to use an HI greater than 1 as a threshold of concern?
3. What does an HI greater than 1 represent when the HQs used to calculate the HI are individually less than 1?
4. Is the RfD an appropriate criterion of toxicity?



In answering the first question, the SAB committee remarked that there is concern about the approach of using an RfD derived HI/HQ as a basis for adding risks from exposures to complex mixtures because the RfD is only an indirect index of potency. The EPA HIs depend upon RfDs, which in turn, depend upon effect levels (e.g., NOAEL) divided by an uncertainty factor. The SAB notes that potency should be defined by the form of the dose-response relationship, not by a single point on the dose-response function.

In relation to the second question, the SAB committee stated that an HI equal to unity has a rational and meaningful basis for defining a threshold of concern, but the committee “does not see any value to use numbers other than ‘1’ in defining a threshold of concern.” The SAB comments that the HI approach is not based upon a linear dose-response relationship and that using the HI may even be “inappropriate if there are interactions of the chemicals in the mixture which cannot be fully characterized by a combination of dilution-type interaction and independent mechanisms of action.”

To answer the third question, the SAB committee indicated that the interpretation of an HI greater than unity may be based on several factors:

- If two or more agents involved share the same mechanism of toxicity, their doses could well be additive.
- If they act upon two or more sites, they could be supra-additive,
- If they each act by different toxicological mechanisms, additivity of risks for a common endpoint is not necessarily to be expected.

The SAB recommends considering that there is a potential increase of risk when the HI exceeds unity. However, the committee warns that without a more complete understanding of interaction mechanisms, there cannot be a statement of how rapidly this increase occurs.

Finally, the SAB noted that if experimentally determined RfDs for specific mixtures were available, then the HQ of the mixture would be an indication of risk relative to the RfD. Currently, chemicals in a mixture are assessed for joint action by computing the ratio of exposure to RfD, then adding these quotients to obtain the HI. According to the SAB, comparisons of HQs for different agents are not meaningful. Because the RfDs are based on dose such as NOAELs that are derived from the critical effect in an assay, the resulting HI may encompass a spectrum of toxic endpoints and risk levels.

5.3 Issues and Regulator Dialogue

5.3.1 Chemical Mixture Issues

To perform CERCLA risk assessments, assessors must evaluate quantitative relationships between exposure and the effects in the studies to identify which effects are of concern, i.e., dose-response assessments. However, toxicological information on specific mixtures found at CERCLA sites is rarely



available, and even if such data existed, monitoring for mixtures or modeling the movement of mixtures across space and time present technical problems (USEPA, 1989). One scientific paper suggested toxicological procedures that “may be performed to evaluate whether a significant health risk is posed by exposure of men to a mixture of chemicals that may be present because of improper chemical waste disposal practices.” This paper concluded that “with current techniques and the present state of knowledge, there is no ideal way of approaching the problem of assessing the toxicity of exposure of man to mixtures of chemicals; it is a goal which will not be obtainable in the foreseeable future” (Neal, 1983).

If sufficient data are not available on the effects of the chemical mixture, the current approach is to assume dose additivity. For carcinogens, simple additivity of risk is used; for noncarcinogens, an HI approach was developed where there is concern for potential adverse effects if the sum of the hazard quotients for several chemicals with the same toxic endpoint exceeds unity. Dose additivity, however, introduces uncertainties into the risk assessment. The following issues were identified:

Dose Additivity Can Lead to Errors If Synergistic or Antagonistic Interactions Occur

In addition to considering the contributions of individual agents, assessors must also consider the combined effects of agents present, taking into account the modes of action, when known, of the organs or systems affected; the possible joint severity of the effects; all and any synergism or antagonism that may be present (USEPA, 1992). Dose additivity is based on the assumption that the components in the mixture have the same mode of action and elicit the same effects and have independent mechanisms of action (meaning that the thresholds for a given chemical are unaffected by exposures from other chemicals) (USEPA, 1993).

A “toxicological interaction” may be defined as a condition in which exposure to two or more chemicals results in a quantitatively or qualitatively altered biological response relative to that predicted from the action of a single chemical (Murphy, 1983). Since the mechanisms of action for most compounds are not well understood, the justification of the assumption of dose addition will often be limited to similarities in pharmacokinetic and toxicological characteristics (e.g., apparent target organ). According to EPA, several commentators have expressed concern that it was difficult to define sufficient similarity and that the guidelines should give more details concerning similar mixtures. EPA agreed with the comments, but indicated that “the best indicators of similarity in terms of risk assessment are yet to be determined [51 ER 34014].

If some of the chemicals interact synergistically, then the condition $HI=1$ may not afford adequate protection. On the other hand, if the individual chemicals have independent mechanisms of action, then the criterion $HI=1$ may be overly protective. The Guidelines for the Health Risk Assessment of Chemical Mixtures (USEPA, 1986a) state in this respect that “dose additive models are not the most biologically plausible approach if the compounds do not have the same mode of toxicologic action,” and that “additivity can lead to substantial errors in risk estimates if synergistic or antagonistic interactions occur.”



Summing HQs Treats All RfDs Equally

The EPA is currently addressing the appropriateness of RfDs as a criterion of toxicity (USEPA, 1993). The concept of RfD was first published in Reference Dose (RfD): Description and Use in Health Risk Assessments (Barnes and Dourson, 1988). This paper describes EPA's approach and rationale to solve "perceived difficulties" with the concept of acceptable daily intake (ADI), safety factor, or margin of safety. The concept of reference dose was introduced "to avoid use of prejudicial terms (e.g., 'safety' and 'acceptable'), to promote greater consistency in the assessment of noncarcinogenic chemicals, and to maintain the functional separation between risk assessment and risk management" (Barnes and Dourson, 1988). The position paper delineates the scientific shortcomings and difficulties in utilizing the "traditional" approach:

1. A too narrow a focus on the NOAEL ignores the information on the shape of the dose-response curve.
2. There are questions about the selection of the appropriate adverse effect.
3. There is a lack of guidelines to address the reliability of toxicity studies due to the number of animals used.

Barnes and Dourson also note that the derivation of RfDs involves the use of uncertainty factors (UF) and modifying factors (MF) which depend upon the professional assessment of scientific uncertainties in the toxicological studies (e.g., the completeness of the overall data base and the number of species tested). The following factors are used in deriving an RfD:

1. 10-fold factor to account for the variation in sensitivity among human populations,
2. 10-fold factor to account for the uncertainty involved in extrapolating from animal data to humans,
3. 10-fold factor to account for the uncertainty involved in extrapolating from less than chronic NOAELs to chronic NOAELs,
4. 10-fold factor to account for the uncertainty involved in extrapolating from LOAELs to NOAELs, and
5. use of professional judgment to determine the MF (it is greater than 0 and less than or equal to 10).

Because each RfD is based on a critical effect (e.g., NOAEL, LOAEL), the resulting sum of HQs (i.e., the HI) contains a spectrum of toxic endpoints (e.g., death, weight-loss, skin rashes, etc.). Also, the addition of RfDs includes adding data sets with disparate levels of confidence.



Cancer-causing Substances are Treated Equally When Summing Slope Factors

EPA evaluates available toxicological data from experimental animals and from epidemiological studies of human populations to determine the carcinogenicity of chemical substances. Based on the amount and type of the data available, EPA assigns a weight-of-evidence classification. The addition of slope factors for multiple chemicals in a mixture sums all carcinogens equally, regardless of their carcinogenicity classification (see Chapter 1 for the classification scheme).

Upper 95th Percentile Estimates of Potency Are Not Strictly Additive

The dose-response curves from animal toxicological experiments are based on data sets derived from high administered doses. The estimation of a slope factor at the low end of the dose-response curve requires extrapolation of the data set to lower exposure levels. There are various mathematical models that have been developed to extrapolate from high to low response doses (e.g., linearized multistage model, Weibull, probit, logit, one-hit, etc.) The choice of an extrapolation model is outlined in Guidelines for Carcinogen Risk Assessment (USEPA, 1986d). The guidelines recommend fitting the experimental data set to the linearized multistage model which assumes that the low-end portion of the dose-response curve is linear. The carcinogenic slope factors published by EPA are the slopes of these curves calculated as an upper 95th percentile confidence limit of the probability that a chemical will cause cancer. It has been mathematically proven that the product of 95th percentiles will result in “compounding conservatism” (Taylor, 1993). RAGS notes that when adding cancer slope factors from multiple chemicals, “the total cancer risk estimate might become more conservative” (USEPA, 1989).

5.3.2 Regulator Dialogue

Review of CERCLA guidance documents revealed that various assumptions are made to determine the levels of risk to human health from exposures to multiple chemicals. According to SPHEM, the results for multiple chemicals “should not be interpreted too strongly,” and the interpretation of the HI for a particular site requires the use of professional judgment (USEPA, 1986c). Because of the uncertainties involved in toxicological effects of chemical mixtures, the guidelines recommend a thorough discussion of all assumptions in the assessment of health risk from chemical mixtures.

As discussed previously, there is a great deal of uncertainty involved in adding HQs. One method that can be used to reduce this uncertainty, which is also recommended in the guidance documents, is to calculate an HI for each affected target organ. The HQs for chemicals that affect different target organs should not be summed for one or multiple exposure pathways. The IRIS database and HEAST specify which target organ is affected (critical effect) by a substance when the RfD value is presented.

Uncertainties are also introduced into the risk assessment if risks from carcinogenic chemicals with different weight-of-evidence values are summed. The only known human carcinogens are Group A chemicals. The other groups’ risks are based mostly on animal studies, with their inherent uncertainties for predicting human carcinogenicity. Situations could exist where a less extensive and costly remedial alternative may be chosen based on cancer risks summed only within the same weight-of-evidence classification, while another more extensive and costly alternative might be required based on risks



associated with summed cancer risk, regardless of their weight-of-evidence classification. However, even when summing carcinogens with the same weight-of-evidence classification, the result will be conservative because the slope factors are 95th percentiles, which, as seen in the previous section, are not strictly additive. Thorough description of such issues in the uncertainty section of the risk assessment will present the remedial decisionmaker with insight that could bear significantly on the remedial selection process.

EPA and ATSDR are currently developing and supporting research programs designed to gain an understanding of the mechanisms of interactions to predict how specific mixtures of toxicants will interact. The ATSDR is under U.S. congressional mandate to conduct health assessments at all National Priority List (NPL) sites, including federal facilities. A Memorandum of Understanding (MOU) between ATSDR and the Department of Energy (DOE) describes the role ATSDR plays at DOE sites, including the preparation of toxicological profiles for substances requested by DOE (MOU, 1991). CERCLA Sections 104(i) (3) and (5) also mandate the preparation of toxicological profiles by ATSDR to support CERCLA activities.

DOE may appropriately decide to sponsor toxicological studies for a particular chemical mixture that is present at various DOE facilities. The time and money spent on the toxicity study may well be worth the effort if the results of the study can reduce the risk and uncertainty of simply adding the HQs of the individual chemicals in the mixture. The following initiatives were suggested to determine how the risk of exposure to a mixture compares to the risk from exposure to each chemical alone (Murphy, 1983):

1. search existing literature for laboratory, clinical, or epidemiological studies that deal with exposures to the combination of chemicals;
2. initiate laboratory or epidemiological studies to test for interactive effects of the specific combination of chemicals; and
3. use toxicokinetic and toxicodynamic characteristics of individual chemicals to predict potential for altered health risks arising from exposure to mixtures.

There are few reports of laboratory or epidemiological studies, however, that have addressed the toxic interactions of chemical mixtures, particularly from mixtures that might arise from a chemical waste dump. Comprehensive toxicological testing of the combination of chemicals to which humans may conceivably be exposed is of "Herculean proportion" (Murphy, 1983). Thus, it is necessary to consider the basic principles underlying the mechanisms of toxic interactions in order to predict the effects of chemical mixtures. The scientific paper concludes that predicting the likelihood of increased risk due to multichemical exposures requires detailed information concerning each of the components. Assessors should perform a structure activity relationship (SAR) analysis on the individual chemicals in the mixture before initiating expensive testing.

5.4 References

Barnes, D.G. and Dourson, M. 1988. Reference Dose (RfD): Description and Use in Health Risk Assessments. *Regulatory Toxicology and Pharmacology*. Vol. 8, pp. 471-486.



MOU. 1991. Memorandum of Understanding Between ATSDR and DOE on the Development of Toxicological Profiles for Hazardous Substances and Health Assessments and Related Activities at DOE Facilities, October 10, 1990, in Health Assessment and Other Activities of the Agency for Toxic Substances and Disease Registry, U.S. DOE Office of Environmental Guidance, RCRA/CERCLA Division EH-231, DOE/EH-006/0891, August 1991.

Murphy, S.D. 1983. General Principles in the Assessment of Toxicity of Chemical Mixtures. In: Assessing Toxic Interactions, Environmental Health Perspectives Vol. 48, pp. 141-144.

Neal, R.A. 1983. Protocol for Testing the Toxicity of chemical Mixtures. In: Testing for Chemical Mixtures, Environmental Health Perspectives Vol. 48, pp. 137-139.

Taylor, A.C. 1993. Unpublished manuscript (Harvard School of Public Health, 1992). In: The Magnitude of Compounding Conservatism in Superfund Risk Assessments, Risk Analysis, Vol. 13, No. 2, April 1993.

USEPA. 1986a. Guidelines for the Health Risk Assessment of chemical Mixtures. U.S. Environmental Protection Agency. [51 FR 34014].

USEPA. 1986b. Guidelines for Estimating Exposures. U.S. Environmental Protection Agency. [51 FR 34042].

USEPA. 1986c. Superfund Public Health Evaluation Manual. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/1-86/060.

USEPA. 1986d. Guidelines for Carcinogen Risk Assessment. U.S. Environmental Protection Agency. [51 FR 33992].

USEPA. 1988. Proposed Guidelines for Exposure-Related Measurements. U.S. Environmental Protection Agency. Washington, D.C. [53 FR 48830].

USEPA. 1989. Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual (Part A). U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/1-89/002.

USEPA. 1990. Guidance for Data Usability in Risk Assessment. Interim Final. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/G-90/008.

USEPA. 1992. Guidelines for Exposure Assessment, U.S. Environmental Protection Agency. [57 FR 22888].

USEPA. 1993. An SAB Report: Superfund Site Health Risk Assessment Guidelines. Review of the Office of Solid Waste and Emergency Responses Draft Risk Assessment Guidance for Superfund Human Health Evaluation Manual by the Environmental Health Committee. U.S. Environmental Protection



Agency, Office of the Administrator, Science Advisory Board Washington, D.C. EPA-SAB-EHC-93-007.



Chapter 6: Radiation Risk Assessment

6.1 Introduction

The U.S. Environmental Protection Agency (EPA) recommends that both a chemical risk assessor and a radiation risk assessor be on site for a Remedial Investigation/Feasibility Study. This is because there are major differences in the procedures used to characterize chemical and radionuclide contaminants. This chapter defines the differences between chemical and radiation risk assessments.

The principal adverse biological effects associated with ionizing radiation from radioactive substances in the environment are carcinogenicity, teratogenicity, and mutagenicity. Carcinogenicity is the ability to produce neoplastic changes that result in carcinomas or cancerous tumors. This is a stochastic effect and is considered to be the limiting deleterious effect at the dose levels expected at DOE Superfund sites. Teratogenicity and mutagenicity are the nonstochastic, noncarcinogenic effects associated with exposure to radiation. Teratogenicity is the ability to induce or increase the incidence of congenital malformations, which are permanent structural or functional deviations produced during embryonic growth and development. Mutagenicity is the ability to induce genetic mutation in the nuclei of either body cells or reproductive cells.

Radiation-induced genetic effects have not been observed in human populations, and extrapolation from animal data reveals that risks per unit exposure are smaller than, or comparable to, the risk of cancer. In addition, the genetic risks are spread over several generations. The risks per unit exposure of serious teratogenic effects are greater than the risks of cancer. However, there is a possibility of a threshold, and the exposures must occur over a specific period of time during gestation to cause the effect. (Teratogenic effects can be induced only during the nine months of pregnancy, whereas genetic effects are induced during the 30-year reproductive generation and cancer can be induced at any point during the lifetime.) Therefore, the cumulative risk of cancer maybe many times greater than the risk of genetic or teratogenic effects due to the potentially longer period of exposure. Consequently, the carcinogenic effects typically are used as the sole basis for assessing radiation-related human health risks of a site contaminated with radionuclide.

The organization of this chapter is slightly different than that of the preceding chapters. The preceding chapters discussed one aspect of the baseline risk assessment, while this chapter discusses all aspects of the risk assessment as it is related to radiation. After the discussion of the statutory and regulatory history, the chapter is organized into sections on exposure, toxicity, and risk. The conclusion section will summarize the issues that are pertinent to radiation which may be important in a regulatory dialogue.



6.2 Discussion of Radiation Risk Assessment in Statutes and Regulations

6.2.1 Statutory and Regulatory Radiation Risk Assessment Framework

CERCLA was enacted to reduce and mitigate human exposures to release-s of “any pollutant or contaminant which may present an imminent and substantial danger to the public health or welfare” (CERCLA, 1980). The definition of a hazardous substance in Section 101(14) of CERCLA includes “any element, compound, mixture, solution, or substance designated pursuant to section 102 of this Act” and “any hazardous air pollutant listed under section 112 of the Clean Air Act.” Section 102(a) of CERCLA states that “the Administrator shall promulgate and revise as may be appropriate, regulations designating as hazardous substances, in addition to those referred to in section 101(14) of this title, such elements, compounds, mixtures, solutions, and substances which, when released into the environment may present substantial danger to the public health or welfare or the environment.” In 40 CFR Part 302.4 the Administrator listed radionuclide as being hazardous substances. Section 112(b) of the Clean Air Act lists radionuclide as being hazardous air pollutants. Thus, radionuclide are incorporated into the baseline risk assessment protocol through statutes and through the regulatory process.

6.3 Exposure

6.3.1 Exposure Pathways

Assessors use mathematical extrapolation models (e.g., EPA’s computer model “RADRISK”) to quantify the relationship between cancer incidence and exposure to radioactive materials. These models estimate the largest possible linear slope (within the 95 percent Upper Confidence Limit) at low extrapolated doses consistent with the data. This “radiocarcinogenicity slope factor” is the “maximum likelihood estimate of the age-averaged lifetime total excess cancer risk per unit intake or exposure” (EPA’s IRIS-computer data base). Assessors use the RADRISK computer code to estimate dose rates from ingestion or inhalation of radioactive materials. The DFSOIL code is used to calculate kerma and energy flux of photons in the air at one meter above the ground surface. Kerma, which stands for K inetic E nergy R eleased in M aterial, is defined as a unit of exposure, expressed in rads, that represents the kinetic energy transferred to charged particles per unit mass of irradiated medium when indirectly ionizing (uncharged) particles, such as photons (x-rays or gamma-rays) or neutrons, traverse the medium. (If all of the kinetic energy is absorbed “locally,” the kerma is equal to the absorbed dose.) Then the DOSFACTOR code is used to convert the estimates of air kerma obtained from DFSOIL to organ dose rates. To generate the slope factors, assessors use the calculated dose rate with risk models in conjunction with life table analysis. However, the true risk to humans, although not identifiable, is not likely to be the upperbound estimate; it may, in fact, be lower. EPA’s Office of Radiation and Indoor Air (ORIA) calculates cancer slope factors for radionuclide of potential concern at Superfund sites. These values are listed in EPA’s Health Effects Assessment Summary Tables (USEPA, 1994a), not IRIS.

*Rad stands for Radiation Absorbed Dose and is a measure of the energy imparted to matter by radiation. 1 Rad - 100 ergs per gram.



The pathways of exposure and the mathematical models used to evaluate the potential health risks associated with radionuclide in the environment are similar to those used for evaluating chemicals of concern, except that external radiation is unique for radionuclide and inhalation of volatiles and dermal absorption are more significant exposure pathways for chemicals than for radionuclide. The behavior of a radionuclide in the environment with regard to its transport and inter-media transfer is determined by the same physical/chemical processes that govern chemical contaminants. Consequently, the types of data needed for a radiation risk assessment are similar to three required for a chemical risk assessment. The primary differences lie in the procedures used to characterize the radionuclide contaminants. For example, in addition to exposure due to ingestion, inhalation, and direct contact, radiation emitted from photon sources (i.e., gamma rays) is an external penetrating exposure. Therefore, gamma emitters, whether they are internal or external, are important in risk assessments. Alpha and beta emitters are only important in radiation risk calculations when they are internal (inhaled or ingested).

For inhalation and ingestion, the slope factors are the central estimates (i.e., median or 50th percentile values) of the age-averaged, lifetime excess cancer incidence (fatal and non-fatal cancer) risk per unit of activity intake. For external exposure, the slope factors are the central estimates of the age-averaged lifetime excess cancer incidence risk for each year of exposure to a unit activity concentration of photon-emitting radionuclide. They can also be important in skin absorption depending upon the “carrier” chemical with which the radionuclide is associated (mixed waste) or attached (radio-labelled or “tagged”). If the radio-labelled or mixed waste chemical is absorbed through the skin, then the alpha- or beta-emitting radionuclide would be considered as an internal emitter (e.g., dimethyl sulfoxide [DMSO]) mixed with a radionuclide, or DMSO labelled with Carbon-14). If the alpha- or beta-emitters are not mixed with or tagged to a dermally absorbed chemical, then internal exposures to these radionuclide should not be considered (USEPA, 1994b).

6.3.2 Exposure Assessment

Despite the differences between the way exposures are expressed for radionuclide and chemicals, the approach to exposure assessment is essentially the same, with the following exceptions: the consideration of external (penetrating photon radiation) exposures, conversion of radiation exposures to dose equivalents, and the fate and transport models must be made specific to radiation exposure to account for the ingrowth and decay processes of radionuclide. Additionally, different time scales must be considered in a radiation risk assessment because of the radioactive decay process. For example, some radionuclide not only “decay away” but there is an “ingrowth” of “new” radioactive decay products. For example, plutonium-241, which has a half-life of 14.4 years, decays to americium-241, which has a half-life of 432.2 years. This illustrates an example in which the daughter is longer lived and more toxic than the parent. Therefore, each such radioactive progeny may also become dominant contributors to the total radiation exposure assessment over a period of several hundred years.

6.3.3 Radiation Dosimetry

Radiation dosimetry can be defined as the amount of energy deposited in living tissue due to internal and external exposures to ionizing radiation. The potential adverse effects of this amount of energy deposited in living tissue are proportional to energy deposition. Therefore, the term “dose,” when



used in radiation exposure, is defined as the energy imparted to a unit mass of tissue, whereas “chemical dose” means the mass of chemical penetrating into an organism.

6.4 Toxicity

6.4.1 Toxicity Assessment

The first step in a toxicity assessment for radionuclides is hazard identification, which is a determination of whether exposure can increase the incidence of an adverse health effect. Then, a dose response assessment is used to quantify the toxicity and characterize the relationship between the dose of the contaminant administered or received and the incidence of adverse health effects in the exposed population. There is no need for an extensive discussion of toxicity, mainly because exposure to any radioactive substance is, by definition, assumed to be hazardous (USEPA, 1989a). An extensive body of literature exists on radiation carcinogenesis in man and animals that indicates that ionizing radiation can be considered “pancarcinogenic” (i.e., it acts as a complete carcinogen in that it serves as both an initiator and a promotor and can induce cancers in almost any tissue or organ).

Each radionuclide produces unique radiation characteristics that can affect different organs in the exposed individual. **EPA has** calculated the annual radiation dose equivalent from each radionuclide to each organ dose from a continuous lifetime exposure with a constant exposure rate. Using these calculations, assessors can estimate the average excess number of all types of radiation-induced fatal cancers per year for the corresponding dose equivalents received during that year and relevant preceding years. By using epidemiological data, extrapolation from high radiation doses to low doses, and hypothetical models for projecting risk through a lifetime, the excess number of radiation-induced fatal cancers can be determined. EPA has also calculated each radionuclide slope factor by dividing the excess fatal cancer risk for that radionuclide by the mortality-to-incidence risk ratio for the types of cancer induced by that radionuclide (USEPA, 1989b).

This helps assessors evaluate cancer incidence and determine the probability that fatal cancer will occur at a particular site. The use of the mortality-to-incidence risk ratio and the site-specific relative risk model are the major differences between estimating cancer risk for radionuclide and estimating it for chemical carcinogens. This is because EPA does not incorporate the mortality-to-incidence ratio in the cancer slope factors for chemical carcinogens. Chemical carcinogen risks are calculated on cancer incidence, while radionuclide cancer risks are calculated on cancer deaths. (Chemical carcinogens are based on laboratory animal experiments and radiation cancers are based on groups of humans exposed to low-LET radiations, such as the Japanese atomic bomb survivors and medical patients treated with radiation). The mortality-to-incidence ratio is used for radionuclide to convert cancer deaths to cancer incidence. The underlying population rates for mortality and incidence vary differently with respect to age. Therefore, age-specific incidence is greater than mortality, that is, it increases less steeply with age.

Most sources of environmental contamination come from inhalation and ingestion rather than external exposure and result in a nonuniform distribution of radioactive material in the body so that some organ systems receive much higher doses than others. For example, since iodine radioisotopes concentrate preferentially in the thyroid, the dose to this organ can be orders of magnitude larger than the average dose



to the body. To determine the probability that fatal cancer occurs at a particular organ site, EPA has used the incidence risk coefficients and mortality-to-incidence ratios from the BEIR V report (NAS, 1990). However, because not all forms of thyroid cancer can be induced by radiation and, for those that are, a more reasonable mortality-to-incidence ratio would be 0.1, EPA has used that value in its calculations. Likewise, lung cancer incidence and mortality have both shown an increasing trend between 1970 and 1980. Since incidence precedes mortality, an uncorrected mortality-to-incidence ratio gives a low estimate of the fraction of those persons who, having been diagnosed with lung cancer, will die of that disease. Therefore, a mortality-to-incidence ratio of 0.94, based on long-term survival studies by the National Cancer Institute for lung cancer, has been used. It is generally accepted that the risk estimates for the individual sites are less certain than are the risk estimates for all sites combined.

EPA discusses in its recent report, "Estimating Radiogenic Cancer Risks" (USEPA, 1994b) that it has revised its methodology for deriving radionuclide slope factors in the HEAST document- Instead of using the BEIR III dosimetry, EPA used BEIR V dosimetry in the revised methodology. The relative biological effect (RBE) value for alpha particles has been revised to 20 from 8, except for leukemia (RBE is 1) and breast cancer (RBE is 10). For all cancers (except breast cancer), EPA assumed a dose and dose rate effectiveness factor (DDREF) of 2 (i.e., the risk per unit dose is reduced by a factor of 2 for low-level radiation exposures). For breast cancer, EPA assigned a DDREF of 1. Before 1993, EPA assigned a DDREF of 1 for all cancers. EPA also revised the risk estimates for leukemia based on new epidemiological data. The agency obtained the life table data from the 1979-1981 census data for the U.S. population. In the previous methodology, EPA used the U.S. population life table data during the years 1969-1971. Using the revised methodology, the cancer risk estimate has increased. For example, for low-linear energy transfer (LET) radiation (see Section 6.5.1) the lifetime fatal risk estimate associated with uniform whole-body irradiation of the U.S. population has increased by 24%, from $3.92 \times 10^{-4}/\text{rem}^{**}$ to $5.09 \times 10^{-4}/\text{rem}$ for fatal cancer risk. This corresponds to an incidence risk estimate of $7.61 \times 10^{-4}/\text{rem}$. Although the results from the revised methodology were not included in the 1994 HEAST document, it is probable that the results will replace the current values in the near future (USEPA, 1994b).

As for the nonstochastic (noncarcinogenic) radiation effects, very little quantitative data, particularly at low-dose exposures, are available on mutagenesis. The majority of the evidence supporting the mutagenic character of ionizing radiation comes from extensive studies of animals. Mutation rates calculated from these studies have been extrapolated to humans and form the basis for estimating the genetic impact of ionizing radiation on humans. The teratogenic effects of radiation are better known because the fetus is much more sensitive to radiation than the mother. However, the age of the fetus at the time of exposure is the most important factor in determining the extent and type of damage from radiation exposure. Malformations produced in the irradiated embryo depend on which cells, tissues, or organs were most actively differentiating at the time of exposure. Embryos are most sensitive just after implantation until approximately eight weeks into the term; the greatest risk microcephaly (brain damage resulting in mental retardation), occurs from radiation exposures at 8 to 15 weeks.

**REM stands for Roentgen Equivalent Man and is defined as the unit of dose equivalent. The dose equivalent in "rem" is numerically equal to the absorbed dose in "rad" multiplied by the "Quality Factor" which is an LET dependent factor by which absorbed doses are multiplied to obtain a quantity which corresponds more closely to the degree of biological effect produced by x-rays or low-energy gamma rays. More simply, the rem is a measure of equivalence for the relative biological effect of radiations of different types and energies on man.



Compared to chemicals, the dose-response assessment of radionuclide is straightforward; that is, the type of effects, the probability, and the likelihood of any one of several possible adverse health effects occurring depends on and increases with the radiation dose. The severity of the effect is, however, independent of dose. Estimates of human health effects are based primarily on single, usually high (acute) doses of radiation. To describe these effects as a function of dose, assessors use the “linear model.” That model assumes that there is no threshold for the induction of cancer or genetic effect (a conservative assumption and model). There are very few data on the effects of radiation at low doses or the effects of chronic, long-term exposure in humans.

6.4.2 Radiation Health Effects in Humans

Four major, scientifically august bodies have been responsible for collecting and evaluating data on the human health effects of ionizing radiation: the Committee on the Biological Effects of Ionizing Radiation (BEIR) of the National Research Council/National Academy of Science, the National Council on Radiation Protection and Measurements (NCRP), the International Commission on Radiological Protection (ICRP), and the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). In the United States, EPA is responsible for developing guidelines for radiation risk assessment and has relied on the published evaluations of these groups.

6.5 Risk

6.5.1 Cancer Risks

For radiation risk evaluation, the “type” of radiation is usually separated into either low or high Linear Energy Transfer (LET) effects: LET refers to the rate at which energy is deposited as the particle or gamma ray travels through matter. Radionuclides that emit radiation as alpha particles or neutrons are classed in the high LET radiation category; beta particles, x-rays, and gamma rays are considered low LET radiation. Some radionuclides emit both types of radiation (e.g., radium-226 emits both high LET alpha and low LET gamma radiation). By far the more dangerous, more cytotoxic, and more carcinogenic of the two is high LET radiation. However, that does not mean that low LET is not also dangerous, cytotoxic, and carcinogenic. For fatal cancers, the lifetime exposure period has a risk factor of $5.09 \times 10^{-4}/\text{rad}$ for low LET radiation and $3.1 \times 10^{-3}/\text{rad}$ for high LET. The corresponding incidence risk factors for all radiation-induced cancers (lifetime exposure) is $7.6 \times 10^{-4}/\text{rad}$ for low LET and $5.0 \times 10^{-3}/\text{rad}$ for high LET (USEPA, 1994b).

6.5.2 Genetic Risks

The genetic effects of ionizing radiation have been studied extensively in plants, animals, and various human populations such as the Japanese atomic-bomb survivors. Results of the A-bomb studies have consistently yielded estimates of genetic effects that imply lower risks in humans than in animals. This indicates that humans are less sensitive to radiation induction of mutations in germ cells and that the risks derived from animal data will be conservative in humans. As a result of this, BEIR V (NAS, 1990) and UNSCEAR (UNSCEAR, 1988) have based their genetic risk estimates on the lower 95 percent



confidence limit for the Japanese data, which is consistent with the mutation rate doubling doses found in mice (doubling dose is the dose that doubles the incidence of genetic defects).

The doubling dose for humans is estimated to be 100 rem; the expected genetic effects per rem per 30-year generation (the generally accepted reproductive span) are less than one to about 100 per million liveborn offspring for multi-generations. The natural incidence for genetic anomalies from all causes ranges from 400 to 30,000 per million liveborn offspring. EPA currently estimates that exposure to 1 rad per generation of lowdose-rate, low-LET radiation will induce 260 cases of serious heritable disorders per 10^6 live births in all generations. For high-LET radiation, the estimate is 690 serious heritable disorders per 10^6 live births in all generations. These risks are based on BEIR III (NAS, 1980), which are essentially the same as in BEIR V (NAS, 1990). The main difference lies within the reassessment of doses assigned to the A-bomb survivors, the effect of which, in general, will increase the risk of low-LET radiation calculated according to a particular model. Attempts to estimate doubling doses from data on Japanese atomic-bomb survivors have consistently led to values larger than those derived from the animal data, and, consequently, they imply lower risks. Although risks calculated from animal data have large confidence intervals, estimates from those exposed to radiation in Hiroshima and Nagasaki are known with even less precision. In spite of these uncertainties, the data suggest a real difference, with the estimated lower 95% confidence limit of the human data approximating the median of a large number of values obtained in mice. If it is assumed that the apparent difference is real, humans would be less sensitive to radiation induction of mutations in germ cells than mice, and the risks in BEIR III should be considered more conservative. The BEIR V Committee stated that despite all the careful work that has gone into their collection and analysis of the human data, they are in no better position to decide the issue than the previous committees (BEIR I, HI, & IV. Note: The BIER II report was strictly a cost/benefit analysis.)

6.5.3 Developmental Risks

Developmental or teratogenic effects are somatic effects resulting from exposure of the unborn, in-utero, to ionizing radiation. These effects differ from genetic effects in that they cannot be passed on to other generations but can include severe mental retardation, microcephaly, and other structural abnormalities. The extrapolation of animal data to humans is extremely difficult because of the significant differences in fetal development rates. EPA's current estimate is 4,000 effects per rad during 8 to 15 weeks of gestation for low LET radiation (mainly x- or gamma ray radiation) (USEPA, 1994b).

6.5.4 Radiation Risk Calculation Methodology

The methodology for estimating the total lifetime excess cancer risks due to continuous, lifetime exposure, based on ICRP 23's recommended 70-year life span, is broken down into risk characterization for internal (inhalation or ingestion) and external (mainly gamma emitters) exposures.

Internal Exposure

The internal risk characterization is calculated from:



$$\text{Risk} = I \times \text{SF}$$

Where:

Risk = cancer incidence, expressed as a unitless probability

I = lifetime radionuclide intake (pCi)

SF = slope factor (pCi)⁻¹

The slope factor is either a HEAST value for a particular radionuclide or the sum of the HEAST slope factors for that radionuclide and its short-lived progeny to account for ingrowth (USEPA, 1989a; USEPA, 1989b).

External Exposure

External risk characterization for gamma-emitting radionuclide in surface soil (photon-emitting radionuclide distributed uniformly in a thick layer of soil, expressed as risk/yr per pCi/gram of soil) is calculated from:

$$\text{Risk} = (\text{SF})[(C_s)(\text{EF})(\text{ED})(\text{ET})(1-\text{SH})]$$

Where:

Risk = risk of cancer incidence, expressed as a unitless probability

SF = radionuclide slope factor, (risk/yr/pCi/g) from EPA HEAST tables

C_s = radionuclide soil concentration (pCi/g)

EF = modifying factor, fraction of year exposed (unitless)

ED = exposure duration (years)

ET = fraction of day exposed (unitless)

SH = shielding factor (titles)

External slope factors do not include the radiation contributions from radioactive decay progeny. In order to include this additional, and often substantial, radiation in the overall risk calculations, a computer program (Rad Decay) must be used to predict future radiation levels from progeny when parent isotopes are decayed over a period of time.



The calculation of a risk characterization for gamma emitters from sources other than surface soil is

$$\text{Risk} = (\text{DE})(\text{RC})$$

Where:

Risk = risk of cancer incidence (titles probability)

DE = total dose equivalent (rem)

RC = cancer risk coefficient (rem-l)

This deviation is necessary because the EPA slope factor method is not applicable to gamma-ray exposures from sources other than contaminated surface soils. The cancer risk coefficient is not radionuclide-specific. Consequently, the same coefficient is used in all cases to which this method applies.

6.6 Radiation Units Conversion

6.6.1 SI Units

The transition to the International System of Units (SI) has been recommended by numerous international technical and regulatory organizations and it is the policy of the United States that regulations should not impede this transition. To ensure a smooth transition to SI units, international and domestic organizations have recognized that there are circumstances where there is a need for showing information in both the SI and the customary units (NAS, 1990).

The Curie and Becquerel are units of measure of the quantity or activity of radioactive material which indicates the rate that atoms in the material are giving off radiation or disintegrating. The Curie (Ci) is equal to 37 billion disintegrations per second whereas the Becquerel (Bq) is equal to only one disintegration per second. The sievert (Sv) and the rem are units of measuring absorbed energy from all types of radiation in human tissue (dose equivalent health effects). The Gray (Gy) and rad are the units of measuring the absorbed dose of radiation energy in matter.

6.6.2 Conversion Factors

- ◆ Becquerel (Bq) = 1 disintegration per second = 2.7×10^{-11} Ci
Curie (Ci) = 3.7×10^{10} disintegrations per second = 3.7×10^{10} Bq
- ◆ Gray (Gy) = 1 joule per kilogram = 100 rad
Rad = 100 erg per gram = 0.01 Gy
Rem = 0.01 Sievert (Sv)



- ◆ Sievert (Sv) = 100 rem

For radon and short-lived radon daughters only:

Working Level (WL) = 1.3×10^5 MeV of alpha energy in 1 liter of air (approximately = 100 pCi of radon-222 alpha energy released from decay daughters)

Working Level Month (WLM) = Exposure from 1 WL of radon daughters for 170 working hours

6.7 Regulator Dialogue

The statutory and regulatory history shows that radionuclide effects are to be considered in the baseline risk assessment process. The guidance documents reveal that risk from radionuclide and other chemicals are calculated differently. An expert in radiation risk should be consulted to ensure that the risks calculated for the radionuclides have been estimated properly. Mortality-to-incidence risk ratio data is included in cancer risk calculations for radionuclide. Radioactive decay progeny must be considered for each radionuclide at the site.

Gamma emitters must be considered for internal and external exposures. Gamma radiation is also an externally penetrating exposure. Alpha and beta emitters should only be considered for internal exposures. The exception to this is if the alpha or beta emitter is associated or attached to a dermally absorbed chemical.

6.8 References

NAS. 1980. "Committee of the Biological Effects of Ionizing Radiations (BEIR III), The Effects on Populations of Exposure to Low Levels of Ionizing Radiation," National Academy of Sciences, National Research Council. National Academy Press. Washington, D.C.

NAS. 1990. Health Effects of Exposure to Low Levels of Ionizing Radiation. National Academy of Sciences, National Research Council, Committee of the Biological Effects of Ionizing Radiation, BEIR V. NAS Press. Washington, D.C.

UNSCEAR. 1988. Effects and Risks of Ionization Radiation, Report to the General Assembly. United Nations Scientific Committee on the Effects of Atomic Radiation Sources Sales No. #88. IX. 7, United Nations, New York, 1988.

USEPA. 1989a. "Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual, Part A, U.S. Environmental Protection Agency, Washington, D.C. EPA/540/1-89/002.

USEPA. 1989b. "Background Information Document-Environmental Impact Statement for NESHAPs Radionuclide. Volume 1. Risk Assessment Methodology." U.S. Environmental Protection Agency. Washington, D.C. EPA/520/1-89-005.



USEPA. 1990. "National Oil and Hazardous Substance Pollution Contingency Plan (Final Rule)." U.S. Environmental Protection Agency. Washington, D.C. 40 CFR 300; FR 8666.

USEPA. 1994a. "Health Effects Assessment Summary Tables." FY-1994 Annual. U.S. Environmental Protection Agency. Washington D.C. EPA 540/R-94/020, March 1994.

USEPA. 1994b. "Estimating Radiogenic Cancer Risks." U.S. Environmental Protection Agency. Washington, D.C. EPA 402-R-93-076, June 1994.



Chapter 7: Noncancer Health Endpoints

7.1 Introduction

The toxicity assessment consists of two components: hazard identification and dose response evaluation. Hazard identification determines whether exposure to an agent can cause an increase in the incidence of a particular adverse health effect (e.g., birth defects) and whether the adverse health effect is likely to occur in humans. Dose response evaluation quantitatively evaluates the toxicity information and characterizes the relationship between the dose of the contaminant administered or received and the incidence of adverse health effects in the exposed population.

Noncancer toxicity values (e.g., reference doses) are derived from the quantitative dose-response relationship data (USEPA, 1989), from both human and animal studies, although human epidemiological studies are rarely available. Therefore, animal studies are the primary basis for developing noncancer health endpoint toxicity values. These values are expressed as reference doses (RfDs) for oral exposures and reference concentrations (RfCs) for inhalation exposures (see Chapter 1 for more details on their derivation). Noncancer health endpoints are addressed in the toxicity assessment section of a baseline risk assessment. The Science Advisory Board (SAB) (USEPA, 1990a) recommended to EPA that “for assessment of non-cancer human health risks the Agency should try to establish a risk assessment framework consistent with that used for carcinogens.” But, at present, there are only proposed guidelines for reproductive risk (USEPA, 1988a and 1988b) and final guidelines for developmental risks (USEPA, 1991). Guidelines for deriving other noncancer toxicity values do not exist. Guidelines for neurotoxicity are being developed.

7.2 Discussion of Noncancer Health Endpoints in Statutes, Regulations, and Guidelines

7.2.1 Statutory and Regulatory Noncancer Toxicity Assessment Framework

As with radionuclide, CERCLA, SARA, and the NCP (USEPA, 1990b) do not specifically address noncancer health risks, but the broad definitions of pollutant or contaminant do include noncancer health endpoints (see Section 6.2.1). In responding to comments on alternative toxicity values proposed by Potential Responsible Parties (PRPs), the NCP stated:

EPA will, of course, consider such public comments submitted on toxicity. However, it is important to note that the Superfund risk assessment process typically relies heavily on existing toxicity information or profiles that EPA has developed on specific chemicals. EPA believes that the use of a consistent data base of toxicological information is important in achieving comparability among its risk assessments.



This data base is the Integrated Risk Information System (IRIS). The NCP also stated that:

. . . where no toxicological information is available in EPA's data base, then EPA routinely considers other available information, including information provided by PRPs or other interested parties Key assumptions and uncertainties in both contaminant toxicity and human and environmental exposure estimates must be documented in the baseline risk assessment, as well as the sources and effects of uncertainties and assumptions on the risk assessment results. Exposure assumptions or other information, such as additional toxicity information, may be evaluated to determine whether the risks are likely to have been under- or overestimated.

On the confidence of a toxicity value in IRIS, the NCP pointed out that "a high confidence in a toxicity value reflects a consensus that the value is not likely to change." The corollary to this would be that a value with a low confidence would be more likely to change.

7.2.2 General Guidance for Noncancer Toxicity Assessment

As discussed in the introduction, toxicity assessment contains two components hazard identification and dose response evaluation. Deriving a toxicity value requires toxicological expertise; therefore, it is beyond the scope of the Superfund Public Health Evaluation Manual (SPHEM) (USEPA, 1986a) and Risk Assessment Guidance for Superfund (RAGS) (USEPA, 1989) to give guidance on this aspect of the toxicity assessment. However, these documents do give guidance on what to do with the toxicity value once it has been derived and presented in IRIS.

Superfund Public Health Evaluation Manual (SPHEM)

SPHEM (USEPA, 1986a) discusses acceptable intakes for subchronic exposures (AIS) and acceptable intakes for chronic exposures (AIC)." AICS and AISs are derived from methods similar to RfDs, but the methodology was not as strict as that for RfDs, and Health Effects Assessment (HEA) documents. These values are determined by identifying the no-observed-adverse-effect-level (NOAEL) in a study and dividing the NOAEL by several uncertainty factors. The uncertainty factors are as follows: 10 for extrapolation from animals to humans, 10 for different sensitivities with the human population, and 10 for the use of a subchronic NOAEL to derive a chronic (AIC) value. The AIS and AIC values for chemicals that produce the same toxic effects are utilized in the risk characterization step to derive the hazard index. Many of the AIS and AIC values for noncarcinogenic effects were supplied in Appendix A of SPHEM.

Risk Assessment Guidance for Superfund (RAGS). Volume 1: Human Health Evaluation Manual (Part A)

RAGS points out that the toxicity assessment has already been performed for many chemicals. Toxicity values and information can be obtained from IRIS, Health Effects Assessment Summary Tables (HEAST) (USEPA, 1994), EPA drinking water criteria documents, drinking water Health Advisory summaries, ambient water quality criteria documents, air quality criteria documents, ATSDR, and EPA's



undergone extensive peer review; thus, it will require an experienced toxicologist familiar with EPA toxicity assessments to present successfully any new data in the baseline risk assessment.

Toxicity values are expressed as reference doses (RfDs) for oral exposures, and reference concentrations (RfCs) for inhalation exposures. They are both derived using the same methodology. The terms acceptable daily intakes (ADIs), acceptable intakes for chronic exposures (AIC), and acceptable intake-s for subchronic exposures (AIS) have been superseded by RfDs. Chronic RfDs are defined as “an estimate (with uncertainty spanning perhaps an order of magnitude or greater) of a daily exposure level for the human population, including sensitive subpopulations, that is likely to be without an appreciable risk of deleterious effects during a lifetime” (USEPA, 1989). Chronic RfDs are used to evaluate the noncancer effects for exposure periods between seven years and a lifetime; subchronic RfDs (RfD_s) are used to evaluate the noncancer effects for exposure between two weeks and seven years; and developmental RfDs (RfD_{dt}), are used for a single exposure event. RfD_{ss} do not appear in IRIS because they have not gone through verification by an intra-agency workgroup. RfD_{dt}s are still under development and have not been placed in IRIS or HEAST. Inhalation RfDs (RfD_i) are derived in a similar manner as oral RfDs, but the dynamics of the respiratory system and its diversity across species, as well as the differences in the physiochemical properties of the chemicals, must also be considered.

In cases where there is a lack of human data, analysts use animal data along with professional judgement to determine a value for RfD. Professional judgement involves an assessment of the relevance and scientific quality of the experimental studies, including the use of the appropriate animal model. If data from several animal studies are evaluated, EPA first seeks to identify animal models that are likely to be most relevant to humans based on biological rationale (e.g., metabolic and pharmacokinetic data). If a relevant animal model is not available, then “as a matter of science policy, the study on the most sensitive species (the species showing a toxic effect at the lowest administered dose) is selected as the critical study for the basis of the RfD” (USEPA, 1989). EPA assumes that humans are as sensitive to contaminants as the most sensitive animal species.

The assessment must then identify the critical toxic effect. “The effect characterized by the lowest-observed-adverse-effect-level’ (LOAEL) after dosimetric conversions is referred to as the critical toxic effect” (USEPA, 1989). The critical toxic effect can include any non-cancer toxic end point, which includes reproductive, developmental, and genetic effects. “After the critical study and toxic effect have been selected, EPA identifies the experimental exposure level representing the highest level tested at which no adverse effects (including the critical toxic effect) were demonstrated. This highest ‘no-observed-adverse-effect-level,’ (NOAEL) is the key datum obtained from the study of the dose-response relationship” (USEPA, 1989). The NOAEL of the critical toxic effect is chosen because it is assumed that “if the critical effect is prevented, then all toxic effects are prevented” (USEPA, 1989).

The RfD is calculated by dividing NOAEL (or LOAEL) for the critical toxic effect by uncertainty factors (UFs) and a modifying factor (MF). The appropriate NOAEL (or LOAEL) is divided by the product of all the applicable UFs and the MF (Barnes and Dourson, 1988). The uncertainty factors are 10 for extrapolation from animals to humans, 10 for different sensitivities within the human population, 10 for the use of a subchronic NOAEL, and 10 if a LOAEL is used to derive the chronic RfD value. The MF reflects a “qualitative professional assessment of additional uncertainties in the critical study and in the entire data base for the chemical not explicitly addressed by the preceding uncertainty factors”



(USEPA, 1989). This value ranges from 1 to 10, and the default value is 1. The use of the RfD in the risk characterization step is explained in Chapter 5, Chemical Mixtures.

Assessors should discuss the degree of confidence in the toxicity value(s) in the risk assessment. RAGS notes that “The degree of confidence ascribed to a toxicity value is a function of both the quality of the individual study from which it was derived and the completeness of the supporting data base.” The degree of confidence assigned to a toxicity value involves the use of professional judgement. RAGS states that the following factors add to the confidence of the evidence that the contaminant poses a hazard to humans

- similar effects across species, strains, sex, and routes of exposure;
- clear evidence of a dose-response relationship;
- a plausible relationship among data on metabolism, postulated mechanism of action, and the effect of concern;
- similar toxicity exhibited by structurally related compounds; and
- some link between the chemical and evidence of the effect of concern in humans.

According to EPA, “High uncertainty (low confidence, low strength of evidence) indicates that the toxicity value might change if additional chronic toxicity data become available. Low uncertainty (high confidence) is an indication that a value is less likely to change as more data become available, because there is consistency among the toxic responses observed in different species, sexes, study designs, or in dose-response relationships” (USEPA, 1989).

Because professional judgement plays a predominant role in selecting the critical study and in calculating the confidence level in the toxicity value, legitimate differences in this judgement may be negotiated. For example, assessors may debate which critical study should be used to derive the RfDs. Another issue is whether the most sensitive species was chosen over the more biological appropriate animal model. The confidence in the toxicity value, on the other hand, is related to the study design of the experiment. Were proper laboratory protocols followed? Does a new study have a better study design? For a new toxicity value to be accepted, the new study will need to have a better study design than the already accepted critical study. An experiment that does not produce definitive results will have a lower confidence. A new study that has a better study design and gives more definitive results will be more easily accepted than a poorly designed study that produces uncertain results. Risks from the old study and the new study must both be presented.

7.2.3 Guidelines for Reproductive Toxicity Assessments

There are two proposed guidelines for reproductive toxicity assessments, Proposed Guidelines for Assessing Female Reproductive Risk (USEPA, 1988a) and Proposed Guidelines for Assessing Male Reproductive Risk (USEPA, 1988b). Final reproductive risk assessment guidelines have not been



published. These two documents give guidelines on laboratory testing protocols, toxicity indices, end points, and their interpretation. Both guidelines point out that there are no mathematical models developed for the dose-response analysis, therefore, RfDs are derived as previously described, by applying uncertainty factors to a NOAEL or LOAEL.

The RfD is derived from one dose point, NOAEL or LOAEL, and therefore the current RfD approach does not take the shape or slope of the dose-response curve into consideration when deriving the RfD value. Two different chemicals may potentially produce similar NOAELs or LOAELs, but have significant differences in the slope of the dose-response curve. Deriving a RfD from the NOAEL or LOAEL would produce similar toxicity values for both chemicals. Deriving the RfD from the dose-response curve in this hypothetical situation could produce different toxicity values, and therefore risk estimates. Both guidelines address the issues of sexual behavior, fertility, and pregnancy outcomes.

Proposed Guidelines for Assessing Female Reproductive Risk

These guidelines state:

Ideally, study designs for all reproductive toxicity evaluations should include a high dose that produce-s some indication of maternal or adult toxicity (i.e., a level which produces a statistically significant reduction in body weight, weight gain, or specific organ toxicity, but no more than 10% mortality), a low dose which demonstrates a no observed effect level (NOAEL) for adult and offspring effects, and at least one intermediate dose level. A concurrent control group treated with the vehicle used for agent administration should be included (USEPA, 1988a).

Protocols used for both female and male reproductive risk include single and multiple generation studies. EPA is currently evaluating the continuous breeding protocol. Guidelines on conducting tests have been published by the Office of Pesticide Programs (USEPA, 1982) and the Office of Toxic Substances (USEPA, 1985). In addition to considering test protocol, these agencies also consider the appropriate route of exposure, number of animals per dose group, range between doses, and the relevance of the test system to humans. These guidelines point out the need for well conducted studies.

Reliance on the NOAEL places substantial importance on the power of the study to detect low-dose effects. Poorly designed studies employing insensitive measures may produce higher NOAELs than those from a well-designed and well-conducted study. Risk assessments based on such data may underestimate the actual human risk. Conversely, use of a NOAEL from a study in which there were wide intervals between doses may overestimate the actual risk (USEPA, 1988a).

Many of the testing protocols call for both the female and the male to be dosed with the contaminant. If adverse effects are seen with this testing protocol, it is difficult to determine whether the effect was mediated through the female, male, or both. To determine a female-only mediated effect, treated females must be mated with untreated males.



The indices that can be used for assessing female reproductive toxicity areas follows: male mating index, male fertility index, female mating index, female fertility index, female fecundity index, parturition index, gestation index, live litter size, live birth index, viability index, lactation index, weaning index, and preweaning index. The guidelines point out that “the gestation index... may provide limited information, since litters with only one pup are counted the same as those with more than one pup,” and “the live birth index varies proportionally with the number of stillborn in each litter. The viability of all offspring at birth cannot always be observed immediately after birth. Cannibalization of the pups is another phenomenon that occurs in rodents and can obscure the interpretation of this index (USEPA, 1988a).” Other indices include alterations in the onset of puberty, alterations in the reproductive cycle, oocyte toxicity, premature reproductive senescence, ovary weight and morphology, uterine weight and histology, and pituitary gland weight and histology.

Proposed Guidelines for Assessing Male Reproductive Risk

Many of the issues addressed in the female reproductive test protocols are also applicable to the male reproductive test protocols. An additional testing protocol used for male reproductive risk is the dominant lethal test. Duration of dosing is critical for male reproductive risk because “damage that is limited to spermatogonial stem cells will not appear in the caudal epididymis or in ejaculates for 8 to 14 weeks, depending on the test species” (USEPA, 1988 b). For humans, spermatogenesis is 12 weeks in duration, damaged sperm will appear in the ejaculate anywhere from 1 to 12 weeks depending on which stage was affected. The study design must consider this delayed effect. With some agents that bioaccumulate, the full impact on a given cell type could be delayed, as could the impact on functional end points such as fertility. The dosing regime is different for the highest dose in this guideline, “the highest dose should induce toxicity but not mortality” (USEPA, 1988b). No explanation is given as to why mortality is not desired for male reproductive tests, and up to 10% mortality is acceptable for female reproductive tests. Test guidelines specify the “use of 20 males and enough females to produce at least 20 pregnancies for each treatment group in each generation in the multigeneration reproduction test. However, 20 pregnancies are often achieved by mating two females per male and using less than 20 males per treatment group” (USEPA, 1988b). The guidelines point out that “in such cases, the statistical treatment of the data should be examined carefully,” and “in assessing male reproductive toxicity, the male remains the unit of statistical analysis. Using the female as the statistical unit inflates the sample size and may distort data analysis and interpretation” (USEPA, 1988b). To determine a male-only mediated effect, treated males must be mated with untreated females.

Male reproductive toxicity endpoints routinely evaluated for risk include the following: body weight, organ weights (testes, epididymides, seminal vesicles, prostate, and pituitary gland), organ histopathology, mating ratio, pregnancy ratio, litter size, pre- and post-implantation loss, number of live/dead pups, sex ratios, malformations, birth and postnatal weights, and survival. Organ weights are not the most sensitive measure of toxicity. For example, “damage to the testes may often be detected as a weight change only at doses higher than those required to produce significant effects in other measures of gonadal status” and “studies may report accessory sex gland weights with or without expression of the secreted fluids. Weights without fluids show less variability than weights in the presence of the secreted fluid” (USEPA, 1988b). Histopathological examination of the tissues is considered a sensitive tool for evaluating potential reproductive risks. Proper fixation of the tissue is important because, the “use of formalin fixation combined with paraffin embedding of the testis results in artifacts in control as well as



treated tissue” (USEPA, 1988b). Histopathological evaluations will not detect all reproductive effects (for example, genetic damage to the germ cell, decreased sperm motility, and an increase in abnormal sperm forms). Fertility and pregnancy outcomes through breeding studies are required to detect these effects, although these tests are considered to be insensitive as measures of reproductive injury. One reason for this is that “in some strains of rats and mice, sperm production can be reduced by 90% without compromising fertility” (USEPA, 1988b). Human sperm production does not have the extra capacity that rodents exhibit, and therefore the fertility potential of humans is far less than that of test species. Other male reproductive endpoints evaluated include the following: sperm count (for human studies this is very important), sperm morphology, sperm motility, sperm-cervical mucus penetration, *in vitro* fertilization, hormone evaluation, reproductive organ biochemical markers, and sexual behavior. For sexual behavior, the site of semen deposition can be strongly influenced by the sexual preparedness of the female rat. Reduced preparedness in the female rat could result in lower fertility index, which might erroneously be attributed to a spermatotoxic effect.

For both female and male reproductive risk evaluations, interpretation of these indices in new studies should be performed by an experienced reproductive toxicologist. For new studies to be considered by EPA, their study designs must be better than current studies, and the results should be more definitive. In other words, their needs to be less uncertainty associated with the new study than the currently accepted studies.

7.2.4 Guidelines for Developmental Toxicity Assessments

Two final guidelines have been published, Guidelines for the Health Assessment of Suspect Developmental Toxicants (USEPA, 1986b) and Guidelines for Developmental Toxicity Risk Assessment (USEPA, 1991a). These guidelines only address developmental toxicity, but they are closely related to the reproductive toxicity guidelines because of the organ systems involved. These guidelines have indicated that animal studies appear to be good predictors of human developmental toxicity. These studies have also shown that humans appear to be the most sensitive species, sometimes by a factor of 100 or more. As with reproductive toxicity evaluations, the study design and interpretation of the results are the two areas of interest that will be negotiated between a currently accepted study and any new study that is to be presented by DOE. Evaluations of study design and interpretation of the results should be performed by an experienced developmental toxicologist because “a great deal of scientific judgement based on experience with developmental toxicity data and with principles of experimental design and statistical analysis may be required to adequately evaluate such data” (USEPA, 1986b). The uncertainty associated with a new study should be less than the currently accepted study before it can be expected that EPA will seriously consider the new study.

Guidelines for the Health Assessment of Suspect Developmental Toxicants

The study design for developmental tests is the same as the female reproductive toxicity test protocols (see Section 7.2.3). These guidelines added, “The route of exposure should be based on expected human exposure considerations, although data from other routes may sometimes be useful, especially if supported by pharmacokinetic information.”



These guidelines discuss 51 maternal and developmental toxicity endpoints that are evaluated for development risk assessments. It is beyond the scope of this document to discuss all of these endpoints and their significance. The most sensitive statistical endpoint is change in fetal weight. The need for careful interpretation of results was stated:

Although statistical analyses are important in determining the effects of a particular agent, the biological significance of data should not be overlooked. For example, with the number of end points that can be observed in developmental toxicity studies, a few statistically significant differences may occur by chance. On the other hand, apparent trends with dose may be biologically relevant even though statistical analyses do not indicate a significant effect (USEPA, 1991a).

One area of concern that the public commented on in the guidelines was developmental effects produced only at maternally toxic doses. The guidelines stated that “current information is inadequate to assume that developmental effects at maternally toxic doses result only from the maternal toxicity; rather, when the lowest observed effect level is the same for the adult and developing organisms, it may simply indicate that both are sensitive to that dose level. Moreover, the maternal effects may be reversible while effects on the offspring may be permanent.” Several known human developmental toxicants (e.g., smoking, alcohol) produce their effects at minimally toxic adult doses (USEPA, 1986b). This issue was addressed further in the 1991 guidelines.

Guidelines for Developmental Toxicity Risk Assessment

Revisions to the 1986 guidelines include combining the hazard identification and dose-response evaluation, and developing the RfD_d and RfC_d values. “Hazard identification/dose-response evaluation involves examining all available experimental animal and human data and the associated doses, routes, and timing and duration of exposures to determine if an agent causes developmental toxicity and/or maternal or paternal toxicity in that species and under what exposure conditions.” The current use of NOAELs or LOAELs to derive RfDs does not take into account the variability of the data or the slope of the dose response curve. EPA is evaluating the use of the benchmark dose method to derive RfDs to remove the limitations in using NOAELs and LOAELs. The approaches taken in these guidelines are based on four assumptions

1. A contaminant that causes an adverse effect in experimental animals will potentially pose a threat to humans following the appropriate exposure.
2. The four manifestations of developmental toxicity (death, structural abnormalities, growth alteration and functional deficits) are all of concern. The guidelines state that “there is usually at least one experimental species that mimics the types of effects seen in humans, but in other species tested, the type of developmental perturbation may be different. Thus, a biologically significant increase in any of the four manifestations is considered indicative of an agent’s potential for disrupting development and producing a developmental hazard.”



3. “The types of developmental effects seen in animal studies are not necessarily the same as those that may be produced in humans.”
4. For developmental toxicants, a threshold is assumed for the dose-response curve.

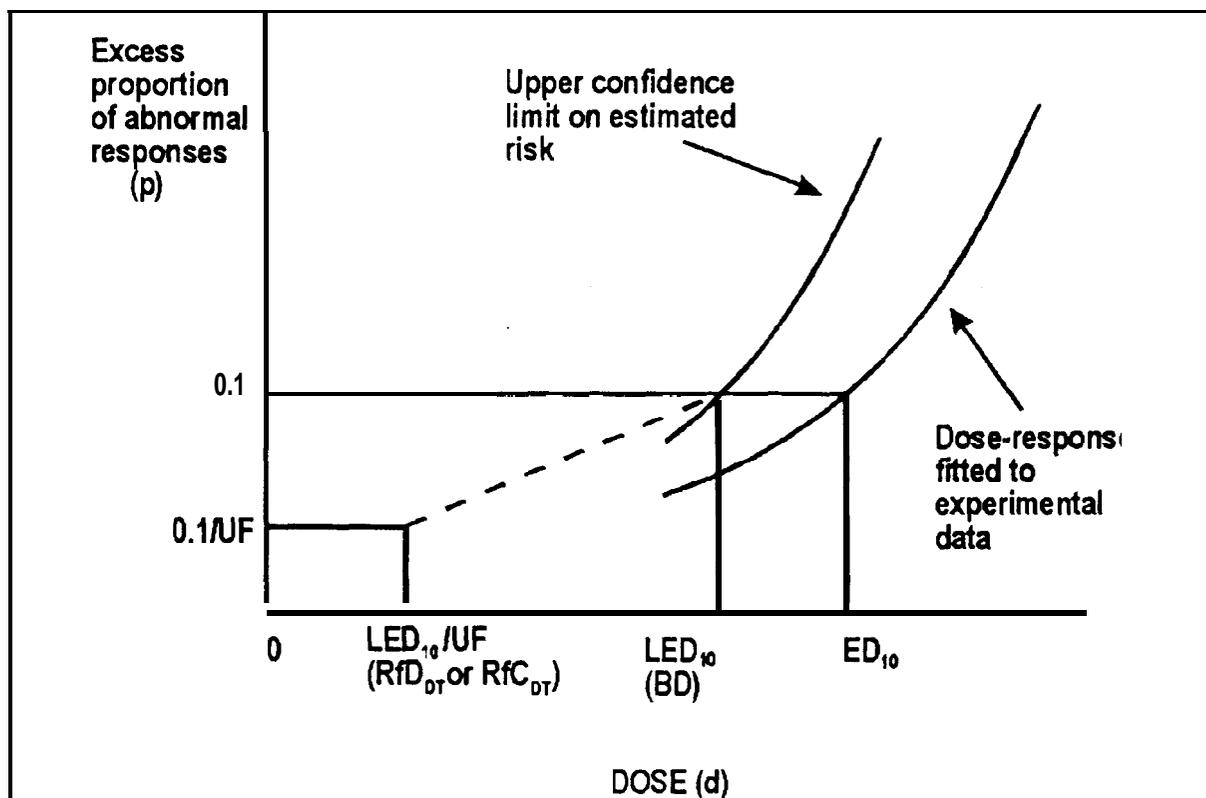
The study design cited in the 1991 guidelines is not significantly different from that presented in the 1986 guidelines. The only change was the use of a NOAEL for the low dose as opposed to a NOEL. It was explained that if the high dose produced excessive maternal toxicity (i.e., a dose that is significantly greater than the minimally toxic level), then results of the study would be difficult to interpret and of limited value. For selection of the test species, the SAB recommended that “the basic position of the Agency should be to use data from the most relevant species, and that use of data from the most sensitive species should be the default position” (USEPA, 1991). If a new, well-designed study is performed with a more relevant species, then the results from the new study can be a point for negotiation.

The end points of developmental toxicity considered in the 1991 guidelines are the same ones as in the 1986 guidelines, except that the 1991 guidelines added a discussion on functional deficits. Routine testing for functional deficits traditionally has not been required, but studies in developmental neurotoxicity are starting to be required by EPA under certain conditions. Generic developmental neurotoxicity test guidelines have been published (USEPA, 1991b). These guidelines also mention that offspring body weight is a sensitive indicator for developmental toxicity and they stress the importance of interpreting the results of a study from both a biological and statistical standpoint. They say that some variations may be statistically increased, but because they have a natural background of occurrence the variation may not be biologically significant (e.g., 12 or 13 ribs in rabbits). On the other hand, a variation may not be statistically significant but it may be biologically significant. These guidelines point out that “if a given study control group exhibits an unusually high or low incidence of postimplantation loss compared to historical controls, then scientific judgement must be used to determine the adequacy of the study for risk assessment purposes.”

Maternal toxicity and developmental toxicity were extensively discussed in the guidelines. It was again stated that if developmental effects are seen at minimal maternal toxic doses, then the contaminant is considered to be a potential developmental toxicant. When developmental effects are seen at minimal maternal toxicity levels, it is assumed that both the mother and the offspring are sensitive at the same dose. If maternal toxicity is produced at a lower dose than developmental effects, the results of the study become more uncertain. How this policy affects the risk assessment was stated as follows: “From a risk assessment point of view, whether a developmental effect is or is not secondary to maternal toxicity, does not impact on the selection of the NOAEL or other dose-response methodology.” The reason for this is because the NOAEL is derived for the critical effect. As discussed earlier, it is assumed that if the critical toxic effect is prevented then all toxic effects will be prevented. For example, if maternal toxicity is observed at an exposure lower than developmental toxicity, the NOAEL will be derived from the maternal critical toxic effect, and it would be assumed that the developmental toxic effect would automatically be prevented. This issue requires careful evaluation by an experienced toxicologist to determine the exposure levels for maternal and developmental toxicity. Another associated issue that should be evaluated is a comparison of maternal toxicity to other adult toxicity values. The pregnant or lactating female may be more sensitive than the rest of the adult population,



Because the use of the NOAEL or LOAEL does not consider variations in the data or the shape of the dose-response curve, EPA has begun evaluating the benchmark dose. Figure 7.1 explains the benchmark dose approach. The SAB strongly suggested “the use of a benchmark dose approach to replace the NOAEL” (USEPA, 1991a). EPA is researching the mathematical models to be used in this approach.



Source: US

This graphical illustration of the benchmark dose is based on Crump (1984) and Kimmel and Gaylor (1988). The benchmark dose (BD) is derived by modeling the data in the observed range, selecting an incidence level within or near the observed range (e.g., the effective dose to produce a 10% increased incidence of response, the ED_{10}), and determining the upper confidence limit on the model. The upper confidence value corresponding to, for example, a 10% excess in response is used to derive the BD which is the lower confidence limit on dose for that level of excess response, in this case, the LED_{10} . The RfD_u or RfC_u estimated by applying uncertainty factors (UF) to the BD would be greater than or equal to the BD/UF .

Figure 7.1 Benchmark Dose Approach

7.3 Issues and Regulator Dialogue

7.3.1 Noncancer Health Endpoint Issues

The statutory and regulatory history shows that noncancer toxic effects are to be included in the baseline risk assessment process. The history also indicates that alternative toxicity values from PRPs may



be considered, but that EPA prefers to use values that it has derived. Values supplied by PRPs are most likely to be considered when there are no existing values or when the confidence in the existing value is low. Alternative toxicity values also can be presented in the uncertainty section to “determine whether the risks are likely to have been underestimated or overestimated” (USEPA, 1990b).

The guidance documents focused on the confidence placed in a toxicity value and the interpretation of toxicological studies. Toxicity values developed from studies with high uncertainty might be changed with new data. Professional judgement is involved in selecting the critical study, interpreting the results, and determining the level of confidence in a study. All of these judgments should be performed by an experienced toxicologist. There are no general guidelines for assessing noncancer toxicity effects. Proposed guidelines exist for reproductive risk, and final guidelines exist for developmental toxicity. EPA is beginning to research alternative methods to develop RfDs because the existing methodology does not take into consideration variations in the data or the shape of the dose-response curve.

Alternative Toxicity Values Can Be Presented in the Risk Assessment

Both the regulations and the guidelines indicate that alternative toxicity values may be considered by EPA. There are generally three reasons to present new toxicity values:

- If there are no existing value(s) in IRIS.
- If the value in IRIS is assigned a low confidence.
- If the estimation of risk using existing values in IRIS have been under- or overestimated.

It will require an experienced toxicologist, however, to assist DOE in negotiating new toxicity values. Toxicity values in IRIS are peer reviewed and are placed in the data base only after they have been accepted by a consensus of scientific opinion. Presentation of any new toxicity value will be working against a peer-reviewed, EPA-accepted value, if a value already exists in IRIS. The remaining issue points will discuss various aspects of studies that should be considered when presenting new toxicity values.

Appropriate Study Design

Study design includes selection of the appropriate animal model, and the dosing regime. EPA’s policy is that the most relevant animal model, based on biological rationale, be selected first. “EPA first seeks to identify the animal model that is most relevant to humans based on a defensible biological rationale, for instance, using comparative metabolic and pharmacokinetic data” (USEPA, 1989). If a relevant model is not available, then the most sensitive species should be chosen, since it is assumed that humans are as sensitive as the most sensitive animal tested. If a new study is available that has used a more relevant animal model than the existing study, then DOE can negotiate the use of the new study. There must be biological and pharmacokinetic data available to prove that the new animal model is more relevant than the currently accepted test animal.



Dosing regime includes the concentration of the contaminant, schedule, and route of administration. Typically three doses are utilized in animal studies: 1) a high dose that produces toxicity, but not more than 10% mortality; 2) a NOAEL dose, and 3) an intermediate dose. Scheduling of the dose is critical for some toxicity endpoints (e.g., reproductive, developmental). For example, a contaminant may adversely affect only one stage of development or one stage of spermatogenesis. The route of administration should be relevant to human exposures, “the route of exposure should be based on expected human exposure considerations” (USEPA, 1986b). Any new study that is presented to EPA must follow the appropriate dosing regime before the study can be expected to be seriously considered by the Agency.

Selection and Interpretation of Toxicity Endpoints

The appropriate selection of toxicity endpoints for the NOAEL is very important because some endpoints are more sensitive than others, and some endpoints can give ambiguous results. For example, for female reproductive toxicity the gestation index “may provide limited information; since litters with only one pup are counted the same as those with more than one pup” (USEPA, 1988a). Some toxicity endpoints are time sensitive, therefore selection of when to measure the endpoint may be crucial for detecting a toxic effect. For example, contaminants may only effect one stage of spermatogenesis.

It is beyond the scope of this document to discuss all of the possible issues involved with the appropriate selection and interpretation of the various toxic endpoints; there are 51 endpoints for developmental toxicity. This chapter has discussed some of the issues for reproductive and developmental toxicity risks. An experienced toxicologist will be needed to assist in negotiating new studies.

7.3.2 Regulator Dialogue

All of the above issues must be considered when presenting any new studies to EPA. “The degree of confidence ascribed to a toxicity value is a function of both the quality of the individual study from which it was derived and the completeness of the supporting data base” (USEPA, 1989). The confidence in any study is associated with all of the above issues. Any new study that is presented to EPA should have a better study design and clearer interpretation of the results than the study used to derive the toxicity value in IRIS. If these conditions are not met, it cannot be expected that EPA will seriously consider the new study as an alternative to the existing study. Many of these issues can also be applied to cancer toxicity studies.

The above discussion indicates that EPA may consider alternative toxicity values in the risk assessment. It also indicates that alternative values will probably only be seriously considered when either the IRIS data base does not have a value, or when a value in the data base has a low confidence assigned to it. Alternative toxicity values may also be presented in the uncertainty section of the baseline risk assessment if it is believed that the risks are underestimated or overestimated when calculated using the values from IRIS. Neither CERCLA, SARA, nor the NCP gave guidance on how to conduct a toxicity assessment for noncarcinogens. Guidelines for deriving reproductive and developmental toxicity values are addressed in guidance documents. There are no guidelines for deriving other noncancer toxicity values.



7.4 References

Barnes, D.G. and Dourson, M. 1988. Reference Dose (RfD): Description and Use in Health Risk Assessments. *Regulatory Toxicology and Pharmacology*. Vol. 8, pp. 471-486.

USEPA. 1982. Pesticide Assessment Guidelines, Subdivision F. Hazard Evaluation: Human and Domestic Animals. U.S. Environmental Protection Agency, Office of Pesticides and Toxic Substances, Washington, D.C. EPA-540/9-82-025.

USEPA. 1985. Toxic Substances Control Act Test Guidelines: Final Rules. U.S. Environmental Protection Agency, Office of Pesticides and Toxic Substances, Washington, D.C. 50 FR 39426 and 50 FR 39433.

USEPA. 1986a. Superfund Public Health Evaluation Manual (SPHEM). U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/1-86/060.

USEPA. 1986b. Guidelines for the Health Assessment of Suspect Developmental Toxicants. U.S. Environmental Protection Agency, Office of Health and Environmental Assessment. Washington, D.C. 51 FR 34028.

USEPA. 1988a. Proposed Guidelines for Assessing Female Reproductive Risk U.S. Environmental Protection Agency, Office of Health and Environmental Assessment. Washington, D.C. 53 FR 24834.

USEPA. 1988b. Proposed Guidelines for Assessing Male Reproductive Risk U.S. Environmental Protection Agency, Office of Health and Environmental Assessment. Washington, D.C. 53 FR 24850.

USEPA. 1989. Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual (Part A) (RAGS). U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/1-89/002.

USEPA. 1990a. Reducing Risk: Setting priorities and Strategies for Environmental Protection. U.S. Environmental Protection Agency, Science Advisory Board. Washington, D.C. SAB-EC-90-021.

USEPA. 1990b. National Oil and Hazardous Substances Pollution Contingency Plan (NCP). U.S. Environmental Protection Agency. 55 FR 8666.

USEPA. 1991a. Guidelines for Developmental Toxicity Risk Assessment. Final. U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Washington, D.C. 56 FR 63798.

USEPA. 1991b. Pesticide Assessment Guidelines, Subdivision F. Hazard Evaluation: Human and Domestic Animals. Addendum 10: Neurotoxicity, Series 81, 82, and 83. U.S. Environmental Protection Agency, Office of Pesticides and Toxic Substances. Washington, D.C. EPA 540/09-91-123.



USEPA. 1994. Health Effects Assessment Summary Tables (HEAST) Annual FY 1992. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. OERR 9200.6-303 (92-1); NTIS No. PB92-921199.



Chapter 8: Institutional Controls in Baseline Risk Assessments

8.1 Introduction

Institutional controls are remedial alternatives “which limit human activities at or near facilities, to protect health and the environment and assure continued effectiveness of the program” (USEPA, 1990). Examples of institutional controls include land and resource use and deed restrictions, provisions for alternative water supplies, and well-drilling prohibitions (USEPA, 1990).

The EPA states in the National Oil and Hazardous Substances Pollution Contingency Plan (NCP) (USEPA, 1990) that institutional controls are considered “limited action alternatives,” and that baseline risk assessments are not the “proper place to take institutional controls into account.” There are instances, however, where institutional controls are not precluded from being described and/or factored into alternative exposure scenarios. This chapter provides an overview of how the use of institutional controls have been considered in CERCLA activities

8.2 Discussion of Institutional Controls in Statutes, Regulations, and Guidelines

8.2.1 Statutes

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) of 1980 [42 U.S.C. 9601], and the Superfund Amendments and Reauthorization Act (SARA) of 1986, passed by the U.S. Congress, are the statutes that establish the broadly defined goal of reducing and mitigating human exposures to hazardous wastes. Section 121 of CERCLA, Clean-up Standards, indicates a strong preference for the selection of cost-effective permanent remedial alternatives. CERCLA defines “removal” as the cleanup or removal of released hazardous substances from the environment; actions taken in the event of the threat of release of hazardous substances; actions to monitor, assess, and evaluate the release of hazardous substances; the disposal of removed material; and other actions to prevent, minimize, or mitigate damage to public health or to the environment [42 USC 9601 et. seq.]. In addition, CERCLA indicates that the term “removal” also includes “security fencing or other measures to limit access” (CERCLA, Sections 101-23 and 101-24).

8.2.2 Regulations

CERCLA statutes are implemented by regulations contained in the NCP of 1985 and its revisions in 1990 (USEPA, 1985; 1990). The NCP requires that a Remedial Investigation and Feasibility Study (RI/FS) be conducted at CERCLA sites, and that the RI/FS assess the “baseline risk posed by the contaminants under investigation” (USEPA, 1990).

EPA indicates that institutional controls are “a necessary supplement when some waste is left in place,” although they “should not substitute for more active response measures that actually reduce, minimize, or eliminate contamination (USEPA, 1990). Examples of institutional controls include land and resource use and deed restrictions, well-drilling prohibitions, and provisions for an alternative water



supply (USEPA, 1990). Section 300.430(a)(1) of the 1990 NCP directs the development of alternatives based on engineering controls, and “as necessary institutional controls, which limit human activities at or near facilities, to protect health and environment, ” The preamble to the 1990 NCP explained that “institutional controls may be used as a supplement to engineering controls over time but should not substitute for active response measures as the sole remedy unless active response measures are not practicable” (USEPA, 1988).

In response to comments on the purpose of risk assessments, EPA clarified in the 1990 NCP that a risk assessment “provides a consistent process for evaluating and documenting threats to human health and the environment posed by hazardous material at sites.” EPA also stated in the same document that the objectives of the risk assessment are to:

1. provide an analysis of baseline risk (i.e., the risks that exist if no remediation or institutional controls are applied to a site) and
2. use the risks and exposure pathways developed in the baseline risk assessment to target chemical concentrations associated with levels of risk that will be adequately protective of human health for a particular site (i.e., remediation goals).

8.2.3 Guidelines

The human health evaluation process was delineated initially in the Superfund Public Health Evaluation Manual (SPHEM) (USEPA, 1986), and later revised and published as Risk Assessment Guidance for Superfund (RAGS) (USEPA, 1989). The baseline risk assessment is defined as “an analysis of the potential adverse health effects (current or future) caused by hazardous substance releases from a site in the absence of any actions to control or mitigate these releases (i.e., under an assumption of no action).” RAGS further states that baseline risks are “risks that might exist if no remediation or institutional controls were applied at a site” (USEPA, 1989). The use of institutional controls in CERCLA risk assessments is addressed in RAGS Part B, Development of Risk-Based Preliminary Remediation Goals (PRGs) (USEPA, 1991a), and in RAGS Part C, Risk Evaluation of Remedial Alternatives (USEPA, 1991b). RAGS Part B provides guidance on using toxicity values and exposure information to derive risk-based PRGs. PRGs are the standards that the remedial alternatives must meet to achieve the criteria set forth in Section 300.430(e)(9)(iii) of the NCP. According to RAGS Part B, the calculation of PRGs involves identifying the most appropriate future land use for the site, which may become complicated because the assumptions for the site may be different from the land use in the surrounding area. For example, RAGS Part B discusses waste managed on site in a residential area, stating that PRGs for groundwater are based on residential exposures, and the PRGs for soils are based on industrial land use “with some management or institutional controls” (USEPA 1991a). RAGS Part C provides assistance on using risk information to evaluate (1) remedial alternatives during the FS and (2) the selected remedial alternative during and after its implementation. RAGS Part C specifically notes that if a remedial alternative relies on institutional controls “to reduce or eliminate exposure to contaminated media, then the ability of these controls to maintain protectiveness should be considered” (USEPA 1991 b). RAGS Part C also remarks that for sites where institutional controls are employed “the concentrations of chemicals



in a contaminated medium may remain the same as the baseline concentrations. The risk will have been reduced or eliminated however, by mitigation or elimination of the exposure pathway” (USEPA, 1991c).

8.3 Issues and Regulator Dialogue

8.3.1 Institutional Controls Issues

The NCP indicates that in instances where the balancing of trade-offs among remedial alternatives results in no practicable engineering remediation (e.g., treatment, removal, capping), institutional controls may be the selected remedial activity. Paragraph 300.68(i) of the NCP specifies that “the appropriate extent of remedy will be determined by the lead agency’s selection of a cost-effective remedial alternative that effectively mitigates and minimizes threats to, and provides adequate protection of public health and welfare and the environment” (USEPA, 1990). Although Site-specific institutional controls may ultimately be the selected remedial action, there are incongruent policies on how they may be addressed in baseline risk assessments. The following issues have been identified:

Evaluation of Institutional Controls

EPA responded to comments made on performing baseline risk assessments assuming that institutional controls were in place and effective at preventing exposure. The Agency indicated in the 1990 NCP that the baseline risk assessment is not the “proper place to take institutional controls into account” (see also USDOE, 1992). According to EPA, the proper place to take institutional controls into account is in the process outlined in RAGS Part C, Risk Evaluation of Remedial Alternatives. RAGS Part C indicates that mitigation or elimination of the exposure pathway may reduce or eliminate the risk from a contamination source where the contaminant concentration has remained the same (USEPA, 1991b).

Institutional Controls in Exposure Scenario Development

Exposure assessment includes the characterization of a site with respect to its physical characteristics as well as those of the human populations (USEPA, 1986). An exposure scenario includes facts, data, assumptions and professional judgments about how exposure takes place. According to Guidelines for Exposure Assessment (USEPA, 1992), the development of exposure scenarios addresses the following:

- Exposure Setting - The physical setting where exposure takes place.
- Exposure Pathways - The pathway from source to exposed population.
- Chemical Characterization - The amounts, locations, environmental, fate, environmental pathways, variation of concentration with time, etc.



- Population Characterization - Identification of exposed populations, and the profile of contact with a chemical based on behavior, location as a function of time, characteristics of the population, etc.

The NCP states that “EPA encourages the taking of early actions, under removal or remedial authority, to abate the immediate threat to human health and the environment” and that these actions are “prior to or concurrent with conduct of an RI/FS” (USEPA, 1990). The NCP also states that “a completed baseline risk assessment generally will not be available or necessary to justify an interim action.” Given the dynamic nature of CERCLA activities, and in spite of a constant striving to separate risk analysis from risk management, baseline risk assessments often need to look at the accomplishments of early actions: “Has the contaminated soil been removed from the site?” “Are the underground storage tanks still in place?” “Is the security fencing preventing trespassers from contacting the site contaminants?” The answers to these and other questions are inevitably factored into the development of exposure scenarios, and, although institutional controls constitute risk management decisions, it would seem appropriate that the baseline risk assessment could indicate through the use of alternative exposure scenarios the existence of early actions that, according to the NCP “abate the immediate threat to human health and the environment” (USEPA, 1990).

Institutional Controls in Land Use Determination

Characterizing the human population involves determining current and future land use. There are instances where CERCLA sites are categorized as industrial and/or located in areas sensitive to national security (e.g., Department of Energy’s laboratories). In these instances, exposure scenarios are often based on occupational exposure profiles (e.g., 8-hour days, 5 days/week, etc.). Realistically assessing the completeness of an exposure pathway at sites where institutional controls are in place (e.g., 24-hour patrolled and fenced area) may result in the exclusion of, for example, dermal contact with contaminated soil by children, although it may include contact to on-site contaminated groundwater if there is potential for current or future contaminant movement off site. Regarding the estimation of high-end exposure intakes, the Exposure Assessment Guidelines state that “the estimate is by definition intended to fall on the actual (or in the case of future exposures, probable) exposure distribution” (USEPA, 1992).

In determining future land use, RAGS recommends making the most conservative choice (i.e., residential land use). However, RAGS also mentions that “an assumption of future residential land use may not be justifiable if the probability that the site will support residential use in the future is exceedingly small” (USEPA, 1989). The 1990 NCP also states that “the assumption of residential land use is not a requirement of the program but rather is an assumption that may be made, based on conservative but realistic exposures, to ensure that remedies that are ultimately selected for the site will be protective” (USEPA, 1990). The use of professional judgment during the determination of future land use is seen by RAGS as “critical,” and it recommends 1) consulting the remedial project manager and 2) supporting the selection of alternative land use with a “logical reasonable argument” (USEPA, 1989).

“Reasonableness” is discussed in RAGS and the 1990 NCP under the concept of reasonable maximum exposures (RME) as applied to assumptions made during the assessment of human health risks: “RME is the maximum exposure that is reasonably expected to occur at a site” (USEPA, 1989; 1990).



Thus, at CERCLA sites located at non-residential DOE facilities, where a change in land use in the foreseeable future is unlikely, it may be reasonable to assume that future land use will be the same as current use (i.e., non-residential).

The results of the baseline risk assessment will help establish acceptable exposure levels for use in developing remedial alternatives “Exposure estimates for future use of the site will provide the basis for the development of protective exposure levels” (USEPA, 1990). According to EPA, if the future land use is unclear, “risks assuming residential land use can be compared to risks associated with other land uses, such as industrial” (USEPA, 1990). RAGS Part B states that in the absence of site-specific information to select one future land use over another, “it may be appropriate to develop a separate set of risk-based PRGs for each possible land use” (USEPA, 1991a).

8.3.2 Regulator Dialogue

In conclusion, EPA currently directs that the effectiveness of institutional controls not be evaluated during CERCLA baseline risk assessments, but under the authority of RAGS Part C, Risk Evaluation of Remedial Alternatives. However, language in the NCP would appear to indicate that institutional controls could be addressed in a baseline risk assessment as part of the development of current and future exposure scenarios. In such scenarios, land-use patterns may preclude the completeness of an exposure pathway (e.g., 24-hour patrolled and fenced area). EPA states that exposure scenarios as part of a baseline risk assessment “provide a powerful tool to evaluate the potential reduction of exposure and risk for these various options, and consequently are quite useful in many cost-benefit analyses” (USEPA, 1992). EPA also adds that “well-crafted and soundly based exposure scenarios may also help communicate risks and possible options to community groups” (USEPA, 1992).

8.4 References

Defense Cleanup. 1993. Volume 4, Number 6; ISSN: 0083-9735. February 12, 1993.

USDOE. 1992. Use of Institutional Controls in a CERCLA Baseline Risk Assessment. U.S. Department of Energy, Office of Environmental Guidance. Washington, D.C. EH-231-014/1292.

USEPA. 1985. National Oil and Hazardous Substances Pollution Contingency Plan. U.S. Environmental Protection Agency. [50 FR 47912].

USEPA. 1986. Superfund Public Health Evaluation Manual. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/1-86/060.

USEPA. 1988. Reposed Revisions to the National Oil and Hazardous Substances Pollution Contingency Plan. U.S. Environmental Protection Agency. [53 FR 51423].

USEPA. 1989. Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual (Part A). U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/1-89/002.



USEPA. 1990. National Oil and Hazardous Substances Pollution Contingency Plan. U.S. Environmental Protection Agency. Washington, D.C. [55 FR 8666].

USEPA. 1991a. Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual (Part B, Development of Risk-based Preliminary Remediation Goals). U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. OSWER Directive 9285.7-01B, December 1991. NTIS #PB 92-963334.

USEPA. 1991b. Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual (Part C, Risk Evaluation of Remedial Alternatives). U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. OSWER Directive 9285.7-01C. NTIS #PB 92-963334.

USEPA. 1992. Guidelines for Exposure Assessment. U.S. Environmental Protection Agency. Washington, D.C. [57 FR 22888].



Chapter 9: Site-Specific Data Versus Default Factors

9.1 Introduction

In the absence of site-specific information (e.g., contaminant characterization, exposed population factors, etc.), the best choice for describing the actual exposure and risk outcome is by using a combination of factors chosen by the risk assessor. Quantifying exposures is rooted in the use of professional scientific judgement. Improving basic research in the various science branches and its application in the environmental field will inevitably reduce uncertainty in risk estimates.

The need at EPA for greater consistency among various sites has led to the development and evolution of guidance documents that provide agency-wide standard default factors and procedures to be used in the absence of site-specific values. EPA responded to arguments that standard default factors are conservative saying that, in the absence of (or limited) data, the risk estimates should be protective of public health.

9.2 Discussion of Site-Specific Data Versus Default Factors in Statutes, Regulations, and Guidelines

9.2.1 Statutes and Regulations

CERCLA, SARA, and NCP do not provide specific guidance on how to address the absence of site-specific data when performing baseline risk assessments. However, the documents provide general directives regarding risk assessments.

9.2.2 Guidelines

Guidelines for Estimating Exposures

The Federal Register of September 24, 1986, published the final EPA Guidelines for Estimating Exposures (USEPA, 1986a), as well as the responses to comments by the public and by the EPA Scientific Advisory Board (SAB). The guidelines, which provide EPA with a framework for performing exposure assessments, indicated that the ideal exposure assessment would be based on data derived from environmental measurements, but recognized that data gaps would be a common problem. When environmental data are limited they direct that modeling be used to estimate exposures and that properly identified assumptions and “order of magnitude estimates” be utilized to delineate exposure areas of concern (USEPA, 1986a).

The guidelines state that uncertainty evaluation is an important part of all exposure assessments because both data and assumptions carry varying degrees of uncertainty that impact the accuracy of exposure assessments. The guidelines recognize the existence of uncertainties in measurements of environmental contamination, and in the estimation of those concentrations when direct measurements are



unavailable. They state that “reliable, analytically-determined values must be given precedence over estimated values” (USEPA, 1986a).

Commentors expressed concern that the guidelines allow assessors “too much latitude in choice of approach and do not assure that all data, sources, limitations, etc., are considered before an exposure assessment is conducted.” EPA replied that the generality of the guidelines is deliberate “in order to accommodate the development of exposure assessments with different levels of detail depending on the scope of the assessment.” Other commentors asked for further guidance to address situations where different exposure models give different results. EPA indicated the necessity of evaluating the uncertainties associated with source data and assumptions, “whether the exposure assessment is based on measurements or simulation model estimates” (USEPA, 1986b). EPA also replied to concerns that worst-case estimates would be used when data are limited or nonexistent “The guidelines do not encourage the use of worst-case assessments, but rather the development of realistic assessments based on the best data available” (USEPA, 1986b). However, the guidelines emphasize that EPA will err on the side of public health when evaluating uncertainties if data are limited or nonexistent.

Superfund Public Health Evaluation Manual (SPHEM)

The Superfund Public Health Evaluation Manual (SPHEM) was published in October of 1986 to provide detailed guidance on how to conduct a public health evaluation at a Superfund site. Because the actual dose received is generally uncertain, the exposure assessment requires the use of complex exposure models that are based on incomplete knowledge of how hazardous substances are transported and undergo transformation in the environment, and how they affect human health. SPHEM indicates that the most appropriate models for Superfund sites are “simple environmental fate models using conservative (i.e., reasonable worst case) assumptions” (USEPA, 1986b).

SPHEM outlines estimation methods for determining indicator chemical concentrations when actual data are not available on the extent and duration of human exposure before remediation. Although the approach was toward “worst-case” scenarios, SPHEM also indicates that “this conservative approach can be modified based on site-specific information to the contrary,” and that “if more accurate site-specific information is available, it can be used to give a better representation of risk at the site” (USEPA, 1986b). In addition, SPHEM provides several examples of how to use the standard assumptions and how to make adjustments based on more accurate site-specific data (e.g., intake and body weight information for the exposed population). Following are SPHEM guidelines on this topic:

- “It is essential to collect sufficient environmental sampling data so that if contamination has reached a human exposure point, some actual data may be used in the evaluation of potential effects.”
- “At most sites, a combination of site monitoring data and environmental modeling results will be required to estimate chemical concentrations at exposure points.”
- “...at all sites the available monitoring data must be reviewed thoroughly and used to the extent possible. For example, monitoring data should always be used to assist in



selection, calibration, and verification of chemical fate models and to help in the estimation of source terms (i.e., release rates) for these models.”

SPHEM also recommends that risk assessment consult other sources of site-specific information. In the case of determining human exposures, SPHEM states that “in the event that data from human monitoring in the site vicinity (e.g., blood or tissue analyses, genetic testing data) are available or such monitoring is planned, the Agency for Toxic Substances and Disease Registry (ATSDR) should be consulted. ATSDR should take the lead in conducting any human monitoring and in assessing the current health status of people near the site based on human monitoring data” (USEPA, 1986b).

Superfund Exposure Assessment Manual (SEAM)

SEAM, published as a final document in April of 1988, provided guidance for assessing contaminant release, environmental fate and transport, and human exposure to contaminants emanating from hazardous waste sites. SEAM was developed to give consistency in conducting exposure assessments at Superfund sites. It compiled and integrated various methodological approaches published by EPA and others.

SEAM recognizes that the approach to conducting exposure assessments is conservative: “While it is traditional in exposure assessments to make conservative assumptions in the absence of data, such assumptions must be reasonable . . .” However, it warns of the possibility that multiple conservative assumptions may result in extreme and unrealistic assessments: “Use of reasonably conservative assumptions at each step may produce cumulative assessment results that are overly conservative and thus unreasonable.”

SEAM provides analytical procedures supplementing SPHEM. According to SEAM the procedures were intended to be flexible, as illustrated in the following passage:

The user of this manual should understand that these analytical procedures are intended to be applied site-specifically. No two sites will be exactly alike in terms of the extent and complexity of contamination, of contaminant migration, or of potentially exposed populations. Therefore, the specific analytical procedures to be applied in all Superfund exposure assessments cannot be freed in general. Instead, the approach and methods applied to conducting an exposure assessment must be tailored to address existing site conditions (USEPA, 1988b).

Risk Assessment Guidance for Superfund, Volume I (RAGS)

RAGS, published in December of 1989, constitutes the present conceptual framework for CERCLA risk assessments. The exposure assessment process and the quantification of exposures is delineated in RAGS as follows: “...the exposure assessor calculates chemical-specific exposures for each exposure pathway. Exposure estimates are expressed in terms of the mass of substance in contact with the body per unit body weight per unit time” (USEPA, 1989a). RAGS states that the selection of exposure factors in CERCLA exposure assessments should result in “an estimate of the reasonable maximum



exposure” (USEPA, 1989a). RAGS also indicates that “...a determination of ‘reasonable’ cannot be based solely on quantitative information, but also requires the use of professional judgment. ”

The Exposure Factors Handbook (EFH)

The The Exposure Factors Handbook (EFH), intended to serve as a support document to the EPA's 1986 Guidelines for Estimating Exposures, provides basic equations for estimating exposure for various exposure scenarios. The EPA's guidelines for estimating exposures, as delineated in SEAM, were expanded and improved in EFH (USEPA, 1989b). The guidelines were developed to promote consistency among the various exposure assessment activities, and toward standardizing exposure assessment calculations. The handbook demonstrates how to apply standard default factors to specific exposure scenarios when site-specific data are not available. For each scenario, the handbook provides the following:

- the basic equation for estimating exposure;
- recommended default values for each parameter in the exposure equation (the default values are presented as averages [intended to represent typical values], ranges [derived from distributions, where possible, basing the lower end on the 50th percentile and the upper end on the 90-95th percentile], and frequent y distributions); and
- justification for each recommended value.

The EFH points out that the analyst “needs to be aware of uncertainties that result from using conservative assumptions when data are lacking,” and that when it is not feasible to acquire measured release rates, assessors could base estimates on contaminant concentration measurements in relevant source media (e.g., basing an estimate of groundwater contaminant concentration on measured concentrations in contaminated soil) (USEPA, 1989b). EFH reminds the risk analyst that no two sites are identical in the nature and extent of contamination. Therefore, the analytical procedures applied in each assessment should be site-specific.

Research to Improve Health Risk Assessments (RIHRA)

Concerns raised about uncertainties and how assumptions are made in risk assessments prompted the establishment of EPA programs and revisions of guidance documents. One of the programs established by EPA was labeled Research to Improve Health Risk Assessments (RIHRA). The program's primary objective was to identify the factors that produced the variability and uncertainty in Superfund exposure assessments. RIHRA published a report entitled “Exposure Assessment at Superfund Sites” (USEPA, 1989c). The report observed that SPHEM and SEAM were considered the “primary guidance documents relied [upon] most exclusively by the EPA regional offices” for use in preparing CERCLA risk assessments. Deficiencies in the guidance documents were supplemented by the EPA regions with open scientific literature, communications with EPA headquarters, contractors, etc. In addition, the RIHRA report identified supplemental guidance documents prepared by EPA Region I.



Supplemental Guidance to RAGS: EPA Region I Guidance

Responsibility for determining and explaining the guidance rationale for the exposure assumptions fell on the various EPA regional administrators. EPA Region I (Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont), for instance, formed a Risk Assessment Group that released the “Region I Supplemental Manual to Risk Assessment Guidance for the Superfund Program” (USEPA, 1989d). As with SPHEM and SEAM, this guidance provided for a reportable range of exposure values, but it also called for a greater imperative to communicate and substantiate exposure assumptions and choice of exposure parameters. While no attempt was made to clarify terms such as “reasonable,” Region I guidance provided for a set of default exposure parameters and recommended more communication with EPA remediation project managers (RPMs). The suggested default factors were to be used in the absence of site-specific data.

Supplemental Guidance to RAGS: Standard Default Exposure Factors

An EPA risk assessment intra-agency group was formed in March of 1990 “to address concerns regarding inconsistencies among exposure assumptions in Superfund risk assessments.” This group released an interim final document entitled “Supplemental Guidance to RAGS: Standard Default Exposure Factors” (USEPA, 1991a). According to the EPA intra-agency group, the principal reasons for the inconsistencies among exposure assessments included:

- factors derived from site-specific data,
- professional judgment when choosing values for key variables, and
- assumptions based on limited data.

The document provides further guidance on which specific default exposure factors to use when site-specific data are unavailable. It also states that “for factors where there is a great deal of uncertainty, a rationally derived conservative estimate is developed and explained” (USEPA, 1991a). The standard set of default exposure values follows the 1990 NCP directive for quantifying exposures under RME scenarios.

EPA Superfund 30-Day Task Force

Concerns raised about CERCLA exposure assumptions resulted in the creation of the EPA Superfund 30-Day Task Force. The role of this task force was to improve the effectiveness of the CERCLA program. The 30-Day Task Force published the report “Accelerating Superfund Cleanups and Evaluating Risk at Superfund Sites” where it recommended the review of CERCLA risk assessment guidance and policies (USEPA, 1991b). To reduce the uncertainty inherent in risk assessments, the Task Force indicated the need for several groups to review the assumptions, including EPA's Office of Research and Development the Risk Assessment Council, the Science Advisory Board, as well as industry and environmental groups.



Exposure Assessment Methods Handbook (EAMH)

The Exposure Assessment Methods Handbook provides guidance to exposure assessors on methodologies to estimate concentrations of chemicals in the environment (USEPA, 1991c). This document indicates the need to “provide decision makers with the complete spectrum of information concerning the quality of a concentration estimate, including the potential variability in the estimated concentration, the inherent variability in the input parameters, data gaps, and the effect these data gaps have on the accuracy or reasonableness of the concentration estimates developed” (USEPA, 1991c). The EAMH advises assessors to identify and prioritize “microenvironments” at a given site for exposure determination, as discussed in the following passage.

Total human exposure assessment methodologies are often limited by the simplistic nature of developed exposure scenarios and frequently-used default values for input parameters. Such simplified approaches may not always account specifically for variations in exposure parameters or for the multitude of microenvironment in which people are exposed via a given exposure pathway and a given exposure route on a daily basis. Prioritization of microenvironment for an exposure assessment is dependent on human activities (i.e., durations and frequencies of exposures in different microenvironment), pollutant concentrations encountered in these microenvironment, and exposure parameters such as inhalation rate that vary according to microenvironment and associated activities. (USEPA, 1991c)

EAMH suggests examining human activity patterns and time-use studies to gather the information needed to select exposure pathways. The handbook also states that “when such information is not readily available, a conservative approach that accounts for all potential exposure routes should be taken” (USEPA, 1991c).

An SAB Report: Superfund Site Health Risk Assessment Guidelines

This SAB report (USEPA, 1993) was published as a result of an SAB meeting on April 7-8, 1992, in Bethesda, Maryland. The meeting was organized to review key issues related to RAGS. One of the report’s conclusions was that the interpretation of an exposure value resulting from combining arithmetic average concentrations at a site with 50th and 90th percentile values for some of the default factors is very difficult to conceptualize. The SAB report recommends that in the absence of further guidance regarding the quantification of exposures at Superfund sites, the risk assessor should present a range of risk estimates.

9.3 Issues and Regulator Dialogue

9.3.1 Site-Specific Data versus Default Factors Issues

CERCLA guidance documents revealed that the evaluation of hazardous waste sites is characterized by numerous sources of uncertainty. The branches of scientific knowledge involved in evaluating human health risks from exposures to contaminants emanating from hazardous waste sites do



not yet provide for definite conclusions. This inability stems from the sources of uncertainty being rooted in the dynamic variability associated with natural systems, with the individual variability among the human population related to behavior and physiology, and with the assumptions made when filling data gaps in required information.

The guidelines for exposure assessment, as delineated in SEAM, EFH Guidelines for Exposure Assessment, and other documents, were developed to promote consistency among EPA exposure assessment activities. The parameters used in exposure intake calculations have often been revised by EPA to underline new policies and default factors to be followed in CERCLA risk assessments. Following are the issues related to the use of site-specific data versus standard default values:

Limited Site-Specific Data Warrants the Use of Conservative Default Factors

The current policy guiding CERCLA risk assessments is the RME (see Chapter 4 of this guidance). The RME definition and applicable policies are found in Guidelines for Exposure Assessment (USEPA; 1992a). The Supplemental Guidance to RAGS: Calculation of the Concentration Term (USEPA, 1992b) and Supplemental Guidance to RAGS: Standard Default Exposure Factors (USEPA, 1991a) are also consulted to provide a better understanding of practical issues in the RME. The first document shows how the concentration term in the RME equation is calculated using the 95% UCL on the mean, explains the significance of the RME, and discusses the basic concepts concerning the concentration term. The Supplemental Guidance to RAGS: Standard Default Exposure Factors provides for the standard default exposure factors to be used in the Superfund program. The exposure factors in this guidance are considered the most appropriate, and are intended to be used under the RME scenario.

The National Resources Defense Council and the Environmental Defense Fund have declared in the popular press that assumptions contained in Supplemental Guidance to RAGS: Standard Default Exposure Factors result in “abandoning the reasonable worst-case scenario” and provide “less protection to the public” (BNA, 1991). However, the Chemical Manufacturers Association indicated that a “30-year exposure duration is a more reasonable assumption than 70 years,” and views the guidance as a “step in the right direction, moving toward a more realistic worst-case assumption” (BNA, 1991). The EPA rationale for the new default values to be used when site-specific information is lacking was designed “to facilitate more consistent evaluation of the risks posed by the Superfund sites,” and the guidance “attempts to reduce unwarranted variability” (USEPA, 1991a).

Responding to public comments expressing concerns that worst-case estimates would be used as a result of conservative default factors when data are limited or absent, the EPA stated in Guidelines for Estimating Exposures (USEPA, 1986a) that “the Guidelines do not encourage the use of worst-case assessments, but rather the development of realistic assessments based on the best data available. However, the Agency will err on the side of public health when evaluating uncertainties when data are limited or nonexistent.”



Site-Specific Data are Preferred to Standard Default Factors

A memorandum from the former Assistant Surgeon General Richard Guimond released in March of 1992 indicated that EPA CERCLA risk assessments relied “heavily on site-specific assessments of human and environmental risk in determining the need for remedial action, in identifying contaminants of concern and critical exposure pathways, and in determining protective cleanup levels” (USEPA, 1992c). Guimond suggested that the EPA rationale be based on the belief that site-specific circumstances provide more appropriate decision-making in protecting populations from site contaminants. The following passage from Guimond’s memorandum highlights the issue:

Superfund guidance indicates that valid site-specific information on exposure factors --particularly human behavior patterns--be used in exposure assessments. In the absence of site-specific survey data, or in cases where the assessment must examine projected changes in land use, guidance has relied on survey data for other populations, commonly at the national level. Is this approach reasonable?

EPA has recognized that risk assessments “are sometimes delayed because of the need to collect better sampling data, or negotiations with potentially responsible parties over land use, exposure assumptions, and chemical toxicity” (USEPA, 1992c). To address the need for more efficient risk assessments, CERCLA guidance documents have evolved toward a full description of risk wherein quantitative estimates are associated with characterization of uncertainty. However, consideration must be given to how greatly the risk estimates may vary depending on whether site-specific data or default values are used. For example, the following specific situations may require different data:

- High-risk populations may warrant use of site-specific data in place of national data.
- Recreational activities (e.g., fishing) may warrant use of surveys.
- Monitoring of background samples is necessary when natural or other suspected sources of contaminants may contribute to overall risk.
- Monitoring of water supplies and water distribution points may be necessary.

9.3.2 Regulator Dialogue

In many cases it may be worth the extra expenditure of resources to increase the amount of site-specific data available for use in a given risk assessment. Because they typically are conservative, the use of default factors because of a lack of site-specific data often results in overestimation of risks. Thus, the use of site-specific data may result in reduced risk estimates, and therefore possibly reduce the costs of cleanup. As described in Chapters 3 and 4, the selection of models and input parameters for the models can be negotiated, as can the exposure scenario as described in Chapter 8. EPA guidance documents clearly indicate that site-specific data has general preference over standard default factors.



9.4 References

- BNA. 1991. Environment Reporter. The Bureau of National Affairs Inc. Washington, D.C. pp. 258, May 31, 1991.
- USEPA. 1986a. Guidelines for Estimating Exposures. U.S. Environmental Protection Agency. [51 FR 34042].
- USEPA. 1986b. Superfund Public Health Evaluation Manual. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/1-86/060.
- USEPA. 1988. Superfund Exposure Assessment Manual. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/1-88/001.
- USEPA. 1989a. Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual (Part A). U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/1-89/002.
- USEPA. 1989b. Exposure Factors Handbook, U.S. Environmental Protection Agency, Office of Health and Environmental Assessment. Washington, D.C. EPA 600/8-89/043.
- USEPA. 1989c. Exposure Assessment at Superfund Sites. U.S. Environmental Protection Agency, Environmental Monitoring Systems Laboratory. Las Vegas, NV. EPA 600/X-89/381.
- USEPA. 1989d. Supplemental Manual to Risk Assessment Guidance for the Superfund Program. U.S. Environmental Protection Agency Region I. U.S. Environmental Protection Agency. EPA 901/5-89-001.
- USEPA. 1991a. Supplemental Guidance to RAGS: Standard Default Exposure Factors. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. OSWER Directive: 9285.6-03.
- USEPA. 1991b. Accelerating Superfund Cleanups and Evaluating Risk at Superfund Sites. In: Superfund 30-Day Task Force Report. U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. Washington, D.C.
- USEPA. 1991c. Exposure Assessment Methods Handbook. U.S. Environmental Protection Agency, Exposure Assessment Group, Office of Health and Environmental Assessment. Washington, D.C. EPA 600/2-91.
- USEPA. 1992a. Guidelines for Exposure Assessment. U.S. Environmental Protection Agency. [57 FR 22888].



USEPA. 1992b. Supplemental Guidance to RAGS: Calculating the Concentration Term. U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. Washington, D.C. Publication 9285.7-081.

USEPA. 1992c. Charge for SAB Review of Superfund Human Health Evaluation Manual. Memorandum from Richard J. Guimond, Assistant Surgeon General, USPHS/Deputy Assistant Administrator. U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. Washington, D.C. March 4, 1992.

USEPA. 1993. An SAB Report: Superfund Site Health Risk Assessment Guidelines. Review of the Office of Solid Waste and Emergency Responses Draft Risk Assessment Guidance for Superfund Human Health Evaluation Manual by the Environmental Health Committee. U.S. Environmental Protection Agency, Office of the Administrator, Science Advisory Board. Washington, D.C. EPA-SAB-EHC-93-007.



Chapter 10: Data Gaps, Uncertainty, and Professional Judgement

10.1 Introduction

Uncertainty in risk assessments is rooted in the dynamic variability associated with natural systems, the individual variability among human behavior and physiology, and the methods designed to characterize both. Risk estimates in CERCLA risk assessments are conditional on a number of assumptions made throughout the assessment. For example, a set of risk estimates may be developed for surface water ingestion based on contaminant concentrations that were modeled from a monitored up-gradient contaminant source (e.g., ground water underneath a landfill or a leaking above-ground storage tank). The numerous assumptions involved in conceptual models of environmental characterization, and the choices of what values to use in various assessment parameters, are the product of professional judgments made by the risk assessors.

Concerns raised about uncertainties and how assumptions are made in risk assessments prompted the EPA to establish programs to investigate and resolve such issues and to revise guidance documents accordingly. One of the programs established by EPA was labeled Research to Improve Health Risk Assessments (RIHRA). The program's primary objective was to identify the factors that produced the variability and uncertainty in CERCLA exposure assessments. RIHRA published a report entitled Exposure Assessment at Superfund Sites (USEPA, 1989a). In this report, RIHRA observed that deficiencies in the primary guidance documents used in preparing CERCLA risk assessments, specifically SPHEM (USEPA, 1986a) and SEAM (USEPA, 1988), were being supplemented with open scientific literature, communications with EPA headquarters, contractors, etc.

Continuing concerns raised about CERCLA exposure assumptions resulted in the creation of the EPA Superfund 30-Day Task Force to improve the effectiveness of the CERCLA program. The 30-Day Task Force published the report Accelerating Superfund Cleanups and Evaluating Risk at Superfund Sites where it recommended that CERCLA risk assessment guidance and policies be reviewed (USEPA, 1991a). In addition, to reduce the uncertainty inherent in risk assessments, the Task Force recommended that assumptions be reviewed by EPA's Office of Research and Development, the Risk Assessment Council, the Science Advisory Board, and industry and environmental groups.

EPA has recognized that risk assessments "are sometimes delayed because of the need to collect better sampling data, or negotiations with potentially responsible parties over land use, exposure assumptions, and chemical toxicity" (USEPA, 1992a). To address the need for more efficient risk assessments, CERCLA guidance documents have evolved to encompass a full description of risk balancing quantitative estimates with characterizations of uncertainty.



10.2 Discussion of Data Gaps, Uncertainty, and Professional Judgement in Statutes, Regulations and Guidelines

10.2.1 Statutes and Regulations

CERCLA, SARA, and the NCP do not provide specific guidance on how to address uncertainty characterization in baseline risk assessments. Comments to Section 300.430(d) of the 1990 NCP criticized the use of EPA's toxicity values because they incorporate uncertainty factors that overestimate levels of risk [55 FR 8711]. EPA recognized the incorporation of uncertainty factors into the toxicity values, but the agency responded that the magnitude of the uncertainty factors is based on the confidence in the toxicity studies, and are not directly related to toxicity. "Larger uncertainty factors are generally used to ensure that protective levels are identified when considering data with greater uncertainty" (USEPA, 1990a).

The preamble to the NCP points out that "the results of the baseline risk assessment are used to understand the types of exposures and risks." To better understand exposures and risks, the NCP recommends that assessors document "the sources and effects of uncertainties and assumptions on the risk assessment results" (USEPA, 1990a).

10.2.2 Guidelines

Guidance documents that were developed to support CERCLA risk assessments address uncertainty in greater detail. Guidance on how to conduct CERCLA risk assessments was initially provided in the Superfund Public Health Evaluation Manual (SPHEM) (USEPA, 1986a). Later, SPHEM was revised and published as Risk Assessment Guidance for Superfund (RAGS) (USEPA, 1989b). In addition to SPHEM and RAGS, EPA developed further guidance supporting CERCLA risk assessments, specifically the Superfund Exposure Assessment Manual (SEAM) (USEPA, 1988), the Exposures Factors Handbook (EFH) (USEPA, 1989c), and various exposure assessment guidelines (USEPA, 1986b; 1992b). These guidance documents acknowledge the existence of data gaps and the uncertainty resulting from those data gaps, as well as from the various assumptions made to fill these gaps. Following is a discussion of how each guidance document addresses uncertainty in risk assessments and how they have contributed to a greater understanding of the issue.

Guidelines for Estimating Exposures

The Federal Register of September 24, 1986, (USEPA, 1986b) published the EPA Guidelines for Estimating Exposures, as well as the EPA responses to comments from the public and the EPA Scientific Advisory Board (SAB). The guidelines, which provide EPA with a framework for performing exposure assessments, indicated that the ideal exposure assessment would be based on data derived from environmental measurements, but recognized that data gaps would be a common problem. When environmental data are limited, EPA directs assessors to use modeling to estimate exposures, and to use properly identified assumptions and "order of magnitude estimates" to delineate exposure areas of concern (USEPA, 1986b).



The guidelines state that uncertainty evaluation is an important part of all exposure assessments because both data and assumptions carry varying degrees of uncertainty that impact the accuracy of the assessment. The method used for assessing uncertainty depends on several factors including the underlying parameters being estimated the type and extent of available data, and the estimation procedures used. If the data used in the exposure assessment were a result of statistical modeling, justification of the model should be included. The guidelines recognize the existence of uncertainties in measurements of environmental contamination, and in the estimation of those concentrations when direct measurements are unavailable, and state that “reliable, analytically-determined values must be given precedence over estimated values” (USEPA, 1986b).

The guidelines contain a section of EPA responses to public comments on the proposed guidelines. Commentors expressed concern that the guidelines allowed assessors “too much latitude in choice of approach and do not assure that all data, sources, limitations, etc. are considered before an exposure assessment is conducted.” EPA replied that the generality of the guidelines is deliberate “in order to accommodate the development of exposure assessments with different levels of detail depending on the scope of the assessment.” Other commentors asked for further guidance to address situations where different exposure models give different results. The EPA indicated the necessity of evaluating the uncertainties associated with source data and assumptions, “whether the exposure assessment is based on measurements or simulation model estimates” (USEPA, 1986b). The EPA also replied to concerns that worst-case estimates would be used when data are limited or nonexistent “The guidelines do not encourage the use of worst-case assessments, but rather the development of realistic assessments based on the best data available” (USEPA, 1986b). However, the guidelines emphasize that EPA will err on the side of public health when evaluating uncertainties if data are limited or nonexistent.

Superfund Public Health Evaluation Manual (SPHEM)

The Superfund Public Health Evaluation Manual (SPHEM) provides detailed guidance on how to conduct a public health evaluation at a Superfund site. SPHEM did not explicitly address uncertainty in risk assessments, but it did call for a listing of the most significant factors increasing the uncertainty of the risk assessment. Because the actual dose received is generally uncertain, the exposure assessment requires the use of complex exposure models that are based on incomplete knowledge of how hazardous substances are transported and undergo transformation in the environment and how they affect human health. SPHEM indicates that the most appropriate models for Superfund sites are “simple environmental fate models using conservative (i.e., reasonable worst case) assumptions.”

Exposure assessments performed under SPHEM were directed toward estimating a range of exposure scenarios a best estimate and an upper-bound scenario. According to SPHEM, this approach would provide “not only an estimate of the risk magnitude but also a good indication of the overall uncertainty of the analysis” (USEPA, 1986a).

Superfund Exposure Assessment Manual (SEAM)

SEAM provided guidance for assessing contaminant release, environmental fate and transport, and human exposure to contaminants emanating from hazardous waste sites. SEAM was developed to give



consistency in conducting exposure assessments at Superfund sites. It compiled and integrated various methodological approaches published by EPA and others.

On communicating the uncertainty associated with the estimated level of risk, SEAM recommends including a standard deviation or the 95% confidence limit. As indicated in the earlier Guidelines for Estimating Exposures, SEAM also suggested that “further research was needed on the use of a distributional approach to characterize exposure uncertainty” (USEPA, 1988).

EPA Region I Supplemental Guidance

EPA Region I (Connecticut Maine, Massachusetts, New Hampshire, Rhode Island, Vermont) released the Region I Supplemental Manual to Risk Assessment Guidance for the Superfund Program (USEPA, 1989d). The EPA Region I Guidance indicated that uncertainties and limitations are addressed in the final section of the risk assessment. According to this guidance, the final section “should clearly state the major limitations, sources of uncertainty, and, if possible, provide an indication as to whether they have resulted in over- or under-estimations of risk.” Following are examples of uncertainties and limitations:

- sample data that may tend to bias results (e.g., adverse weather conditions, heterogeneity of sample data),
- methodology used to compile and analyze the data (e.g., detection limits not documented),
- reliance upon non-validated models that predict contaminant fate and transport,
- variations in human behavior, and
- dose-response uncertainties (e.g., extrapolation of potency across routes of exposure, application of potency estimates to mixtures).

EPA Region I guidance called for a greater imperative to communicate and substantiate exposure assumptions and choice of exposure parameters. It also recommended a sensitivity analysis to determine which parameters have the greatest influence on the resulting risk estimates. Region I guidance provided for a set of default exposure parameters and recommended more communication with EPA remediation project managers.

The Exposure Factors Handbook (EFH)

The EPA’s guidelines for estimating exposures, as delineated in SEAM, were expanded and improved in the Exposure Factors Handbook (EFH) (USEPA, 1989c). The guidelines were developed to promote consistency among the various exposure assessment activities and toward standardizing exposure assessment calculations. The handbook demonstrates how to apply standard default factors to specific exposure scenarios when site-specific data are not available. This handbook was intended to serve as a



support document to EPA's 1986 Guidelines for Estimating Exposures. It provides basic equations for estimating exposure for various exposure scenarios.

The EFH points out that the analyst "needs to be aware of uncertainties that result from using conservative assumptions when data are lacking," and that, when it is not feasible to acquire measured release rates, estimates could be made based on contaminant concentration measurements in relevant source media (e.g., ground water contaminant concentration estimation based on measured contaminated soil concentrations) (USEPA, 1989c). EFH also describes approaches for dealing with uncertainty (e.g., sensitivity appraisals, Monte-Carlo simulations, and use of monitoring data to calibrate the model).

The EHF illustrated that the analyst is expected to have "a strong technical background in engineering or the sciences" and that it may be necessary for the analyst to obtain and use the original source documentation for the analytical methods. It also cautioned that care should be taken when interpreting modeling results because of the additive effect of using many conservative assumptions. The EHF also stated that "the U.S. EPA encourages ongoing communication between site analysts and experts in various exposure and health impact assessment fields."

Risk Assessment Guidance for Superfund, Volume I (RAGS)

RAGS, published in December of 1989, provides the current conceptual framework to be used when conducting CERCLA risk assessments. RAGS admits not being able to provide guidance to all circumstances arising at a site. RAGS states that users of the manual "must exercise technical and management judgment, and should consult with EPA regional risk assessment contacts" (USEPA, 1989b). RAGS emphasizes the appropriateness of the personnel involved in conducting the risk assessments because various assumptions and judgments are required during the process. RAGS recognizes the following general types of uncertainties associated with risk assessments:

- selection of contaminants of concern,
- chemical monitoring data (sampling and analysis),
- chemical fate modeling,
- exposure intake parameters,
- toxicity values, and
- summing exposure intakes across multiple pathways.

RAGS describes how to summarize and discuss the uncertainties in (1) site-specific exposure assessments and (2) general toxicity evaluations. Regarding exposure assessments, RAGS identified the following components responsible for uncertainties:



- Definition of physical setting: Characterization of the physical setting involves many professional judgments and assumptions about land uses, exposure pathways, and selection of contaminants of concern.
- Model applicability and assumptions: The mathematical expression of an exposure model (ground water transport model) is an approximation of site-specific environmental conditions. Because the currently available models are only partially validated and employ various simplifying assumptions, the risk estimates will be impacted by the uncertainties in the models. Characterizing model uncertainties involves (1) listing/summarizing key model assumptions and (2) indicating the direction and magnitude of the impact of the model (i.e., whether it overestimates or underestimates the risk levels and by how much).
- Exposure parameter value uncertainty: Significant site data gaps require that assumptions be made for certain parameters. Characterizing parameter uncertainties involves (1) listing all key exposure parameters (e.g., body weight, exposure duration, etc.); (2) describing the measured or assumed parameter distributions, including the shape of the distribution (e.g., log-normal), mean (geometric or arithmetic), total range, and percentiles; and (3) presenting parameter uncertainties in graphic form.

Regarding toxicity assessments, RAGS delineated the characterization of toxicity uncertainties as encompassing:

- listing weights-of-evidence for carcinogens,
- presenting how the data were derived (e.g. human or animal studies, duration of study, etc.),
- listing extrapolations from less-than-lifetime exposures to lifetime cancer risks,
- presenting information on potential synergistic or antagonistic interactions, and
- presenting qualitative information for each substance not included in quantitative assessment.

Guidance for Data Useability in Risk Assessment (GDURA)

Guidance for Data Useability in Risk Assessment (GDURA) was published to present an overview of the data collection and evaluation issues that affect the quality and usability of risk assessments (USEPA, 1990b). This guidance discusses how the quality of environmental data impacts the level of certainty of the risk assessment and stresses the importance of analyzing data limitations during the risk characterization. The document reviews the issues affecting the level of confidence in each component of the risk assessment.



To address uncertainties during hazard identification, GDURA indicates the need for describing the degree of confidence associated with the analytical sampling and analyses. In relation to uncertainties in exposure assessments, GDURA recommends (1) presenting the range of values for the chemicals monitored and the factors used in developing intake estimates and (2) summarizing the major assumptions made and how they affect the final exposure. During the toxicity assessment, GDURA indicates the importance of providing the degree of confidence on toxicity values (i.e., weight-of-evidence for cancer slopes, and uncertainty and modifying factors for RfDs). Finally, GDURA recommends that assessors provide an overview of the methods used for uncertainty analysis and include, along with numerical results, statements regarding limitations and uncertainties.

Supplemental Guidance to RAGS: Standard Default Exposure Factors

An EPA risk assessment intra-agency group was formed in March of 1990 “to address concerns regarding inconsistencies among exposure assumptions in Superfund risk assessments,” and released an interim final document entitled Supplemental Guidance to RAGS: Standard Default Exposure Factors (USEPA, 1991b). According to the EPA intra-agency group, there are two main reasons for exposure assessment inconsistencies:

- professional judgment when choosing values for key variables and
- assumptions based on limited data.

The document provides further guidance on which specific default exposure factors to use when site-specific data are unavailable. It also states that “for factors where there is a great deal of uncertainty, a rationally-derived conservative estimate is developed and explained” (USEPA, 1991b).

Exposure Assessment Methods Handbook (EAMH)

The Exposure Assessment Methods Handbook was published to provide guidance to exposure assessors on methodologies for estimating concentrations of chemicals in the environment (USEPA, 1991c). This document dedicates a chapter to Characterization and Analysis of Uncertainties in the Sampling, Monitoring, and Modeling of Environmental Concentrations of Contaminants. This chapter indicates that analysis of uncertainties can “provide decision makers with the complete spectrum of information concerning the quality of a concentration estimate, including the potential variability in the estimated concentration, the inherent variability in the input parameters, the existence of data gaps, and the effect those data gaps have on the accuracy or reasonableness of the concentration estimates developed” (USEPA, 1991c). The handbook identifies six causes of uncertainty in exposure assessments:

- Measurement errors: Uncertainty caused by random and systematic errors in measurement techniques (e.g., chemical analysis).
- Indirect empirical or generic data: Uncertainty caused by applying indirect data (e.g., use of a structurally similar chemical where chemical-specific data is lacking).



- Variability of natural systems: Uncertainty caused by inherent random variability in environmental- and concentration-related parameters (e.g., river flow, wind speed, ingestion rate, etc.).
- Environmental modeling: Uncertainty caused by simplifying approximations required in mathematical algorithms.
- Sampling errors: Uncertainty caused by sampling selection, number of samples, sample accuracy and precision, and sampling frequency.
- Professional judgement: Uncertainty caused by using professional judgments in every step of the assessment (e.g., evaluation of information, interpretation of results, etc.).

After identifying uncertainties, assessors are recommended to qualitatively and quantitatively analyze the impacts of these uncertainties on the estimation results. The qualitative analysis includes “a listing of possible variations in each parameter that would encompass a reasonable range of actual expected concentration conditions,” and a statement of the impact of pertinent assumptions. A qualitative analysis should “transmit the level of confidence in the results to the decision maker and aid in determining future actions.” For a quantitative analysis, the handbook identifies the following methods: (1) sensitivity analysis, (2) mean and variance of concentrations, (3) Monte Carlo simulation, and (4) confidence interval for concentration characteristics.

Finally, the handbook stresses the importance of how the results of uncertainty analyses are presented. The presentation should include the identification of the most sensitive parameters, statements of qualitative and quantitative uncertainties, major data gaps, and summary of the uncertainties for the overall concentration estimation.

Guidance for Risk Assessment

This document was released as part of a February 1992 memorandum from EPA Deputy Administrator Henry Habicht. The memorandum directs that the risk characterization section of the risk assessment must identify important uncertainties as a “discussion on confidence in the assessment.” He further directs that “the uncertainty analysis should reflect the type and complexity of the risk assessment, with the level of effort for analysis and discussion of the uncertainty corresponding to the level of effort for the assessment” (USEPA, 1991d). Finally, Habicht also stressed that when scientific assumptions are used, they need to be discussed, along with implications of using alternative assumptions.

Supplemental Guidance to RAGS: Calculating the Concentration Term

This supplemental guidance was designed to explain how assessors should calculate the concentration term to be used in exposure intake equations under the framework of the reasonable maximum exposure (RIME). The supplemental guidance states that the RME “is intended to account for both variability in exposure parameters and uncertainty in the contaminant concentration” (USEPA, 1992c). It defines the concentration term as the result of the calculation of the 95% upper confidence limit (UCL)



on the arithmetic average (mean) of the environmental samples. The rationale for using the 95% UCL value is that statistical confidence limits are “the classical tool for addressing uncertainties of a distribution average” (USEPA, 1992c).

Guidelines for Exposure Assessment

The Guidelines for Exposure Assessment, published in response to recommendations from EPA's SAB and the general public (USEPA, 1992b), replaced the Guidelines for Estimating Exposures published in 1986 and the Proposed Guidelines for Exposure-Related Measurements published in 1988. The guidelines outline the current theoretical principles to be used for exposure assessments in the CERCLA program.

Specifically, the guidelines introduce uncertainty “characterization” and uncertainty “assessment” as two activities that lead to varying degrees of sophistication in describing uncertainty. According to the guidelines, the characterization phase involves a qualitative discussion of the decisions that lead to the selection and rejection of specific data. The assessment phase is more quantitative in nature and may involve simple measures and techniques, such as ranges and sensitivity analysis, or more complex quantitative methodologies, such as probabilistic uncertainty analysis. For the less complex exposure assessments, where quantitative information is limited, the guidelines indicated that the uncertainty characterization may be all that is necessary.

The Guidelines for Exposure Assessment provides several options for dealing with data gaps

- collect new data,
- narrow the scope of the assessment where possible,
- use conservative assumptions,
- utilize models to estimate the conservativeness of assumptions,
- make use of applicable surrogate data, or
- utilize professional judgement,

The Guidelines for Exposure Assessment states that “the utility of [professional judgement] depends on the confidence placed in the estimate. Expert opinion based on years of observation of similar circumstances usually carries more weight than anecdotal information. The assessor must discuss the implications of these estimates in the uncertainty analysis” (USEPA, 1992b).



10.3 Issues and Regulator Dialogue

10.3.1 Data Gaps, Uncertainty, and Professional Judgement Issues

Review of CERCLA guidance documents reveals that there are numerous sources of uncertainty involved in evaluating human health risks from exposures to contaminants emanating from hazardous waste sites. EPA has declared that “no risk assessment is certain,” and that the function of a risk assessment is to provide “a best estimate of potential current and future risk along with the limitations associated with the estimates” (USEPA, 1990b).

Uncertainty analysis is the last step in the risk characterization. However, the analysis of uncertainty is a required procedure in every component of the risk assessment (i.e., during hazard identification, exposure assessment, toxicity assessment, and risk characterization). In the 1986 Guidelines for Estimating Exposures, EPA encouraged the evaluation of uncertainty in each aspect of the exposure assessment and stressed the importance of estimating the level of uncertainty in risk assessments so that decisions based on the risk assessment will reflect total uncertainty. However, RAGS states that “even in the most comprehensive analyses, it will generally be true that not all of the sources of uncertainty can be accounted for” (USEPA, 1989b). Nevertheless, insofar as possible an indication of the likely impact of uncertainties on the risk estimates obtained also should be provided (i.e., an indication of whether the uncertainties tend to drive risk estimates up or down). To date, however, risk assessors often have not provided such insight to decision makers. In a recent review and analysis of the degree to which risk assessments were adhering to the guidance provided by EPA Headquarters, the General Accounting Office reported that in 19 out of 20 baseline risk assessments reviewed did not adequately follow EPA’s guidance for disclosure of uncertainties in the assessment (GAO, 1994). Of the 20 assessments, 18 failed to include information on the possible ranges of values for various exposure parameters, 10 did not indicate how the uncertainties in the assessment affected the risk estimates obtained, and 7 did not provide the basis for selection of values or assumptions.

Exposure Assumptions and Toxicity Values are Great Sources of Uncertainty

Regarding the relative impact of data gaps, uncertainties, and assumptions made during the four components of a CERCLA risk assessment, EPA has stated that “uncertainties in toxicological measures and exposure assessments are greater than uncertainties in environmental analytical data and usually have a more significant effect on the uncertainty of the risk assessment” (USEPA, 1990b). The guidelines for exposure assessment, as delineated in SEAM, the Exposure Factors Handbook, the Guidelines for Exposure Assessment, and other documents, were developed to promote consistency among EPA exposure assessment activities. However, EPA has often revised the parameters used in exposure intake calculations to correspond with new policies and default factors to be followed in CERCLA risk assessments. Thus, the methodology used to assess exposure can introduce uncertainty in the overall risk assessment.

It is important to acknowledge the uncertainties in toxicity values because the exposure intake estimates are compared to them in the risk characterization step. Since human data seldom are available or adequate to estimate the toxicity values, risk estimates are generally based on experimental animal results. Cancer slope factors and reference doses in the EPA IRIS database are, for the most part, derived



from animal toxicological studies. Extrapolation from animal to human populations results in considerable uncertainty. It is believed that the use of uncertainty factors in performing the extrapolation overestimates the risk although the following statement reflects another option:

For chemicals where the dose-response is nearly linear below experimental doses, cancer risk estimates based on animal data are not necessarily conservative; Supralinearity could lead to anticonservative estimates of cancer risk...If the dose-response is nonlinear at low doses to produce cancer risks near zero, then low-dose estimates based on linear extrapolation are likely to overestimate risk and the limits of uncertainty cannot be established (Gaylor et al., 1993).

Uncertainties Tend to Overestimate Risk

Table 10.1 provides an overview of the typical sources of uncertainties associated with the various components of the risk assessment, and the impact of various assumptions required to address data gaps. Review of CERCLA guidance documents indicates that uncertainties associated with the ‘numerous assumptions made during the various phases of the risk assessment most frequently tend to overestimate the levels of risk associated with CERCLA sites.

Table 10.1: Typical Sources of Uncertainty in CERCLA Risk Assessments

Data Gaps/Uncertainty	Assumptions	Impact on Risk Assessment
Hazard Identification		
Insufficient number of samples	Use of various estimation methods	Overestimation
High detection limits	Contaminant level below detection limit	Underestimation
Contaminant degradation during sampling	Degradation occurs	Underestimation
Exposure Assessment		
Limited information on intake factors, population characteristics, exposure duration, etc.	Various assumptions required	Overestimation and/or underestimation



Data Gaps/Uncertainty	Assumptions	Impact on Risk Assessment
Limited or no chemical bioavailability data	100% bioavailability	Overestimation
Limited or no data on degradation, transformation, and fate of chemicals	No degradation and/or transformation	Overestimation and/or underestimation
Limited dermal absorption factors	Conservative default factors	Overestimation
Toxicity Assessment		
Toxicity values for low doses in humans derived from high doses in animal studies	Linearity of dose-response curves at low doses	Overestimation and/or underestimation
Limited information on shape of carcinogenic dose-response curves at low doses	95% upper confidence limit on cancer slope factors	Overestimation
Risk Characterization		
No toxicity information on individual chemicals	Use of RfDs and cancer slope factors of similar chemicals	Overestimation
No toxicity information on individual chemicals	Not factored into quantitative analysis	Underestimation
No interactive toxicity information on mixtures of chemicals	Dose additivity	Overestimation if antagonistic interaction; underestimation if synergistic interaction
Limited quality and size of sources of information	Quantification of risks, but no quantitative analyses of uncertainty possible	Risk assessment open to differing interpretations



Limited Prescribed Protocols to Address Uncertainty

The guidance documents reviewed suggest various procedures for addressing uncertainties. For example, methods exist to assess uncertainty and sensitivity in mathematical models (e.g., differential analysis, response-surface replacement, Monte Carlo methods). However, EPA suggestions are mostly general and do not provide for a specific methodology.

To address the uncertainty encountered in CERCLA risk assessments, RAGS recommends that the risk assessor “fully specify the assumptions and uncertainties inherent in the risk assessment to place the risk estimates in proper perspective” (USEPA, 1989b). EPA recommends a qualitative and/or a semi-quantitative approach that dictates “it is more important to identify the key site-related variables and assumptions that contribute most to the uncertainty than to precisely quantify the degree of uncertainty in the risk assessment” (USEPA, 1989b). Because of the considerable resources required under current practices to enable valid probability data distributions, EPA recognizes that “highly quantitative analysis is usually not practical or necessary” (USEPA, 1989b).

Use of Professional Judgement

Every CERCLA guidance document recommends the use of the best professional judgement when data gaps are encountered in the risk analysis. Because uncertainties inherent in risk assessments can produce a wide range of risk estimates, risk assessors have to make choices among numerous possibilities. According to William Ruckelshaus, former EPA Administrator, “[S]uch choices are influenced by values, which may be affected by professional training, or by ideas about what constitutes good science” (USEPA, 1984). EPA values, rooted in the various congressional mandates to be protective of public health, are biased toward the use of conservative models when data are lacking. This protective bias has often been criticized for producing unrealistic risk estimates, and also for impractical mandates “EPA often has a hard time dealing with uncertainty because personnel with different professional background operate under different statutes, which prompt different attitudes towards uncertainty...The agency cannot develop a rationale and consistent program without agreement on how to handle uncertainty. It must do better in clarifying the often subtle line between science and policy” (CEQ, 1985).

10.3.2 Regulator Dialogue

CERCLA risk assessment guidance documents acknowledge that uncertainties in risk assessments are in part the product of a lack of scientific knowledge (USEPA, 1989b; 1991c). The 16th Annual Report of the Council on Environmental Quality (CEQ, 1985) observes that “scientific uncertainty is pervasive in environmental decision-making,” and that “scientific issues concerning environmental protection often wind up for resolution in a courtroom rather than a laboratory because most of EPA mandates demand decisions for which no firm scientific basis exists.” The decisions, choices, and assumptions made by the various individuals requiring the best professional judgement may result in disparate conclusions.

A Carnegie Foundation publication reports that risk assessment is “a tool for extrapolating from scientific data to a risk number,” using assumptions that are “an admixture of science and policy”



(Carnegie, 1993). The report adds that “the science underlying most risk assessment assumptions is inconclusive,” and relying on those assumptions produces numerical risk estimates that are “highly uncertain and highly variable.” The report also indicates the difficulty in gaining a consensus about science and policy, and concludes that because “the process is assumption-and-value-laden,” its usefulness depends on the understanding of its assumptions and limitations.

In conclusion, data gaps and uncertainty are an integral part of CERCLA risk assessments. Dealing with data gaps and uncertainty may require the use of general default values (usually conservative), the use of mathematical models, or use of assumptions based on professional judgement. Regardless of which method or combination of methods are used to derive quantitative estimates of risk, it is imperative that the sources of uncertainty be clearly documented and evaluated. However, the lack of clear protocols on how to evaluate uncertainty may result in inconsistencies in the application of judgments, resulting in risk assessments being developed differently among CERCLA sites.

The above discussion, and discussions in previous chapters, illustrates that data gaps, uncertainties, and professional judgement are inherent in risk assessments. One method that can be used to remove data gaps is to obtain more site- or chemical-specific information. This information may not always be obtainable, therefore, models will have to be used. The DOE risk assessor should be knowledgeable about the site conditions and all potential exposure models, and input parameters for those models. Because of differing site conditions, no one model will be appropriate for all DOE sites. A thorough knowledge of site conditions and models will enable the risk assessor to determine which model, and input parameters, are most appropriate for a particular site. This knowledge will also enable the assessor to negotiate with EPA as to why certain models and parameters were chosen for that site. Choosing the most appropriate models and input parameters should also help to lower the uncertainty in the risk calculation.

10.4 References

Carnegie. 1993. Carnegie Commission on Science, Technology, and Government. Risk and the Environment: Improving Regulatory Decision Making. Carnegie Foundation, New York June 1993.

CEQ. 1985. Environmental Quality. 16th Annual Report of the Council on Environmental Quality. Council on Environmental Quality. Washington, D.C.

Gaylor, D. W., Chen, J. J., Sheehan, D.M. 1993. Uncertainty in Cancer Risk Estimates. In Risk Analysis, Vol. 13, No. 12, April 1993.

GAO, 1994. Superfund - Improved Reviews and Guidance Could Reduce Inconsistencies in Risk Assessments. U.S. General Accounting Office. Washington, D.C. GAO/RCED-94-220.

USEPA. 1984. Risk in a Free Society. EPA Journal. April 1984.

USEPA. 1986a. Superfund Public Health Evaluation Manual. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/1-86/060.



USEPA. 1986b. Guidelines for Estimating Exposures. U.S. Environmental Protection Agency. [51 FR 34042].

USEPA. 1988. Superfund Exposure Assessment Manual. U.S. Environmental Protection Agency, Office of Remedial Response. Washington, D.C. EPA 540/1-88/001.

USEPA. 1989a. Exposure Assessment at Superfund Sites. U.S. Environmental Protection Agency, Environmental Monitoring Systems Laboratory. Las Vegas, NV. EPA 600/X-89/381.

USEPA. 1989b. Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual (Part A). U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/1-89/002.

USEPA. 1989c. Exposure Factors Handbook. U.S. Environmental Protection Agency, Office of Health and Environmental Assessment. Washington, D.C. EPA 600/8-89/043.

USEPA. 1989d. Supplemental Manual to Risk Assessment Guidance for the Superfund Program. U.S. EPA Region I. U.S. Environmental Protection Agency. EPA 901/5-89-001.

USEPA. 1990a. National Oil and Hazardous Substances Pollution Contingency Plan. U.S. Environmental Protection Agency. [55 FR 8666].

USEPA. 1990b. Guidance for Data Useability in Risk Assessment. Interim Final. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. EPA 540/G-90/008, October 1990.

USEPA. 1991a. Accelerating Superfund Cleanups and Evaluating Risk at Superfund Sites. In: Superfund 30-Day Task Force Report. U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. Washington, D.C.

USEPA. 1991b. Supplemental Guidance to RAGS: Standard Default Exposure Factors. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. Washington, D.C. OSWER Directive: 9285.6-03.

USEPA. 1991c. Exposure Assessment Methods Handbook. U.S. Environmental Protection Agency, Exposure Assessment Group, Office of Health and Environmental Assessment. Washington, D.C. EPA 600/2-91.

USEPA. 1991d. Guidance for Risk Assessment. In: Guidance on Risk Characterization for Risk Managers and Risk Assessors. Memorandum from F. Henry Habicht II to Assistant and Regional Administrators, U.S. Environmental Protection Agency, Office of the Administrator. Washington, D.C. February 26, 1992.



USEPA. 1992a. Charge for SAB Review of Superfund Human Health Evaluation Manual. Memorandum from Richard J. Guimond, Assistant Surgeon General, USPHS/Deputy Assistant Administrator, U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. Washington, D.C. March 4, 1992.

USEPA. 1992b. Guidelines for Exposure Assessment, U.S. Environmental Protection Agency. [57 FR 22888].

USEPA. 1992c. Supplemental Guidance to RAGS: Calculating the Concentration Term. U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. Washington, D.C. Publication 9285.7-081.



APPENDIX A

Annotated Bibliography

Annotated Bibliography: Summary of Risk Assessment Requirements and Guidance

1.0 Statutory and Regulatory Requirements

1.1 Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). 1980. PL 96-510.

In 1980, Congress enacted the Comprehensive, Environmental Response, Compensation, and Liability Act (CERCLA), commonly referred to as Superfund in response to the dangers posed by sudden or otherwise uncontrolled releases of hazardous substances, pollutants, or contaminants into the environment. This statute created the Superfund program, and the need to conduct baseline risk assessments. CERCLA authorized 1.6 billion dollars over five years for a comprehensive program to clean up the worst abandoned or inactive waste sites in the nation. The National Contingency Plan (NCP), the implementing regulation of CERCLA, provides the organizational structure and procedures for preparing and responding to releases of hazardous substances, pollutants, and contaminants. The NCP is codified in 40 CFR 300.

1.2 CERCLA as Amended by SARA.

Superfund Amendments and Reauthorization Act (SARA). 1986. PL 99-499.

The reauthorization of CERCLA occurred in 1986. These amendments, known as the Superfund Amendments and Reauthorization Act (SARA), strengthen the Environmental Protection Agency's (EPA's) mandate to focus on permanent cleanups at Superfund sites, involve the public in decision processes at sites, and encourage States and Federally recognized Indian tribes to actively participate as partners with EPA to address these sites. SARA also expanded EPA's research and development in the area of alternative technologies. The changes to CERCLA Sections 104 (Response Authorities) and 121 (Cleanup Standards) had the greatest impact on the remedial investigation/feasibility study process. Section 121 cleanup standards state a strong preference for remedies that are reliable and provide long-term protection. Section 121(b) remedy selection strategies

- prefer remedial actions that employ treatment that permanently and significantly reduce the volume, toxicity, or mobility of hazardous substances, pollutants, and contaminant,
- discourage the use of off-site transport and disposal without treatment as the least favored alternative where practicable treatment technologies are available; and
- assess the use of alternative treatment technologies or resource recovery technologies and promote their use to the maximum extent possible.



Section 121(c) requires a review of remedial actions at five- year intervals after the initial remedial action as long as hazardous substances, pollutants, or contaminants that may pose a threat to human health or the environment remain at the site. If it is determined that the action has not provided protection to human health and the environment then further remedial action must be considered.

Section 121(d) requires that all Superfund remedial actions meet any Federal standards, requirements, criteria, or limitations that are determined to be legally applicable or relevant and appropriate requirements (ARARs). A provision is included in this section that if State ARARs are more stringent than Federal requirements, the State standards must be followed.

Section 104 of CERCLA requires the Agency for Toxic Substances and Disease Registry (ATSDR) to conduct a health assessment, which is qualitative by nature, for each Superfund site. This health assessment should be distinguished from the EPA Human Health Evaluation which is more quantitative in nature. CERCLA Section 104(i)(5)(F) defines health assessment as follows:

The term “health assessment” shall include preliminary assessments of the potential risks to human health posed by individual sites and facilities, based on such factors as the nature and extent of contamination, the existence of potential pathways of human exposure (including ground and surface water contamination, air emissions, and food chain contamination), the size and potential susceptibility of the community within the likely pathways of exposure, the comparison of expected human exposure levels to the short-term and long-term health effects associated with identified hazardous substances and any available recommended exposure or tolerance limits for such hazardous substances, and the comparison of existing morbidity and mortality data on diseases that may be associated with the observed levels of exposure. The Administrator of ATSDR shall use appropriate data, risk assessments, risk evaluations, and studies available from the Administrator of EPA.

An ATSDR health assessment and the traditional risk assessment should be distinguished from each other.

- The health assessment is qualitative in nature, site specific, and focuses on medical and public health perspectives. Exposure to contaminants are discussed in terms of especially sensitive populations, mechanisms of toxic chemical action, and possible disease outcomes.
- Risk assessments, the framework of EPA’s human health evaluation, differ from health assessments in that they are quantitative, chemical-oriented characterizations that use statistical and biological models to calculate numerical estimates of risk to health.

Both health and risk assessments use data from human epidemiological investigations when available. If human toxicological data are unavailable, the assessments rely on results from animal toxicology studies.



1.3 The National Oil and Hazardous Substances Pollution Contingency Plan.

U.S. Environmental Protection Agency. Washington, D.C. 1985. 50 FR 47912.

The National Contingency Plan (NCP) provides the organizational structure and procedures for preparing and responding to discharges of oil and releases of hazardous substances, pollutants, and contaminants. The NCP is required by Section 105 of CERCLA and by Section 311 of the Clean Water Act. The NCP was published on November 20, 1985, and was codified at 40 CFR 300.

Section 300.68 (Remedial Action) was written to implement objectives of the Superfund Remedial Action program. Objectives of the remedial action specified in the 1985 NCP are “to determine the nature and extent of the threat presented by the release and to evaluate proposed remedies. This includes sampling, monitoring, and exposure assessment, as necessary, and includes the gathering of sufficient information to determine the necessity for and proposed extent of remedial action.” A remedial investigation/feasibility study (RI/FS) shall be undertaken by the lead agent y. Scoping of response actions includes an initial analysis to indicate the extent to which the release or threat of release may pose a hazard to public health or welfare or the environment. In determining whether and what type of remedial and/or removal actions will be considered the following will be assessed:

- population, environmental, and welfare concerns at risk;
- routes of exposure;
- amount, concentration, hazardous properties, environmental fate and transport (e.g., ability and opportunities to bioaccumulate, persistence, mobility, etc.), and form of the substance(s) present;
- hydrogeological factors;
- current and potential ground water use;
- climate;
- the extent to which the source can be adequately identified and characterized;
- whether substances at the site may be reused or recycled;
- the likelihood of future releases if the substances remain on-site;
- the extent to which natural or manmade barriers currently contain the substances, and the adequacy of the barriers;



- the extent to which the substances have migrated or are expected to migrate from the area of their original location, or new location if relocated, and whether future migration may pose a threat to public health, welfare, or the environment;
- the extent to which Federal environmental and public health requirements are applicable or relevant and appropriate to the specific site;
- the extent to which contamination levels exceed applicable or relevant and appropriate Federal requirements or other Federal criteria, advisories, and guidance and State standards;
- contribution of the contamination to air, land, water, and/or food chain contamination problems; and
- ability of the responsible party to implement and maintain the remedy until the threat is permanently abated.

1.4 Final Rule of the National Oil and Hazardous Substances Pollution Contingency Plan.

U.S. Environmental Protection Agency. Washington, D.C. 1990. 55 FR 8666.

The National Contingency Plan [NCP] provides the organizational structure and procedures for preparing and responding to discharges of oil and releases of hazardous substances, pollutants, and contaminants. The NCP is required by Section 105 of CERCLA and by Section 311 of the Clean Water Act. The NCP was published on November 20, 1985 and was codified at 40 CFR 300. A revised version was proposed on December 21, 1988, in response to SARA. The NCP was revised and published in the Federal Register on March 8, 1990. The primary purpose of this final rule was to implement regulatory changes necessitated by SARA and to resolve issues that commentors raised about the proposed rule (1988) and the original NCP.

Section 300.430 (Remedial Investigation-Baseline Risk Assessment) was written to clarify and implement objectives of the Superfund Risk Assessment program. Following are the objectives of the baseline risk assessment (BRA) as specified in the 1990 NCP:

- to provide an analysis of baseline risk (i.e., the risks that exist if no remediation or institutional controls are applied to a site); and
- to use the risks and exposure pathways developed in the BRA to target chemical concentrations associated with levels of risk that will be adequately protective of human health for a particular site.

The revised NCP clarifies several issues regarding the baseline risk assessment:



- The NCP clarifies the relation of ARARs to the BRA; the identification of ARARs is not part of the BRA; it is a separate part of the RI. Nevertheless, ARARs should be addressed consistently in the risk assessment, the remedial investigation/feasibility study, and remedy selection.
- Risk assessments are to be performed on a site-specific basis. This is consistent with CERCLA Section 104(i)(6), which requires the Agency for Toxic Substances and Disease Registry (ATSDR) to perform health assessments for facilities on the proposed and final National Priorities List.
- EPA stated that the reasonable maximum exposure (RME) scenario will still be used by the Agency but it is not considering it as a requirement in the NCP. The RME scenario is a product of factors, such as contaminant concentration and exposure frequency and duration, that are an appropriate mix of values that reflect averages and 95th percentile distributions.
- In considering land use, the risk assessment will consider reasonable future land use from land use development patterns, and such land use assumptions may be associated with the highest (most significant) risk. These considerations will lead to the assumption of residential use as the future land use in many cases.
- EPA clarifies the role of the toxicity assessment component of Superfund risk assessment. Toxicity assessment considers the following: (1) the types of adverse health or environmental effects associated with chemical exposures, (2) the relationship between magnitude of exposure and adverse effects, and (3) related uncertainties such as weight of evidence for chemical carcinogenicity in humans.
- Proposed Section 300.430(d)(4) of the rule has been clarified to indicate that both current and potential exposures and risks are to be considered in the RA. No other changes have been made to the rule on risk assessment,
- In Subpart E, the acceptable cancer range in Section 300.430(e)(2) has been modified from the proposed 10^{-4} to 10^{-6} . EPA's approach allows a pragmatic and flexible evaluation of potential remedies at a site while still protecting human health and the environment. This approach emphasizes the use of 10^{-6} as the point of departure while allowing site- or remedy-specific factors, including potential future uses, to enter the evaluation of what is appropriate at a given site.
- Subpart K will provide a roadmap to those requirements in the NCP that Federal agencies must follow when conducting CERCLA response actions where either the release is on, or the sole source of the release is from, any facility or vessel under their jurisdiction, custody, or control.



2.0 Risk Assessment Guidance

2.1 The Effects on Populations of Exposure to Low Levels of Ionizing Radiation (BEIR III).

National Academy of Sciences (NAS). 1980. National Academy Press. Washington D.C.

This report was prepared by the Committee on the Biological Effects of Ionizing Radiation (BEIR). It deals with the scientific basis of effects of low-dose radiation and encompasses a review and evaluation of scientific knowledge developed since the first BEIR report concerning radiation exposure of human populations. The report concentrates primarily on the long-term somatic and genetic risks to people exposed to ionizing radiation at low doses. Somatic effects also discussed in the report include developmental abnormalities of varying severity caused by fetal or embryonic exposure. This report was utilized in Chapter 10 of Risk Assessment Guidance for Superfund (RAGS) to help in the evaluation of risks posed by exposure to low levels of ionizing radiation. This report was updated by BEIR V. BEIR V is the current report that should be used for evaluating risks from low levels of ionizing radiation.

2.2 Chemical Carcinogens: a Review of the Science and its Associated Principles.

U.S. Environmental Protection Agency. 1985. Office of Science and Technology Policy (OSTP). Washington, D.C.

This document has two stated purposes: (1) to articulate a view of chemical carcinogenesis that scientists generally hold in common today and (2) to draw upon this understanding to compose a series of general principles that can be used to establish guidelines for assessing carcinogenic risk. The document states that “elucidation of the basic mechanisms underlying cancer and the identification of cancer-causing agents and conditions, when coupled to research aimed at identifying and evaluating the problems created by such agents, should provide the optimal administrative bases for making sound and reasonable judgments.”

Part I of this document lays out 31 principles that can be used by various Federal agencies in reviewing their own specific guidelines for performing cancer risk assessments. Part II of the document contains six chapters on the scientific background that went into establishing the 31 principles.

The principles outlined in this document, which form the basis for EPA’s risk assessment of carcinogens, also have been used in several other documents including Guidelines for Carcinogen Risk Assessment and Risk Assessment Guidance for Superfund. Volume 1: Human Health Evaluation Manual (Part A).

2.3 Guidance on Remedial Investigations under CERCLA (RI Guide).

U.S. Environmental Protection Agency. 1985. Office of Solid Waste and Emergency Response. Washington, D.C. EPA 540/G-85/002

This document provides guidance on the conduct of remedial investigations (RIs). It provides personnel conducting remedial investigations the means to plan, prepare, conduct, and conclude RIs. The



- The NCP clarifies the relation of ARARs to the BRA; the identification of ARARs is not part of the BRA; it is a separate part of the RI. Nevertheless, ARARs should be addressed consistently in the risk assessment, the remedial investigation/feasibility study, and remedy selection.
- Risk assessments are to be performed on a site-specific basis. This is consistent with CERCLA Section 104(i)(6), which requires the Agency for Toxic Substances and Disease Registry (ATSDR) to perform health assessments for facilities on the proposed and final National Priorities List.
- EPA stated that the reasonable maximum exposure (RME) scenario will still be used by the Agency but it is not considering it as a requirement in the NCP. The RME scenario is a product of factors, such as contaminant concentration and exposure frequency and duration, that are an appropriate mix of values that reflect averages and 95th percentile distributions.
- In considering land use, the risk assessment will consider reasonable future land use from land use development patterns, and such land use assumptions may be associated with the highest (most significant) risk. These considerations will lead to the assumption of residential use as the future land use in many cases.
- EPA clarifies the role of the toxicity assessment component of Superfund risk assessment. Toxicity assessment considers the following: (1) the types of adverse health or environmental effects associated with chemical exposures, (2) the relationship between magnitude of exposure and adverse effects, and (3) related uncertainties such as weight of evidence for chemical carcinogenicity in humans.
- Proposed Section 300.430(d)(4) of the rule has been clarified to indicate that both current and potential exposures and risks are to be considered in the RA. No other changes have been made to the rule on risk assessment.
- In Subpart E, the acceptable cancer range in Section 300.430(e)(2) has been modified from the proposed 10^{-4} to 10^{-6} . EPA's approach allows a pragmatic and flexible evaluation of potential remedies at a site while still protecting human health and the environment. This approach emphasizes the use of 10^{-6} as the point of departure while allowing site- or remedy-specific factors, including potential future uses, to enter the evaluation of what is appropriate at a given site.
- Subpart K will provide a roadmap to those requirements in the NCP that Federal agencies must follow when conducting CERCLA response actions where either the release is on, or the sole source of the release is from, any facility or vessel under their jurisdiction, custody, or control.



2.0 Risk Assessment Guidance

2.1 The Effects on Populations of Exposure to Low Levels of Ionizing Radiation (BEIR III).

National Academy of Sciences (NAS). 1980. National Academy Press. Washington, D.C.

This report was prepared by the Committee on the Biological Effects of Ionizing Radiation (BEIR). It deals with the scientific basis of effects of low-dose radiation and encompasses a review and evaluation of scientific knowledge developed since the first BEIR report concerning radiation exposure of human populations. The report concentrates primarily on the long-term somatic and genetic risks to people exposed to ionizing radiation at low doses. Somatic effects also discussed in the report include developmental abnormalities of varying severity caused by fetal or embryonic exposure. This report was utilized in Chapter 10 of Risk Assessment Guidance for Superfund (RAGS) to help in the evaluation of risks posed by exposure to low levels of ionizing radiation. This report was updated by BEIR V. BEIR V is the current report that should be used for evaluating risks from low levels of ionizing radiation.

2.2 Chemical Carcinogens: a Review of the Science and its Associated Principles.

U.S. Environmental Protection Agency. 1985. Office of Science and Technology Policy (OSTP). Washington, D.C.

This document has two stated purposes: (1) to articulate a view of chemical carcinogenesis that scientists generally hold in common today and (2) to draw upon this understanding to compose a series of general principles that can be used to establish guidelines for assessing carcinogenic risk. The document states that “elucidation of the basic mechanisms underlying cancer and the identification of cancer-causing agents and conditions, when coupled to research aimed at identifying and evaluating the problems created by such agents, should provide the optimal administrative bases for making sound and reasonable judgments.”

Part I of this document lays out 31 principles that can be used by various Federal agencies in reviewing their own specific guidelines for performing cancer risk assessments. Part II of the document contains six chapters on the scientific background that went into establishing the 31 principles.

The principles outlined in this document, which form the basis for EPA’s risk assessment of carcinogens, also have been used in several other documents including Guidelines for Carcinogen Risk Assessment and Risk Assessment Guidance for Superfund, Volume 1: Human Health Evaluation Manual (Part A.)

2.3 Guidance on Remedial Investigations under CERCLA (RI Guide).

U.S. Environmental Protection Agency. 1985. Office of Solid Waste and Emergency Response. Washington, D.C. EPA 540/G-85/002

This document provides guidance on the conduct of remedial investigations (RIs). It provides personnel conducting remedial investigations the means to plan, prepare, conduct, and conclude RIs. The



document describes the essential steps in the RI process. The remedial investigation is used to characterize a hazardous waste site. Information from the site characterization is used in the toxicity and exposure assessment phases of the baseline risk assessment. Thus, an improperly conducted RI will result in an inaccurate risk assessment. This document was used in the development of the Superfund Public Health Evaluation Manual. It was also revised and incorporated with the Guidance on Feasibility Studies Under CERCLA into the Guidance for Conducting Remedial Investigations and Feasibility Studies Under CERCLA.

2.4 Guidance on Feasibility Studies under CERCLA.

U.S. Environmental Protection Agency. 1985. Office of Solid Waste and Emergency Response. Washington, D. C. EPA 540/G-85/002.

This document, details the process for identifying, evaluating, and selecting remedial action alternatives for hazardous waste sites. Results from the baseline risk assessment assist in determining the scope of the remedial action alternatives. Low risks generally result in more simple remedial action alternatives, while higher risks will generally involve more complicated alternatives. The analysis of the alternatives involves five areas: engineering, institutional, public health, environmental, and cost. The engineering analysis investigates the constructability and reliability of the various alternatives. The institutional analysis evaluates the alternatives in terms of the Federal, State, or local requirements, advisories, or guidance that must be considered to protect public health, welfare, and the environment. The public health analysis includes baseline site evaluation, exposure assessment standards analysis, short- and long-term effects of each alternative, and endangerment assessment. The environmental evaluation includes assessment of adverse impacts if no action is taken and the short- and long-term effects of the remedial action alternatives. The cost analysis evaluates capital and operating costs, and involves present worth and sensitivity analyses. These areas are addressed in separate chapters within the document- It was also revised and incorporated with the Guidance on Remedial Investigations Under CERCLA into the Guidance for Conducting Remedial Investigations and Feasibility Studies Under CERCLA.



2.5 Guidelines for Estimating Exposures.

U.S. Environmental Protection Agency. 1986. Office of Health and Environmental Assessment. Washington, D.C. 51 FR 34042;

Guidelines for Carcinogen Risk Assessment.

U.S. Environmental Protection Agency. 1986. Office of Health and Environmental Assessment. Washington, D.C. 51 FR 33992;

Guidelines for Mutagenicity Risk Assessment.

U.S. Environmental Protection Agency. 1986. Office of Health and Environmental Assessment. Washington, D.C. 51 FR 34006;

Guidelines for the Health Assessment of Suspect Developmental Toxicants.

U.S. Environmental Protection Agency. 1986. Office of Health and Environmental Assessment. Washington D. C. 51 FR 34028;

Guidelines for the Health Risk Assessment of Chemical Mixtures.

U.S. Environmental Protection Agency. 1986. Office of Health and Environmental Assessment. Washington, D. C. 51 FR 34014.

These five guidelines were published together and were intended to be used in assessing the health risks of environmental pollutants. They set forth principles and procedures to guide scientists in the conduct of Agency risk assessments, and they emphasize that risk assessments will be conducted on a case-by-case basis. When the National Research Council (NRC) of the National Academy of Sciences (NAS) published its book entitled *Risk Assessment in the Federal Government: Managing the Process* in 1983, they recommended that Federal regulatory agencies ensure that the risk assessment process be maintained as a scientific effort separate from risk management. All five of these guidelines support this recommendation. As outlined above, the risk assessment process involves four steps: data collection and evaluation (hazard identification), toxicity/dose-response assessment, exposure assessment and risk characterization. The last four of these guidelines provide guidance on the entire risk assessment process in their respective subject areas. The first only addresses the exposure assessment step in the risk assessment process. All five guideline documents have been used in developing other documents which include the Superfund Exposure Assessment Manual, Exposure Factors Handbook and Risk Assessment Guidance for Superfund.

2.6 Superfund Public Health Evaluation Manual (SPHEM).

U.S. Environmental Protection Agency. 1986. Office of Emergency and Remedial Response. Washington, D.C. EPA 5401/1-86/060.

This document was developed to supplement Chapter 5 of the Guidance on Feasibility Studies Under CERCLA. That guidance described what the public health evaluation process was, but it did not describe how to conduct the evaluation. It is the first document published that describes how to conduct a baseline risk assessment. This document also addresses the public health analysis of remedial alternatives. The procedures in this manual were designed to conform to the five guidelines listed in 2.5 above.



2.7 Superfund Exposure Assessment Manual (SEAM).

U.S. Environmental Protection Agency. 1988. Office of Remedial Response. Washington, D.C. EPA 5401/1-88/001.

The analytical procedures outlined in this document provide a complete, integrated framework for the assessment of exposure to contaminants” at or migrating from uncontrolled hazardous waste sites. The application of both monitoring and modeling procedures to the exposure assessment process is outlined. This process considers all contaminant releases and exposure routes. The analytical protocol is structured into five segments:

1. analysis of contaminant release-s from a site into environmental media;
2. evaluation of the transport and environmental fate of the chemicals released;
3. identification, enumeration, and characterization of potential y exposed populations;
4. integrated exposure analysis; and
5. uncertainty analysis.

The analytical protocol provided by SEAM was designed specifically to support the baseline risk assessment process as called for by Guidance for Conducting Remedial Investigations and Feasibility Studies Under CERCLA (USEPA, 1988) and as outlined by the Superfund Public Health Evaluation Manual (USEPA, 1986f). It continues to constitute a key technical resource supporting development of baseline risk assessments as currently directed by Risk Assessment Guidance for Superfund (USEPA, 1989a).

2.8 Recommended Procedures for Implementation of Superfund Risk Assessment Guidelines

U.S. Environmental Protection Agency. 1988. U.S. EPA Region IX. In. Exposure Assessment at Superfund Sites. U.S. Environmental Protection Agency, Environmental Monitoring Systems Laboratory. Las Vegas, NV, EPA 600/X-89/381 1989.

Region IX published 38 recommendations to assist risk assessors in completing a baseline risk assessment, particularly for Region IX. The recommendations covered the areas of exposure and toxicity assessment, indicator chemical identification, environmental fate and transport of chemicals, data presentation, data gaps, and uncertainty. These recommendations were incorporated and published in Exposure Assessment at Superfund Sites. Many of the recommendations made in this document are still currently followed.



2.9 Guidance for Conducting Remedial Investigations and Feasibility Studies under CERCLA.

U.S. Environmental Protection Agency. 1988. Office of Emergency and Remedial Response. Washington, D.C. OSWER Directive 9355.3-01.

This guidance manual combined and replaced the Guidance on Remedial Investigations Under CERCLA and Guidance on Feasibility Studies Under CERCLA. It incorporated the changes made to CERCLA by SARA. It gave a brief overview of the steps involved the baseline risk assessment and stated that the risk assessment provides “the basis for determining whether or not remedial action is necessary and the justification for performing remedial actions.” The results of the BRA will determine the scope of the feasibility study.

2.10 Proposed Guidelines for Assessing Female Reproductive Risk.

U.S. Environmental Protection Agency. 1988. Office of Health and Environmental Assessment. Washington, D.C. 53 FR 24834;

Proposed Guidelines for Assessing Male Reproductive Risk.

U.S. Environmental Protection Agency. 1988. Office of Health and Environmental Assessment. Washington, D. C. 53 FR 24850.

These guidelines describe the procedures to follow in evaluating the potential toxicity of environmental agents to the human male and female reproductive systems. They provide guidance for the interpretation and analysis of studies conducted according to the testing guidelines, for conducting risk assessments and information on other types of studies available when reviewing data on particular agents. The female reproductive guidelines discuss how events in the female reproductive cycle are closely interrelated and how alterations in one event in the cycle can cause alterations in other events in the cycle. The male reproductive guidelines focus on male reproductive function as it relates to sexual behavior, fertility, and male-mediated pregnancy outcomes, plus effects on processes that can affect those functions directly. These are two of three guidelines issued for assessing non-cancer health effects. They are intended to be utilized for the non-cancer toxicity assessment component of the BRA outlined in the Risk Assessment Guidance for Superfund.

2.11 Health Risks of Radon and Other Internally Deposited Alpha-emitters (BEIR IV).

National Academy of Sciences (NAS). 1988. BEIR IV. National Academy Press. Washington, D. C.

This report addresses demonstrated and potential health effects of exposure of human populations to internally deposited alpha-emitting radionuclide and their decay products. The report is divided into the following main categories

- carcinogenic and other health effects of radon, radium, thorium, polonium, uranium, and the transuranic radionuclide;



- genetic, teratogenic, and fetal effects of internally deposited alpha-emitting radionuclide, and
- the scientific bases and mechanisms underlying the biological and health effects, including the relevant physics and dosimetry, radiobiology, anatomy, and physiology.

Where possible, the report presents quantitative risk estimates for cancer induction. This report is utilized in Chapter 10 of Risk Assessment Guidance for Superfund to help in the evaluation of risks posed by internally deposited alpha-emitters.

2.12 Risk Assessment Guidance for Superfund, Volume 1: Human Health Evaluation Manual (Part A)

U.S. Environmental Protection Agency. 1989. Office of Emergency and Remedial Response. Washington, D. C. EPA 540/1-89/002.

Risk Assessment Guidance for Superfund (RAGS) constitutes the present conceptual framework for CERCLA risk assessments. All four steps (data collection and evaluation, exposure assessment, toxicity assessment, and risk characterization) in that process are discussed in detail. The four steps are briefly discussed in Chapter 1. This is the primary guidance document used for conducting baseline risk assessments. The other two documents in this series (see Sections 2.21 and 2.22) discuss remediation goals and alternatives. This document revised and replaced SPHEM. Other guidance currently being used in the development of baseline risk assessments are used in conjunction with the overall protocol outlined in RAGS.

2.13 Exposure Factors Handbook (EFH). U.S. Environmental Protection Agency. 1989.

Office of Health and Environmental Assessment. Washington, D. C. EPA 600/8-89/63.

The purpose of this handbook was to provide a summary of the available data on various factors used in exposure assessments including drinking water consumption; consumption rates of foods including fruits, vegetables, beef, dairy products, and fish; soil ingestion; inhalation rate; skin area; lifetime; activity patterns; and body weight. A number of specific exposure scenarios are identified, along with recommendations for default values to use when site-specific data are not available. Additionally, basic equations using these parameters to estimate exposure levels are also presented for each scenario. Monte Carlo and sensitivity analysis procedures for assessing the uncertainties in exposure assessments are also addressed. Some of the procedures presented in this document were incorporated into RAGS.

2.14 Supplemental Manual to Risk Assessment Guidance for the Superfund Program (SMRAGSP).

U.S. Environmental Protection Agency. 1989. U.S. EPA Region I: EPA 901/5-89-001.

This Region I manual is intended to supplement the Superfund Public Health Evaluation Manual, the Superfund Exposure Assessment Manual, and the Endangerment Assessment Handbook Region I



experience with risk assessments showed that the assessments had wide variability with respect to structure, content, and quality. Therefore, the overall goal of this manual is to improve the quality and consistency of risk assessments performed in Region I. The guidance is intended to be as practical and useful as possible, consequently, it is very explicit on technical matters in all four areas of the baseline risk assessment process.

2.15 Risk Assessment Methodology - Environmental Impact Statement - NESHAPs for Radionuclide - Background Information Document - Volume 1.

U.S. Environmental Protection Agency. 1989. Office of Radiation Programs. Washington, D. C. EPA 520/1-89-005.

This background document involves the National Emission Standards for Hazardous Air Pollutants (NESHAPs). Even though this rule is under the Clean Air Act, it provides information on methods used in radiation risk assessment. This background document provides information on EPA's radiation protection programs and a detailed description of EPA's procedures and methods for estimating radiation doses and risk due to radionuclide emissions to the air. Appendix A describes the environmental transfer factors used in the dose assessment models. Appendix B describes the mechanics of the life table implementation used to estimate risk. Appendix C presents an overview of the quantitative uncertainty analysis techniques currently under review.

2.16 International Commission on Radiological Protection: Recommendations of the Commission - 1990.

International Commission on Radiological Protection (ICRP). ICRP/90/G-01.

This report is intended to be of help to regulatory and advisory authorities at national, regional, and international levels, mainly by providing guidance on the fundamental principles on which appropriate radiological protection can be based. The report is divided into the following subjects:

- the physical quantities and units used in radiological protection and the biological effects of radiation,
- the fundamentals of radiological protection,
- the Commission's main recommendations, and
- the practical implementation of the recommendations.

Earlier versions of this report were utilized in Chapter 10 of RAGS to help in the evaluation of risks posed by exposure to ionizing radiation. These more current recommendations should now be considered in evaluating risks to ionizing radiation.



2.17 Guidance for Data Usability in Risk Assessment.

U.S. Environmental Protection Agency. 1990. Office of Emergency and Remedial Response. Washington, D.C. EPA 540/G-90-008.

EPA has established a Data Useability Workgroup to develop national guidance for minimum data quality requirements to increase the usability of environmental analytical data in the cleanup of hazardous waste sites under CERCLA. This guidance manual provides direction for planning and assessing analytical data collection activities for the baseline human health risk assessment. The manual provides guidance on the following specific topics:

- How to design remedial investigation sampling and analytical activities that meet the data quality and data quantity needs of risk assessors.
- Procedures for assessing the usability of the environmental analytical data obtained in the remedial investigation.
- Options for combining data of varying levels of quality from different sources and incorporating them into the risk assessment.
- Procedures for determining the degree of confidence in the risk assessment based on the uncertainty in the environmental analytical data.
- Guidelines for timing and execution of the various activities.
- Appendices requested by risk assessors and remedial project managers that describe data review summaries, assist in selecting analytical methods to meet required detection limits, and describe data qualifier flags.

2.18 Health Effects of Exposure to Low Levels of Ionizing Radiation (BEIR V).

National Academy of Sciences (NAS). 1990. National Academy Press. Washington, D. C.

This report is an update of the 1980 BEIR III report. Since that report there has been significant developments in the knowledge of the extent of radiation exposures from natural sources and medical uses as well as new data on the late health effects of radiation in humans, primarily the induction of cancer and developmental abnormalities. Advanced computational techniques and models for analysis have become available for radiation risk assessment. This report is divided into the following categories

- heritable genetic effects,
- cellular radiobiology and carcinogenic mechanisms,
- radiation carcinogenesis,



- radiation effects on the fetus, and
- radiation epidemiology and risk modeling.

This report also includes information and analyses from the BEIR IV report that are appropriate for cancer and genetic risk assessment. BEIR V is the current report that should be used for evaluating risks from low levels of ionizing radiation. Guidance for evaluation of risks from radiation can be found in Chapter 10 of Risk Assessment Guidance for Superfund.

2.19 Exposure Assessment Methods Handbook.

U.S. Environmental Protection Agency. 1991. Office of Health and Environmental Assessment. Washington, D. C.

This handbook provides a summary of the available algorithms and parameter values that can be used to determine estimated or modeled concentrations of chemicals in various environmental media, including ambient air, surface water, ground water, fish and shellfish, terrestrial food sources, and soil. Quantitative treatment of changes in concentration of chemicals due to environmental fate processes is provided for ambient air, surface water, and ground water. It also provides an overview of the exposure assessment process and how these methods are integrated within that process. In addition, it presents discussions of methods for characterizing and enumerating exposed populations and of methods for quantitating the statistical uncertainties related to estimation of environmental concentrations.

2.20 Supplemental Guidance to Rags: Standard Default Exposure Factors.

U.S. Environmental Protection Agency. 1991. Office of Emergency and Remedial Response. Washington, D. C. OSWER Directive: 9285.6-03.

This supplemental guidance was published to reduce unwarranted variability in the exposure assumptions used to characterize potentially exposed populations in residential, commercial/industrial, agricultural, and recreational exposure scenarios. This guidance also addresses present and future land use considerations. If values differ between this guidance and RAGS, the values in this supplemental guidance supersede those in RAGS.

2.21 Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual (Part B, Development of Risk-based Preliminary Remediation Goals).

U.S. Environmental Protection Agency. 1991. Office of Emergency and Remedial Response. Washington D.C. PB92-963333.

This guidance manual is based on policies in the Final Rule of the NCP which was published in 1990. Part B provides guidance on using EPA toxicity values and exposure information to derive chemical-specific, risk-based preliminary remedial goals (PRGs) for a CERCLA site. Chemical-specific PRGs are concentration goals for individual chemicals for specific medium and land-use combinations. PRGs provide remedial design staff with long-term targets to use during analysis and selection of remedial



alternatives. PRGs are developed early in the RI/FS process before the baseline risk assessment is completed. Information from PRGs is not used in the baseline risk assessment although information from the RI will be used for both the BRA and the PRGs.

2.22 Risk Assessment Guidance for Superfund-Volume I: Human Health Evaluation Manual (Part C, Risk Evaluation of Remedial Alternatives).

U.S. Environmental Protection Agency. 1991. Office of Emergency and Remedial Response. Washington, D. C. PB92-963334.

This guidance has been developed by EPA to assist RPMs, risk assessors, site engineers, and others in using risk information at CERCLA sites to evaluate remedial alternatives during the FS and to evaluate the human health risk associated with the selected remedial alternative during and after its implementation. This Part provides general guidance to assist in site-specific risk evaluations. It discusses the statutes, regulations, and guidance relevant to the evaluation of remedial alternatives, describes appropriate levels of effort for risk evaluations of remedial alternative discusses the importance of risk communication, addresses the role of the RPM, and describes the need for documentation. PRGs developed using Part B of RAGS will help to evaluate the human risks of remedial alternatives

2.23 Guidelines for Developmental Toxicity Risk Assessment.

U.S. Environmental Protection Agency. 1991. Office of Health and Environmental Assessment. Washington, D. C. 56 FR 63798.

These guidelines outline principles and methods for evaluating data from animal and human studies, exposure data, and other information to characterize risk to human development growth, survival, and function because of exposure prior to conception, prenatally, or to infants and children. It adds new guidance on the relationship between maternal and developmental toxicity, characterization of the health-related data base for developmental toxicity. risk assessment, use of the reference dose or reference concentration for developmental toxicity (RfD_{DT} or RfC_{DT}), and use of the benchmark dose approach. These guidelines replace the Guidelines for the Health Assessment of Suspect Developmental Toxicants. This is one of three guidelines issued for assessing non-cancer health effects. It is intended to be utilized for the non-cancer toxicity assessment component of the BRA outlined in RAGS.

2.24 Guidance for Risk Assessment - Henry Habicht Memorandum.

U.S. Environmental Protection Agency. 1991. Office of The Administrator. Washington, D.C. (February 26, 1992).

This guidance applies to the development evaluation, and description of EPA risk assessments for use in regulatory decision-making. Some of the principles outlined in this guidance describe information expected in EPA risk assessments to the extent practicable, emphasizing that discussion of both data and confidence in the data are essential features of a complete risk assessment. Guidance on exposure risk descriptors (i.e., central tendency, high end of individual risk, population risk and important subgroups) is also presented in this document. This is internal guidance that applies directly to assessments developed under EPA auspices. It also encourages EPA staff to use these principles as guidance in evaluating assessments submitted to EPA from other sources.



2.25 Dermal Exposure Assessment: Principles and Applications.

U.S. Environmental Protection Agency. 1992. Office of Research and Development. Washington, D.C. EPA 600/8-91/011B.

The dermal contact pathways specifically addressed are direct contact with soils, contact with contaminants in water, and contact with vapors. Priority was given to developing procedures oriented toward chronic systemic risks rather than acute local risks. This document:

- summarizes the current state of knowledge concerning dermal exposure to water, soil, and vapor media;
- presents methods for estimating dermal absorption resulting from contact with these media and elaborates upon their associated uncertainties;
- summarizes available chemical-specific experimental data describing the dermal absorption properties and provides predictive techniques to use where data are not available; and
- establishes a procedure for evaluating experimental data for application to exposure assessments.

This document is divided into two parts. Part 1 describes general principles of dermal absorption, while Part 2 presents methods for applying the principles described in Part 1 to human exposure assessments. This document provides valuable information for assessing dermal exposures, but it is an interim report, and therefore the models it addresses should be used with caution.

2.26 Supplemental Guidance to RAGS: Calculating the Concentration Term.

U.S. Environmental Protection Agency, 1992. Office of Solid Waste and Emergency Response. Washington, D.C. Publication 9285.7-081.

This supplemental guidance to RAGS is designed to help explain the concentration term in the reasonable maximum exposure (RME) equation. It presents the general RME equation, explains the significance of the RME, discusses basic concepts concerning the concentration term, describes generally how to calculate the concentration term, and presents examples to illustrate several important points.

2.27 Guidelines for Exposure Assessment.

U.S. Environmental Protection Agency. 1992. Office of Health and Environmental Assessment. Washington, D.C. 57 FR 22888.

These guidelines describe the general concepts of exposure assessment, including definitions and associated units, and provides guidance on planning and conducting an exposure assessment. Guidance is also provided on presenting the results of the exposure assessment and characterizing uncertainty. These guidelines supersede and replace the Guidelines for Estimating Exposures (USEPA, 1986a).



2.28 An SAB Report: Superfund Site Health Risk Assessment Guidelines; Review of the Office of Solid Waste and Emergency Response's Draft Risk Assessment Guidance for Superfund Human Health Evaluation Manual by the Environmental Health Committee.

U.S. Environmental Protection Agency. 1993. Office of the Administrator, Science Advisory Board. Washington, D.C. EPA-SAB-EHC-93-007.

This report is a review of the EPA's Office of Solid Waste and Emergency Response (OSWER) risk assessment methodology. The Science Advisory Board reviewed four broad issue areas relating to Superfund human health risk assessment:

- defining and calculating the reasonable maximum exposure (RME);
- assessing and dealing with exposure to multiple chemicals--using the hazard index/hazard quotient to assess risk;
- reference doses in goal-setting--use of chronic/subchronic reference doses and specific populations to set risk-driven remediation goals; and
- short-term toxicity values--use of appropriate defaults for characterizing less-than-lifetime exposure to toxicants.

3.0 Toxicity Data Sources

3.1 Integrated Risk Information Service (IRIS).

U.S. Environmental Protection Agency. 1991.

IRIS provides numerical toxicity values, reference doses (RfDs), and cancer slope factors for various chemicals for use in Superfund risk assessments. IRIS is an EPA data base containing current health risk and EPA regulatory information for approximately 500 specific substances. It contains summaries of EPA qualitative and quantitative human health information that support two steps (hazard identification and dose response) of the four major steps of the risk assessment process outlined in the National Research Council's 1983 publication, *Risk Assessment in the Federal Government: Managing the Process*.

IRIS was created in 1986 for EPA staff as the official repository of consensus information regarding the areas of hazard identification and dose-response assessment. On June 2, 1988, a Federal Register notice (53 FR 21162) was issued to announce that IRIS was available to the public. The notice described IRIS, the type of information it contained, and how to access the system. It also informed the public about the IRIS Information Submission Desk, which provides an opportunity for public input- Data submission procedures are provided in the Federal Register notice (58 FR 11490) along with a list of the specific work group review schedules. Every six months, the data submission procedures will be reprinted in the Federal Register with a new or revised list of substances for work group review. For the



latest status of the substances scheduled for review, interested persons should check the IRIS data base or contact:

IRIS User Support
U.S. Environmental Protection Agency
26 W. Martin Luther King Drive, (MS-190)
Cincinnati, Ohio 45268
Telephone: (513) 569-7254

The database information supporting risk characterization consists of brief statements on the quality of data and very general statements on confidence in the dose-response evaluation. IRIS consensus information does not include exposure assessment information. IRIS contains RfDs and slope factors that have been verified by the RfD or Carcinogen Risk Assessment Verification Endeavor (CRAVE) Workgroups and, subsequently, is considered to be the preferred source of toxicity information.

Information in IRIS supersedes all other sources. Only if information is not available in IRIS for the chemical being evaluated should other sources be consulted. The data base contains three consensus health hazard information summary sections

- the reference dose for noncancer health effects resulting from oral exposure,
- the reference concentration for noncancer health effects resulting from inhalation exposure, and
- the carcinogen assessment for both oral and inhalation exposure.

IRIS substance files may include supplemental information such as summaries on health advisories, regulatory sections, and physical/chemical properties.

3.2 Health Effects Assessment Summary Tables (HEAST).

U.S. Environmental Protection Agency. 1994. Office of Emergency and Remedial Response. Washington D.C. OERR 9200.6-303 (92-1); NTIS No. PB92-921199.

The HEAST is a comprehensive listing consisting almost entirely of provisional risk assessment information relative to oral and inhalation routes for chemicals of interest to Superfund and RCRA. Entries in the HEAST are limited to chemicals that have undergone review and have the concurrence of individual EPA Program offices. The risk assessment information is not considered as high-quality, EPA-wide consensus information.

Chemicals reviewed by EPA Work Groups are classified according to their status as either verified, not verifiable, or under review. The toxicity values listed in HEAST (other than National Ambient Air Quality standards [NAAQS] or drinking water criteria values) are considered to be provisional. Provisional values are found in HEAST but not in IRIS. Verified numbers are found in both IRIS and HEAST. The HEAST are categorized into the following tables:



- HEAST Table 1: Subchronic and Chronic Toxicity (Other Than Carcinogenicity)
- HEAST Table 2: Alternate Methods-Subchronic and Chronic Toxicity
- HEAST Table 3: Carcinogenicity
- HEAST Table 4A and 4B: Radionuclide Carcinogenicity - Slope Factors

In 1992, HEAST Tables were modified to include: (1) the addition of Chemical Abstract Service Registry Number (CASRN) for each chemical, (2) the identification of the dose level, (3) the identification of target organs, and (4) a description of the critical effects. In addition, an Appendix (Appendix A) has also been developed with the following sections:

- data sources and selection criteria used in HEAST,
- RFD to RFC dose conversions,
- chemical name and CASRN reference,
- effect level definitions, and
- National Ambient Air Quality Standards (NAAQS).



APPENDIX B

Land Use in the CERCLA Remedy Selection Process



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

MAY 25 1995

OFFICE OF
SOLID WASTE AND EMERGENCY
RESPONSE

OSWER Directive No. 9355.7-04

MEMORANDUM

SUBJECT: Land Use in the CERCLA Remedy Selection Process

FROM: Elliott P. Laws
Assistant Administrator

A handwritten signature in black ink, appearing to read "Elliott P. Laws", written over the typed name and title.

TO: Director, Waste Management Division
Regions I, IV, V, VII
Director, Emergency and Remedial Response Division
Region II
Director, Hazardous Waste Management Division
Regions III, VI, VIII, IX
Director, Hazardous Waste Division,
Region X
Director, Environmental Services Division
Regions I, VI, VII

Purpose:

This directive presents additional information for considering land use in making remedy selection decisions under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) at National Priorities List (NPL) sites. The U.S. Environmental Protection Agency (EPA) believes that early community involvement, with a particular focus on the community's desired future uses of property associated with the CERCLA site, should result in a more democratic decisionmaking process; greater community support for remedies selected as a result of this process; and more expedited, cost-effective cleanups.

The major points of this directive are:

- 1 Discussions with local land use planning authorities, appropriate officials, and the public, as appropriate, should be conducted as early as possible in the scoping phase of the Remedial Investigation/Feasibility Study (RI/FS). This will assist EPA in understanding the



Recycled/Recyclable
Printed with Soy/Canola Ink on paper that
contains at least 50% recycled fiber

reasonably anticipated future uses of the land on which the Superfund site is located;

- If the site is located in a community that is likely to have environmental justice concerns, extra efforts should be made to reach out to and consult with segments of the community that are not necessarily reached by conventional communication vehicles or through local officials and planning commissions;
- Remedial action objectives developed during the RI/FS should reflect the reasonably anticipated future land use or uses;
- Future land use assumptions allow the baseline risk assessment and the feasibility study to be focused on developing practicable and cost effective remedial alternatives. These alternatives should lead to site activities which are consistent with the reasonably anticipated future land use. However, there may be reasons to analyze implications associated with additional land uses;
- Land uses that will be available following completion of remedial action are determined as part of the remedy selection process. During this process, the goal of realizing reasonably anticipated future land uses is considered along with other factors. Any combination of unrestricted uses; restricted uses, or use for long-term waste management may result.

Discussions with local land use authorities and other locally affected parties to make assumptions about future land use are also appropriate in the RCRA context. EPA recognizes that RCRA facilities typically are industrial properties that are actively managed, rather than the abandoned sites that are often addressed under CERCLA. Therefore, consideration of non-residential uses is especially likely to be appropriate for RCRA facility cleanups. Decisions regarding future land use that are made as part of RCRA corrective actions raise particular issues for RCRA (e.g., timing, property transfers, and the viability of long-term permit or other controls) in ensuring protection of human health and the environment. EPA intends to address the issue of future land use as it relates specifically to RCRA facility cleanups in subsequent guidance and/or rulemakings.

This guidance is also relevant for Federal Facility sites. Land use assumptions at sites that are undergoing base closure may be different than at sites where a Federal agency will be maintaining control of the facility. Most land management agency sites will remain in Federal ownership after remedial actions. In these cases, Forest Land Management Plans and other resource

management guidelines may help develop reasonable assumptions about future uses of the land. At all such sites, however., this document can focus the land use consideration toward appropriate options.¹

Background:

Reasonably anticipated future use of the land at NPL sites is an important consideration in determining the appropriate extent of remediation. Future use of the land will affect the types of exposures and the frequency of exposures that may occur to any residual contamination remaining on the site, which in turn affects the nature of the remedy chosen. On the other hand, the alternatives selected through the National Oil and Hazardous Substance Contingency Plan (NCP) [55 Fed. Reg. 8666, March 8, 1990] process for CERCLA remedy selection determine the extent to which hazardous constituents remain at the site, and therefore affect subsequent available land and ground water uses.

The NCP preamble specifically discusses land use assumptions regarding the baseline risk assessment. The baseline risk assessment provides the basis for taking a remedial action at a Superfund site and supports the development of remedial action objectives. Land use assumptions affect the exposure pathways that are evaluated in the baseline risk assessment. Current land use is critical in determining whether there is a current risk associated with a Superfund site, and future land use is important in estimating potential future threats. The results of the risk assessment aid in determining the degree of remediation necessary to ensure long-term protection at NPL sites.

EPA has been criticized for too often assuming that future use will be residential. In many cases, residential use is the least restricted land use and where human activities are associated with the greatest potential for exposures. This directive is intended to facilitate future remedial decisions at NPL sites by outlining a public process and sources of information which should be considered in developing reasonable assumptions regarding future land use.

This directive expands on discussions provided in the preamble to the National Oil and Hazardous Substance Contingency Plan (NCP); "Risk Assessment Guidance for Superfund Vol. I, Human Health Evaluation Manual" (Part A) (EPA/540/1-89/002, Dec. 1989); "Guidance for Conducting Remedial Investigations and Feasibility studies Under CERCLA" (OSWER Directive 9355.3-01, Oct. 1988); and

¹Federal agency responsibility under CERCLA 120(h)(3), which relates to additional clean up which may be required to allow for unrestricted use of the property, is not addressed in this guidance.

"Role of the Baseline Risk Assessment in Superfund Remedy Selection Decisions" (OSWER Directive 9355.0-30, April 22, 1991).

This land use directive may have the most relevance in situations where surface soil is the primary exposure pathway. Generally, where soil contamination is impacting ground water, protection of the ground water may drive soil cleanup levels. Consideration of future ground water use for CERCLA sites is not addressed in this document. There are separate expectations established for ground water in the NCP rule section 300.430 (a) (1) (iii) (F) that "EPA expects to return usable ground waters to their beneficial uses wherever practicable, within a timeframe that is reasonable given the particular circumstances of the site."

Objective

This directive has two primary objectives. First, this directive promotes early discussions with local land use planning authorities, local officials, and the public regarding reasonably anticipated future uses of the property on which an NPL site is located. Second, this directive promotes the use of that information to formulate realistic assumptions regarding future land use and clarifies how these assumptions fit in and influence the baseline risk assessment, the development of alternatives, and the CERCLA remedy selection process.

Implementation

The approach in this guidance is meant to be considered at current and future sites in the RI/FS pipeline, to the extent possible. This directive is not intended to suggest that previous remedy selection decisions should be re-opened.

Developing Assumptions About Future Land Use

In order to ensure use of realistic assumptions regarding future land uses at a site, EPA should discuss reasonable anticipated future uses of the site with local land use planning authorities, local officials, and the public, as appropriate, as early as possible during the scoping phase of the RI/FS. EPA should gain an understanding of the reasonably anticipated future land uses at a particular Superfund site to perform the risk assessment and select the appropriate remedy.

A visual inspection of the site and its surrounding area is a good starting point in developing assumptions regarding future land use. Discussions with the local land use authorities and appropriate officials should follow. Discussions with the public can be accomplished through a public meeting and/or other means. By developing realistic assumptions based on information gathered from these sources early in the RI/FS process, EPA may develop

remedial alternatives that are consistent with the anticipated future use.

The development of assumptions regarding the reasonably anticipated future land use should not become an extensive, independent research project. Site managers should use existing information to the extent possible, much of which will be available from local land use planning authorities. Sources and types of information that may aid EPA in determining the reasonably anticipated future land use include, but are not limited to:

- Current land use
- Zoning laws
- Zoning maps
- Comprehensive community master plans
- Population growth patterns and projections (e.g., Bureau of Census projections)
- Accessibility of site to existing infrastructure (e.g., transportation and public utilities)
- Institutional controls currently in place
- Site location in relation to urban, residential, commercial, industrial, agricultural and recreational areas
- Federal/State land use designation (Federal/State control over designated lands range from established uses for the general public, such as national parks or State recreational areas, to governmental . facilities providing extensive site access restrictions, such as Department of Defense facilities
- Historical or recent development patterns
- Cultural factors (e.g., historical sites, Native American religious sites)
- Natural resources information
- Potential vulnerability of ground water to contaminants that might migrate from soil
- Environmental justice issues
- Location of on-site or nearby wetlands
- Proximity of site to a floodplain
- Proximity of site to critical habitats of endangered or threatened species
- Geographic and geologic information
- Location of Wellhead Protection areas, recharge areas, and other areas identified in a State's Comprehensive Ground-water Protection Program

These types of information should be considered when developing the assumptions about future land use. Interaction with the public, which includes all stakeholders affected by the site, should serve to increase the certainty in the assumptions made regarding future land use at an NPL site and increase the

confidence expectations about anticipated future land use are, in fact, reasonable.

For example, future industrial land use is likely to be a reasonable assumption where a site is currently used for industrial purposes, is located in an area where the surroundings are zoned for industrial use, and the comprehensive plan predicts the site will continue to be used for industrial purposes.

Community Involvement

NPL sites are located in diverse areas of the country, with great variability in land use planning practices. For some NPL sites, the future land use of a site may have been carefully considered through local, public, participatory, planning processes, such as zoning hearings, master plan approvals or other vehicles. When this is the case, local residents around the Superfund site are likely to demonstrate substantial agreement with the local land use planning authority on the future use of the property. Where there is substantial agreement among local residents and land use planning agencies, owners and developers, EPA can rely with a great deal of certainty on the future land use already anticipated for the site. For other NPL sites, however, the absence or nature of a local planning process may yield considerably less certainty about what assumptions regarding future use are reasonable. In some instances the local residents near the Superfund site may feel disenfranchised from the local land use planning and development process. This may be an especially important issue where there are concerns regarding environmental justice in the neighborhood around the NPL site. Consistent with the principle of fairness, EPA should make an extra effort to reach out to the local community to establish appropriate future land use assumptions at such sites.

Land Use Assumptions in the Baseline Risk Assessment

Future land use assumptions allow the baseline risk assessment and the feasibility study to focus on the development of practicable and cost-effective remedial alternatives, leading to site activities which are consistent with the reasonable anticipated future land use.

The baseline risk assessment generally needs only to consider the reasonably anticipated future land use; however, it may be valuable to evaluate risks associated with other land uses. The NCP preamble (55 Fed. Reg. 8710) states that in the baseline risk assessment, more than one future land use assumption may be considered when decision makers wish to understand the implications of unexpected exposures. Especially where there is some uncertainty regarding the anticipated future land use, it may be useful to compare the potential risks associated with several land use scenarios to estimate the impact

on human health and the environment should the land use unexpectedly change. The magnitude of such potential impacts may be an important consideration in determining whether and how institutional controls should be used to restrict future uses. If the baseline risk assessment evaluates a future use under which exposure is limited, it will not serve the traditional role, evaluating a "no action" scenario. A remedy, i.e. institutional controls to limit future exposure, will be required to protect human health and the environment. In addition to analyzing human health exposure scenarios associated with certain land uses, ecological exposures may also need to be considered.

Developing Remedial Action Objectives

Remedial action objectives provide the foundation upon which remedial cleanup alternatives are developed. In general, remedial action objectives should be developed in order to develop alternatives that would achieve cleanup levels associated with the reasonable anticipated future land use over as much of the site as possible. EPA recognizes, however, that achieving either the reasonably anticipated land use, or the land use preferred by the community, may not be practicable across the entire site, or in some cases, at all. For example, as RI/FS data become available, they may indicate that the remedial alternatives under consideration for achieving a level of cleanup consistent with the reasonably anticipated future land use are not cost-effective nor practicable. If this is the case, the remedial action objective may be revised which may result in different, more reasonable land use(s).

EPA's remedy selection expectations described in section 300.430(a)(1)(iii) of the NCP should also be considered, when developing remedial action objectives. Where practicable, EPA expects to treat principal threats, to use engineering controls such as containment for low-level threats, to use institutional controls to supplement engineering controls, to consider the use of innovative technology, and to return usable ground waters to beneficial uses to protect human health and the environment. (Some types of applicable or relevant and appropriate requirements (ARARs) define protective cleanup levels which may, in turn, influence post-remediation land use potential.)

In cases where the future land use is relatively certain, the remedial action objective generally should reflect this land use. Generally, it need not include alternative land use scenarios unless, as discussed above, it is impracticable to provide a protective remedy that allows for that use. A landfill site is an example where it is highly likely that the future land use will remain unchanged (i.e., long-term waste management area), given the NCP's expectation that treatment of high volumes of waste generally will be impracticable and the fact that EPA's presumptive remedy for landfills is containment. In such a case,

a remedial action objective could be established with a very high degree of certainty to reflect the reasonably anticipated future land use.

In cases where the reasonably anticipated future land use is highly uncertain, a range of the reasonably likely future land uses should be considered in developing remedial action objectives. These likely future land uses can be reflected by developing a range of remedial alternatives that will achieve different land use potentials. The remedy selection process will determine which alternative is most appropriate for the site and, consequently, the land use(s) available following remediation.

As discussed in "Role of the Baseline Risk Assessment in Superfund Remedy Selection Decisions" (OSWER Directive 9355.0-30, April 22, 1991), EPA has established a risk range for carcinogens within which EPA strives to manage site risks. EPA recognizes that a specific cleanup level within the acceptable risk range may be associated with more than one land use (e.g., an industrial cleanup to 10^{-6} may also allow for residential use at a 10^{-4} risk level.) It is not EPA's intent that the risk range be partitioned into risk standards based solely on categories of land use (e.g., with residential cleanups at the 10^{-6} level and industrial cleanups at the 10^{-4} risk level.) Rather, the risk range provides the necessary flexibility to address the technical and cost limitations, and the performance and risk uncertainties inherent in all waste remediation efforts.

Land Use Considerations in Remedy Selection

As a result of the comparative analysis of alternatives with respect to EPA's nine evaluation criteria, EPA selects a site-specific remedy. The remedy determines the cleanup levels, the volume of contaminated material to be treated, and the volume of contaminated material to be contained. Consequently, the remedy selection decision determines the size of the area that can be returned to productive use and the particular types of uses that will be possible following remediation.

The volume and concentration of contaminants left on-site, and thus the degree of residual risk at a site, will affect future land use. For example, a remedial alternative may include leaving in place contaminants in soil at concentrations protective for industrial exposures, but not protective for residential exposures. In this case, institutional controls should be used to ensure that industrial use of the land is maintained and to prevent risks from residential exposures. Conversely, a remedial alternative may result in no waste left in place and allow for unrestricted use (e.g., residential use) .

Results of Remedy Selection Process

Several potential land use situations could result from EPA's remedy selection decision. They are:

- The remedy achieves cleanup levels that allow the entire site to be available for the reasonably anticipated future land use in the baseline risk assessment (or, where future land use is uncertain, all uses that could reasonably be anticipated).
- The remedy achieves cleanup levels that allow most, but not all, of the site to be available for the reasonably anticipated future land use. For example, in order to be cost effective and practicable, the remedy may require creation of a long-term waste management area for containment of treatment residuals or low-level waste on a small portion of the site. The cleanup levels in this portion of the site might allow for a more restricted land use.
- The remedy achieves cleanup levels that require a more restricted land use than the reasonably anticipated future land use for the entire site. This situation occurs when no remedial alternative that is cost-effective or practicable will achieve the cleanup levels consistent with the reasonably anticipated future land use. The site may still be used for productive purposes, but the use would be more restricted than the reasonably anticipated future land use. Furthermore, the more restricted use could be a long-term waste management area over all or a portion of the site.

Institutional Controls

If any remedial alternative developed during the FS will require a restricted land use in order to be protective, it is essential that the alternative include components that will ensure that it remain protective. In particular, institutional controls will generally have to be included in the alternative to prevent an unanticipated change in land use that could result in unacceptable exposures to residual contamination, or, at a minimum, alert future users to the residual risks and monitor for any changes in use. In such cases, institutional controls will play a key role in ensuring long-term protectiveness and should be evaluated and implemented with the same degree of care as is given to other elements of the remedy. In developing remedial alternatives that include institutional controls, EPA should determine: the type of institutional control to be used, the existence of the authority to implement the institutional control, and the appropriate entity's resolve and ability to

implement the institutional control. An alternative may anticipate two or more options for establishing institutional controls, but should fully evaluate all such options. A variety of institutional controls may be used such as deed restrictions and deed notices, and adoption of land use controls by a local government. These controls either prohibit certain kinds of site uses or, at a minimum, notify potential owners or land users of the presence of hazardous substances remaining on site at levels that are not protective for all uses. Where exposure must be limited to assure protectiveness, a deed notice alone generally will not provide a sufficiently protective remedy. While the ROD need not always specify the precise type of control to be imposed, sufficient analysis should be shown in the FS and ROD to support a conclusion that effective implementation of institutional controls can reasonably be expected.

Suppose, for example, that a selected remedy will be protective for industrial land use and low levels of hazardous substances will remain on site. An industry still may be able to operate its business with the selected remedy in place. Institutional controls, however, generally will need to be established to ensure the land is not used for other, less restricted purposes, such as residential use, or to alert potential buyers of any remaining contamination.

Future Changes in Land Use

Where waste is left on-site at levels that would require limited use and restricted exposure, EPA will conduct reviews at least every five years to monitor the site for any changes. Such reviews should analyze the implementation and effectiveness of institutional controls with the same degree of care as other parts of the remedy. Should land use change, it will be necessary to evaluate the implications of that change for the selected remedy, and whether the remedy remains protective. EPA's role in any subsequent additional cleanup will be determined on a site-specific basis. If landowners or others decide at a future date to change the land use in such a way that makes further cleanup necessary to ensure protectiveness, CERCLA does not prevent them from conducting such a cleanup as long as protectiveness of the remedy is not compromised. (EPA may invoke CERCLA section 122(e)(6), if necessary, to prevent actions that are inconsistent with the original remedy.) In general, EPA would not expect to become involved actively in the conduct or oversight of such cleanups. EPA, however, retains its authority to take further response action where necessary to ensure protectiveness.

Further Information

If you have any questions concerning this directive, please call Sherri Clark at 703-603-9043.

NOTICE : The policies set out in this memorandum are intended solely as guidance. They are not intended, nor can they be relied upon, to create any rights enforceable by any party in litigation with the United States. EPA officials may decide to follow the guidance provided in this memorandum, or to act at variance with the guidance, based on an analysis of specific site circumstances. Remedy selection decisions are made and justified on a case-specific basis. The Agency also reserves the right to change this guidance at any time without public notice.

APPENDIX C

EPA Risk Characterization Program



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D C 20450

THE ADMINISTRATOR

MAR 21 1995

MEMORANDUM

SUBJECT: EPA Risk Characterization Program

TO: Assistant Administrators
Associate Administrators
Regional Administrators
General Counsel
Inspector General

EPA has achieved significant pollution reduction over the past 20 years, but the challenges we face now are very different from those of the past. Many more people are aware of environmental issues today than in the past and their level of sophistication and interest in understanding these issues continues to increase. We now work with a populace which is not only interested in knowing what EPA thinks about a particular issue, but also how we come to our conclusions.

More and more key stakeholders in environmental issues want enough information to allow them to independently assess and make judgments about the significance of environmental risks and the reasonableness of our risk reduction actions. If we are to succeed and build our credibility and stature as a leader in environmental protection for the next century, EPA must be responsive and resolve to more openly and fully communicate to the public the complexities and challenges of environmental decisionmaking in the face of scientific uncertainty.

As the issues we face become more complex, people both inside and outside of EPA must better understand the basis for our decisions, as well as our confidence in the data, the science policy judgments we have made, and the uncertainty in the information base. In order to achieve this better understanding, we must improve the way in which we characterize and communicate environmental risk. We must embrace certain fundamental values

so that we may begin the process of changing the way in which we interact With each other, the public, and key stakeholders on environmental risk issues. I need your help to ensure that these values are embraced and that we change the way we do business.

First, we must adopt as values **transparency** in our decisionmaking process and **clarity in** communication with each other and the public regarding environmental risk and the uncertainties associated with our assessments of environmental risk. This means that we must My, openly, and clearly characterize risks. In doing so, we will disclose the scientific analyses, uncertainties, assumptions, and science policies which underlie our decisions as they are made throughout the risk assessment and risk management processes. I want to be sure that key science policy issues are identified as such during the risk assessment process, that policymakers are fully aware and engaged in the selection of science policy options, and that their choices and the rationale for those choices are clearly articulated and visible in our communications about environmental risk.

I understand that some maybe concerned about additional challenges and disputes. I expect that we will see more challenges, particularly at first. However, I strongly believe that making this change to a more open decisionmaking process will lead to more meaningful public . participation, better information for decisionmaking improved decisions, and more public support and respect for EPA positions and decisions. There is value in sharing with others the complexities and challenges we face in making decisions in the face of uncertainty. I view making this change as essential to the long term success of this Agency.

Clarity in communication also means that we will strive to help the public put environmental risk in the proper perspective when we take risk management actions. We must meet this challenge and find legitimate ways to help the public better comprehend the relative significance of environmental risks.

Second, because **transparency** in decisionmaking and **clarity** in communication will likely lead to more outside questioning of our assumptions and science policies, we must be more vigilant about ensuring that our core assumptions and science policies are consistent and comparable across programs, well grounded in science, and that they fall within a “zone of reasonableness.”

While I believe that the American public expects us to err on the side of protection in the face of scientific uncertainty, I do not want our assessments to be unrealistically conservative. We cannot lead the fight for environmental protection into the next century unless we use common sense in all we do.

These core values of transparency, clarity, consistency, and reasonableness need to guide each of us in our day-to-day work; from the toxicologist reviewing the individual cancer study, to the exposure and risk assessors, to the risk manager, and through to the ultimate decisionmaker. I recognize that issuing this memo will not by itself result in any change. You need to believe in the importance of this change and convey your beliefs to your managers and staff through your words and actions in order for the change to occur. You also need to play an integral role in developing the implementing policies and procedures for your programs.

I am issuing the attached EPA Risk Characterization Policy and Guidance today. I view these documents as building blocks for the development of your program-specific policies and procedures. The Science Policy Council (SPC) plans to adopt the same basic approach to implementation as was used for Peer Review. That is, the Council will form an Advisory Group that will work with a broad Implementation Team made up of representatives from every Program Office and Region. Each Program Office and each Region will be asked by the Advisory Group to develop program and region-specific policies and procedures for risk characterization consistent with the values of **transparency, clarity, consistency, and reasonableness** and consistent with the attached policy and guidance.

I recognize that as you develop your Program-specific policies and procedures you are likely to need additional tools to fully implement this policy. I want you to identify these needed tools and work cooperatively with the Science Policy Council in their development. I want your draft program and region-specific policies, procedures, and implementation plans to be developed and submitted to the Advisory Group for review by no later than May 30, 1995. You will be contacted shortly by the SPC Steering Committee to obtain the names of your nominees to the implementation Team.

A handwritten signature in black ink, appearing to read "Carol M. Browner". The signature is fluid and cursive, with a large initial "C" and "B".

Carol M. Browner

Attachments

March 1995
POLICY FOR RISK CHARACTERIZATION
at the U.S. Environmental Protection Agency

INTRODUCTION

Many EPA policy decisions are based in part on the results of risk assessment, an analysis of scientific information on existing and projected risks to human health and the environment. As practiced at EPA, risk assessment makes use of many different kinds of scientific concepts and data (e.g., exposure, toxicity, epidemiology, ecology), all of which are used to “characterize” the expected risk associated with a particular agent or action in a particular environmental context. Informed use of reliable scientific information from many different sources is a central feature of the risk assessment process.

Reliable information may or may not be available for many aspects of a risk assessment. Scientific uncertainty is a fact of life for the risk assessment process, and agency managers almost always must make decisions using assessments that are not as definitive in all important areas as would be desirable. They therefore need to understand the strengths and the limitations of each assessment, and to communicate this information to all participants and the public.

This policy reaffirms the principles and guidance found in the Agency’s 1992 policy (Guidance on Risk Characterization for Risk Managers and Risk Assessors, February 26, 1992). That guidance was based on EPA’s risk assessment guidelines, which are products of peer review and public comment. The 1994 National Research Council (NRC) report, “Science and Judgment in Risk Assessment,” addressed the Agency’s approach to risk assessment, including the 1992 risk characterization policy. The NRC statement accompanying the report stated, “... EPA’s overall approach to assessing risks is fundamentally sound despite often-heard criticisms, but the Agency must more clearly establish the scientific and policy basis for risk estimates and better describe the uncertainties in its estimates of risk.”

This policy statement and associated guidance for risk characterization is designed to ensure that critical information from each stage of a risk assessment is used in forming conclusions about risk and that this information is communicated from risk assessors to risk managers (policy makers), from middle to upper management, and from the Agency to the public. Additionally, the policy will provide a basis for greater clarity, transparency, reasonableness, and consistency in risk assessments across Agency programs. While most of the discussion and examples in this policy are drawn from health risk assessment, these values also apply to ecological risk assessment. A parallel effort by the Risk Assessment Forum to develop EPA ecological risk assessment guidelines will include guidance specific to ecological risk characterization.

Policy Statement

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

Key Aspects of Risk Characterization

Bridging risk assessment and risk management. As the interface between risk assessment and risk management, risk characterizations should be clearly presented, and separate from any risk management considerations. Risk management options should be developed using the risk characterization and should be based on consideration of all relevant factors, scientific and nonscientific.

Discussing confidence and uncertainties. Key scientific concepts, data and methods (e.g., use of animal or human data for extrapolating from high to low doses, use of pharmacokinetics data, exposure pathways, sampling methods, availability of chemical-specific information, quality of data) should be discussed. To ensure transparency, risk characterizations should include a statement of confidence in the assessment that identifies all major uncertainties along with comment on their influence on the assessment, consistent with the Guidance on Risk Characterization (attached).

Presenting several types of risk information. Information should be presented on the range of exposures derived from exposure scenarios and on the use of multiple risk descriptors (e.g., central tendency, high end of individual risk, population risk, important subgroups, if known) consistent with terminology in the Guidance on Risk Characterization, Agency risk assessment guidelines, and program-specific guidance. In decisionmaking, risk managers should use risk information appropriate to their program legislation.

EPA conducts many types of risk assessments, including screening-level assessments of new chemicals, in-depth assessments of pollutants such as dioxin

and environmental tobacco smoke, and site-specific assessments for hazardous waste sites. An iterative approach to risk assessment, beginning with screening techniques, may be used to determine if a more comprehensive assessment is necessary. The degree to which confidence and uncertainty are addressed in a risk characterization depends largely on the scope of the assessment. In general, the scope of the risk characterization should reflect the information presented in the risk assessment and program-specific guidance. When special circumstances (e.g., lack of data, extremely complex situations, resource limitations, statutory deadlines) preclude a full assessment, such circumstances should be explained and their impact on the risk assessment discussed.

Risk Characterization in Context

Risk assessment is based on a series of questions that the assessor asks about scientific information that is relevant to human and/or environmental risk. Each question calls for analysis and interpretation of the available studies, selection of the concepts and data that are most scientifically reliable and most relevant to the problem at hand, and scientific conclusions regarding the question presented. For example, health risk assessments involve the following questions:

Hazard Identification - What is known about the capacity of an environmental agent for causing cancer or other adverse health effects in humans, laboratory animals, or wildlife species? What are the related uncertainties and science policy choices?

Dose Response Assessment - What is known about the biological mechanisms and dose-response relationships underlying any effects observed in the laboratory or epidemiology studies providing data for the assessment? What are the related uncertainties and science policy choices?

Exposure Assessment - What is known about the principal paths, patterns, and magnitudes of human or wildlife exposure and numbers of persons or wildlife species likely to be exposed? What are the related uncertainties and science policy choices?

Corresponding principles and questions for ecological risk assessment are being discussed as part of the effort to develop ecological risk guidelines.

Risk characterization is the summarizing step of risk assessment. The risk characterization integrates information from the preceding components of the risk assessment and synthesizes an overall conclusion about risk that is complete, informative and useful for decisionmakers.

Risk characterizations should clearly highlight both the confidence and the uncertainty associated with the risk assessment. For example, numerical risk estimates should always be accompanied by descriptive information carefully selected to ensure an objective and balanced characterization of risk in risk assessment reports and regulatory documents. In essence, a risk characterization conveys the assessor's judgment as to the nature and existence of (or lack of) human health or ecological risks. Even though a risk characterization describes limitations in an assessment, a balanced discussion of reasonable conclusions and related uncertainties enhances, rather than detracts, from the overall credibility of each assessment.

“Risk characterization” is not synonymous with “risk communication.” This risk characterization policy addresses the interface between risk assessment and risk management. Risk communication, in contrast, emphasizes the process of exchanging information and opinion with the public - including individuals, groups, and other institutions. The development of a risk assessment may involve risk communication. For example, in the case of site-specific assessments for hazardous waste sites, discussions with the public may influence the exposure pathways included in the risk assessment. While the final risk assessment document (including the risk characterization) is available to the public, the risk communication process may be better served by separate risk information documents designed for particular audiences.

Promoting Clarity, Comparability and Consistency

There are several reasons that the Agency should strive for greater clarity, consistence and comparability in risk assessments. One reason is to minimize confusion. For example, many people have not understood that a risk estimate of one in a million for an “average” individual is not comparable to another one in a million risk estimate for the “most exposed individual.” Use of such apparently similar estimates without further explanation leads to misunderstandings about the relative significance of risks and the protectiveness of risk reduction actions.

EPA's Exposure Assessment Guidelines provide standard descriptors of exposure and risk. Use of these terms in all Agency risk assessments will promote consistency and comparability. Use of several descriptors, rather than a single descriptor, will enable EPA to present a fuller picture of risk that corresponds to the range of different exposure conditions encountered by various individuals and population exposed to most environmental chemicals.

Legal Effect

This policy statement and associated guidance on risk characterization do not establish or affect legal rights or obligations. Rather, they confirm the importance of risk characterization as a component of risk assessment, outline relevant principles, and identify factors Agency staff should consider in implementing the policy.

The policy and associated guidance do not stand alone; nor do they establish a binding norm that is finally determinative of the issues addressed. Except where otherwise provided by law, the Agency's decision on conducting a risk assessment in any particular case is within the Agency's discretion. Variations in the application of the policy and associated guidance, therefore, are not a legitimate basis for delaying or complicating action on Agency decisions.

Applicability

Except where otherwise provided by law and subject to the limitations on the policy's legal effect discussed above, this policy applies to risk assessments prepared by EPA and to risk assessments prepared by others that are used in support of EPA decisions.

EPA will consider the principles in this policy in evaluating assessments submitted to EPA to complement or challenge Agency assessments. Adherence to this Agency-wide policy will improve understanding of Agency risk assessments, lead to more informed decisions, and heighten the credibility of both assessments and decisions.

Implementation

Assistant Administrators and Regional Administrators are responsible for implementation of this policy within their organizational units. The Science Policy Council (SPC) is organizing Agency-wide implementation activities. Its responsibilities include promoting consistent interpretation, assessing Agency-wide progress, working with external groups on risk characterization issues and methods, and developing recommendations for revisions of the policy and guidance, as necessary.

Each Program and Regional office will develop office-specific policies and procedures for risk characterization that are consistent with this policy and the associated guidance. Each Program and Regional office will designate a risk manager or risk assessor as the office representative to the Agency-wide Implementa-

tion Team, which will coordinate development of office-specific policies and procedures and other implementation activities. The SPC will also designate a small cross-Agency Advisory Group that will serve as the liaison between the SPC and the Implementation Team.

In ensuring coordination and consistency among EPA offices, the Implementation Team will take into account statutory and court deadlines, resource i.replications, and existing Agency and program-specific guidance on risk assessment. The group will work closely with staff throughout Headquarters and Regional offices to promote development of risk characterizations that present a full and complete picture of risk that meets the needs of the risk managers.

APPROVED: 
Carol M. Browner, Administrator

DATE: MAR 21 1995

ELEMENTS TO CONSIDER WHEN DRAFTING EPA RISK CHARACTERIZATIONS

March 1995

Background -- Risk Characterization Principles

There are a number of principles which form the basis for a risk characterization:

- Risk assessments should be transparent, in that the conclusions drawn from the science are identified separately from policy judgments, and the use of default values or methods and the use of assumptions in the risk assessment are clearly articulated.
- Risk characterizations should include a summary of the key issues and conclusions of each of the other components of the risk assessment, as well as describe the likelihood of harm. The summary should include a description of the overall strengths and the limitations (including uncertainties) of the assessment and conclusions.
- Risk characterizations should be consistent in general format, but recognize the unique characteristics of each specific situation.
- Risk characterizations should include, at least in a qualitative sense, a discussion of how a specific risk and its context compares with other similar risks. This may be accomplished by comparisons with other chemicals or situations in which the Agency has decided to act, or with other situations which the public may be familiar with. The discussion should highlight the limitations of such comparisons.
- Risk characterization is a key component of risk communication, which is an interactive process involving exchange of information and expert opinion among individuals, groups and institutions.

Conceptual Guide for Developing Chemical-Specific Risk Characterizations

The following outline is a guide and formatting aid for developing risk characterizations for chemical risk assessments. Similar outlines will be developed for other types of risk characterizations, including site-specific assessments and ecological risk assessments. A common format will assist risk managers in evaluating and using risk characterization.

The outline has two parts. The first part tracks the risk assessment to bring forward its major conclusions. The second part draws all of the information together to characterize risk. The outline represents the expected findings for a typical complete chemical assessment for a single chemical. However, exceptions for the

circumstances of individual assessments exist and should be explained as part of the risk characterization. For example, particular statutory requirements, court-ordered deadlines, resource limitations, and other specific factors may be described to explain why certain elements are incomplete.

This outline does not establish or affect legal rights or obligations. Rather, it confirms the importance of risk characterization, outlines relevant principles, and identifies factors Agency staff should consider in implementing the policy. On a continuing basis, Agency' management is expected to evaluate the policy as well as the results of its application throughout the Agency and undertake revisions as necessary. Therefore, the policy does not stand alone; nor does it establish a binding norm that is finally determinative of the issues addressed. Minor variations in its application from one instance to another are appropriate and expected; they thus are not a legitimate basis for delaying or complicating action on otherwise satisfactory scientific, technical, and regulatory products.

PART ONE

SUMMARIZING MAJOR CONCLUSIONS IN RISK CHARACTERIZATION

I. Characterization of Hazard Identification

- A. What "is the key toxicological study (or studies) that provides the basis for health concerns?
 - How good is the key study?
 - Are the data from laboratory or field studies? In single species or multiple species?
 - If the hazard is carcinogenic, comment on issues such as: observation of single or multiple tumor sites; occurrence of benign or malignant tumors; certain tumor types not linked to carcinogenicity; use of the maximum tolerated dose (MTD).
 - If the hazard is other than carcinogenic, what endpoints were observed, and what is the basis for the critical effect?
 - Describe other studies that support this finding.
 - Discuss any valid studies which conflict with this finding.
- B. Besides the health effect observed in the key study, are there other health endpoints of concern?
 - What are the significant data gaps?
- C. Discuss available epidemiological or clinical data. For epidemiological studies:
 - What types of studies were used, i.e., ecologic, case-control, cohort?

- Describe the degree to which exposures were adequately described.
 - Describe the degree to which confounding factors were adequately accounted for.
 - Describe the degree to which other causal factors were excluded.
- D. How much is known about how (through what biological mechanism) the chemical produces adverse effects?
- Discuss relevant studies of mechanisms of action or metabolism.
 - Does this information aid in the interpretation of the toxicity data?
 - What are the implications for potential health effects?
- E. Comment on any non-positive data in animals or people, and whether these data were considered in the hazard identification.
- F. If adverse health effects have been observed in wildlife species, characterize such effects by discussing the relevant issues as in A through E above.
- G. Summarize the hazard identification and discuss the significance of each of the following:
- confidence in conclusions;
 - alternative conclusions that are also supported by the data; significant data gaps; and
 - highlights of major assumptions.

II. Characterization of Dose-Response

- A. What data were used to develop the dose-response curve? Would the result have been significantly different if based on a different data set?
- If animal data were used:
 - which species were used? most sensitive, average of all species, or other?
 - were any studies excluded? why?
 - If epidemiological data were used:
 - Which studies were used? only positive studies, all studies, or some other combination?
 - Were any studies excluded? why?
 - Was a meta-analysis performed to combine the epidemiological studies? what approach was used? were studies excluded? why?
- B. What model was used to develop the dose-response curve? What rationale supports this choice? Is chemical-specific information available to support this approach?
- For non-carcinogenic hazards:
 - How was the RfD/RfC (or the acceptable range) calculated?

- What assumptions or uncertainty factors were used?
- What is the confidence in the estimates?
- For carcinogenic hazards:
 - What dose-response model was used? LMS or other linear-at-low-dose model, a biologically-based model based on metabolism data, or data about possible mechanisms of action?
 - What is the basis for the selection of the particular dose-response model used? Are there other models that could have been used with equal plausibility and scientific validity? What is the basis for selection of the model used in this instance?

C. Discuss the route and level of exposure observed, as compared to expected human exposures.

- Are the available data from the same route of exposure as the expected human exposures? If not, are pharmacokinetic data available to extrapolate across route of exposure?
- How far does one need to extrapolate from the observed data to environmental exposures (one to two orders of magnitude? multiple orders of magnitude)? What is the impact of such an extrapolation?

D. If adverse health effects have been observed in wildlife species, characterize dose-response information using the process outlined in A-C.

III. Characterization of Exposure

- A. What are the most significant sources of environmental exposure?
- Are there data on sources of exposure from different media? What is the relative contribution of different sources of exposure?
 - What are the most significant environmental pathways for exposure?
- B. Describe the populations that were assessed, including as the general population, highly exposed groups, and highly susceptible groups.
- C. Describe the basis for the exposure assessment, including any monitoring, modeling, or other analyses of exposure distributions such as Monte-Carlo or krieging.
- D. What are the key descriptors of exposure?
- Describe the (range of) exposures to: “average” individual “high end” individuals, general population, high exposure group(s), children, susceptible populations.
 - How was the central tendency estimate developed? What factors and/or methods were used in developing this estimate?
 - How was the high-end estimate developed?

- Is there information on highly-exposed subgroups? Who are they?
 - What are their levels of exposure? How are they accounted for in the assessment?
- E. Is there reason to be concerned about cumulative or multiple exposures because of ethnic, racial, or socioeconomic reasons?
- F. If adverse health effects have been observed in wildlife species, characterize wildlife exposure by discussing the relevant issues as in A through E above.
- G. Summarize exposure conclusions and discuss the following
- results of different approaches, i.e. modeling, monitoring, probability distributions;
 - limitations of each, and the range of most reasonable values; and
 - confidence in the results obtained, and the limitations to the results.

PART TWO

RISK CONCLUSIONS AND COMPARISONS

IV. Risk Conclusions

- A. What is the overall picture of risk, based on the hazard identification, dose-response and exposure characterizations?
- B. What are the major conclusions and strengths of the assessment in each of the three main analyses (i.e., hazard identification, dose-response, and exposure assessment)?
- C. What are the major limitations and uncertainties in the three main analyses?
- D. What are the science policy options in each of the three major analyses?
- What are the alternative approaches evaluated?
 - What are the reasons for the choices made?

V. Risk Context

- A. What are the qualitative characteristics of the hazard (e.g., voluntary vs. involuntary, technological vs. natural, etc.)? Comment on findings, if any, from studies of risk perception that relate to this hazard or similar hazards.
- B. What are the alternatives to this hazard? How do the risks compare?

- C. How does this risk compare to other risks?
1. How does this risk compare to other risks in this regulatory program, or other similar risks that the EPA has made decisions about?
 2. Where appropriate, can this risk be compared with past Agency decisions, decisions by other federal or state agencies, or common risks with which people may be familiar?
 3. Describe the limitations of making these comparisons.
- D. Comment on significant community concerns which influence public perception of risk?

VI. Existing Risk Information

Comment on other risk assessments that have been done on this chemical by EPA, other federal agencies, or other organizations. Are there significantly different conclusions that merit discussion?

VII. Other Information

Is there other information that would be useful to the risk manager or the public in this situation that has not been described above?

of high quality. As a first step, a selected number of risk characterization case studies will be developed for use as teaching tools. A "case study" will be an exercise to improve an existing risk characterization, using the information available in an existing risk assessment. While based on actual risk assessments, identifying information (e.g., site identification information) will be removed to avoid any implied judgement

as to the adequacy of the original risk assessment and risk characterization. Examples of case studies may include a chemical assessment, a site-specific assessment, and a screening-level assessment. The case studies will be developed by the risk characterization advisory group, working in consultation with the implementation team, and will be used for discussion at the first risk characterization workshop.

Roundtables and Workshops

EPA decision-makers will be invited to participate in roundtable discussions on risk characterization. In addition, a minimum of two workshops are planned for EPA risk assessors and risk managers.

- ° *Risk Decision-maker Roundtables on Risk Characterization* - The goal will be to determine the types of risk characterization information needed by managers for effective risk-based decision-making.
- ° *Risk Characterization Workshop I* - Will focus on identifying the qualities of "good" risk characterizations, program-specific plans and guidance development, and case studies.
- ° *Risk Characterization Workshop II* - Risk assessors and risk managers will meet to wrap-up program-specific plans and guidance, and discuss any necessary updates to the agency-wide risk characterization guidance.

**GUIDANCE
FOR
RISK CHARACTERIZATION**

**U.S. Environmental Protection Agency
Science Policy Council
February, 1995**

CONTENTS

- I. The Risk Assessment-Risk Management Interface
- II. Risk Assessment and Risk Characterization
- III. Exposure and Risk Descriptors

PREFACE

This guidance contains principles for developing and describing EPA risk assessments, with a particular emphasis on risk characterization. The current document is an update of the guidance issued with the Agency's 1992 policy (Guidance on Risk Characterization for Risk Managers and Risk Assessors, February 26, 1992). The guidance has not been substantially revised, but includes some clarifications and changes to give more prominence to certain issues, such as the need to explain the use of default assumptions.

As in the 1992 policy, some aspects of this guidance focus on cancer risk assessment, but the guidance applies generally to human health effects (e.g., neurotoxicity, developmental toxicity) and, with appropriate modifications, should be used in all health risk assessments. This document has not been revised to specifically address ecological risk assessment, however, initial guidance for ecological risk characterization is included in EPA's Framework for Ecological Risk Assessments (EPA/630/R-92/001). Neither does this guidance address in detail the use of risk assessment information (e.g., information from the Integrated Risk Information System (IRIS)) to generate site- or media-specific risk assessments. Additional program-specific guidance will be developed to enable implementation of EPA's Risk Characterization Policy. Development of such guidance will be overseen by the Science Policy Council and will involve risk assessors and risk managers from across the Agency.

I. THE RISK ASSESSMENT-RISK MANAGEMENT INTERFACE

Recognizing that for many people the term risk assessment has wide meaning, the National Research Council's 1983 report on risk assessment in the federal government distinguished between risk assessment and risk management.

"Broader uses of the term [risk assessment] than ours also embrace analysis of perceived risks, comparisons of risks associated with different regulatory strategies, and occasionally analysis of the economic and social implications of regulatory decisions -- functions that we assign to risk management (emphasis added). (1)

In 1984, EPA endorsed these distinctions between risk assessment and risk management for Agency use (2), and later relied on them in developing risk assessment guidelines (3). In 1994, the NRC reviewed the Agency's approach to and use of risk assessment and issued an extensive report on their findings (4). This distinction suggests that EPA participants in the process can be grouped into two main categories, each with somewhat.. different responsibilities, based on their roles with respect to risk assessment and risk management.

A. Roles of Risk Assessors and Risk Managers

Within the Risk Assessment category there is a group that develops chemical-specific risk assessments by collecting, analyzing, and synthesizing scientific data to produce the hazard identification, dose-response, and exposure assessment portion of the risk assessment and to characterize risk. This group relies in part on Agency risk assessment guidelines to address science policy issues and scientific uncertainties. Generally, this group includes scientists and statisticians in the Office of Research and Development; the Office of Prevention; Pesticides and Toxics and other program offices; the Carcinogen Risk Assessment Verification Endeavor (CRAVE); and the Reference Dose (RfD) and Reference Concentration (RfC) Workgroups.

Another group generates site- or media-specific risk assessments for use in regulation development or site-specific decision-making. These assessors rely on existing databases (e.g., IRIS, ORD Health Assessment Documents, CRAVE and RfD/RfC Workgroup documents, and program-specific toxicity information) and media- or site-specific exposure information in developing risk assessments. This group also relies in part on Agency risk assessment guidelines and program-specific guidance to address science policy issues and scientific uncertainties. Generally, this group includes scientists and analysts in program offices, regional offices, and the Office of Research and Development.

Risk managers, as a separate category, integrate the risk characterization with other considerations specified in applicable statutes to make and justify regulatory decisions. Generally, this group includes Agency managers and decision-makers. Risk managers also play a role in determining the scope of risk assessments. The risk assessment process involves regular interaction between risk assessors and risk managers, with overlapping responsibilities at various stages in the overall process. Shared responsibilities include initial decisions regarding the planning and conduct of an assessment, discussions as the assessment develops, decisions regarding new data needed to complete an assessment and to address significant uncertainties. At critical junctures in the assessment, such consultations shape the nature of, and schedule for, the assessment. External experts and members of the public may also play a role in determining the scope of the assessment; for example, the public is often concerned about certain chemicals or exposure pathways in the-development of site-specific risk assessments.

B. Guiding Principles

The following guidance outlines principles for those who generate, review, use, and integrate risk assessments for decision-making.

1. Risk assessors and risk managers should be sensitive to distinctions between risk assessment and risk management.

The major participants in the risk assessment process have many shared responsibilities. Where responsibilities differ, it is important that participants confine themselves to tasks in their areas of responsibility and not inadvertently obscure differences between risk assessment and risk management.

For the generators of the assessment, distinguishing between risk assessment and risk management means that scientific information is selected, evaluated, and presented without considering issues such as cost, feasibility, or how the scientific analysis might influence the regulatory or site-specific decision. Assessors are charged with (1) generating a credible, objective, realistic, and scientifically balanced analysis; (2) presenting information on hazard, dose-response, exposure and risk; and (3) explaining confidence in each assessment by clearly delineating strengths, uncertainties and assumptions, along with the impacts of these factors (e.g., confidence limits, use of conservative/ non-conservative assumptions) on the overall assessment. They do not make decisions on the acceptability of any risk level for protecting public health or selecting procedures for reducing risks.

For users of the assessment and for decision-makers who integrate these assessments into regulatory or site-specific decisions, the distinction between risk assessment and risk management means refraining from influencing the risk

description through consideration of other factors -- e.g., the regulatory outcome -- and from attempting to shape the risk assessment to avoid statutory constraints, meet regulatory objectives, or serve political purposes. Such management considerations are often legitimate considerations for the overall regulatory decision (see next principle), but they have no role in estimating or describing risk. However, decision-makers and risk assessors participate in an Agency process that establishes policy directions that determine the overall nature and tone of Agency risk assessments and, as appropriate, provide policy guidance on difficult and controversial risk assessment issues. Matters such as risk assessment priorities, degree of conservatism, and acceptability of particular risk levels are reserved for decision-makers who are charged with making decisions regarding protection of public health.

2. The risk assessment product, that is, the risk characterization, is only one of several kinds of information used for regulatory decision-making.

Risk characterization, the last step in risk assessment, is the starting point for risk management considerations and the foundation for regulator decision-making, but it is only one of several important components in such decisions. As the last step in risk assessment, the risk characterization identifies and highlights the noteworthy risk conclusions and related uncertainties. Each of the environmental laws administered by EPA calls for consideration of other factors at various stages in the regulatory process. As authorized by different statutes, decision-makers evaluate technical feasibility (e.g., treatability, detection limits), economic, social, political, and legal factors as part of the analysis of whether or not to regulate and, if so, to what extent. Thus, regulatory decisions are usually based on a combination of the technical analysis used to develop the risk assessment and information from other fields.

For this reason, risk assessors and managers should understand that the regulatory decision is usually not determined solely by the outcome of the risk assessment. For example, a regulatory decision on the use of a particular pesticide considers not only the risk level to affected populations, but also the agricultural benefits of its use that may be important for the nation's food supply. Similarly, assessment efforts may produce an RfD for a particular chemical, but other considerations may result in a regulatory level that is more or less protective than the RfD itself.

For decision-makers, this means that societal considerations (e.g., costs and benefits) that, along with the risk assessment, shape the regulatory decision should be described as fully as the scientific information set forth in the risk characterization. Information on data sources and analyses, their strengths and limitations, confidence in the assessment, uncertainties, and alternative analyses are as important here as they are for the scientific components of the regulatory decision. Decision-makers should be able to expect, for example, the same level of rigor from the economic analysis as they receive from the risk analysis. Risk management decisions involve numerous assumptions and uncertainties regarding technology, economics and social factors, which need to be explicitly identified for the decision-makers and the public.

II. RISK CHARACTERIZATION

A. Defining Risk Characterization in the Context of Risk Assessment

EPA risk assessment principles and practices draw on many sources. Obvious sources include the environmental laws administered by EPA, the National Research Council's 1983 report on risk assessment (1), the Agency's Risk Assessment Guidelines (3), and various program specific guidance (e.g., the Risk Assessment Guidance for Superfund). Twenty years of EPA experience in developing, defending, and enforcing risk assessment-based regulation is another. Together these various sources stress the importance of a clear explanation of Agency processes for evaluating hazard, dose-response, exposure, and other data that provide the scientific foundation for characterizing risk.

This section focuses on two requirements for full characterization of risk. First, the characterization should address qualitative and quantitative features of the assessment. Second, it should identify the important strengths and uncertainties in the assessment as part of a discussion of the confidence in the assessment. This emphasis on a full description of all elements of the assessment draws attention to the importance of the qualitative, as well as the quantitative, dimensions of the assessment. The 1983 NRC report carefully distinguished qualitative risk assessment from quantitative assessments, preferring risk statements that are not strictly numerical.

The term risk assessment is often given narrower and broader meanings than we have adopted here. For some observers, the term is synonymous with quantitative risk assessment and emphasizes reliance on numerical results. Our broader definition includes quantification, but also includes qualitative expressions of risk. Quantitative estimates of risk are not always feasible, and they may be eschewed by agencies for policy reasons. (1)

EPA's Exposure Assessment Guidelines define risk characterization as the final step in the risk assessment process that:

- Integrates the individual characterizations from the hazard identification, dose-response, and exposure assessments;
- Provides an evaluation of the overall quality of the assessment and the degree of confidence the authors have in the estimates of risk and conclusions drawn;
- Describes risks-to individuals and populations in terms of extent and severity of probable harm; and
- Communicates results of the risk assessment to the risk manager. (5)

Particularly critical to full characterization of risk is a frank and open discussion of the uncertainty in the overall assessment and in each of its components. The uncertainty discussion is important for several reasons.

1. Information from different sources carries different kinds of uncertainty and knowledge of these differences is important when uncertainties are combined for characterizing risk.
2. The risk assessment process, with management input, involves decisions regarding the collection of additional data (versus living with uncertainty); in the risk characterization, a discussion of the uncertainties will help to identify where additional information could contribute significantly to reducing uncertainties in risk assessment.
3. A clear and explicit statement of the strengths and limitations of a risk assessment requires a clear and explicit statement of related uncertainties.

A discussion of uncertainty requires comment on such issues as the quality and quantity of available data, gaps in the data base for specific chemicals, quality of the measured data, use of default assumptions, incomplete understanding of general biological phenomena, and scientific judgments or science policy positions that were employed to bridge information gaps.

In short, broad” agreement exists on the importance of a full picture of risk, particularly including a statement of confidence in the assessment and the associated uncertainties. This section discusses information content and uncertainty aspects of risk characterization, while Section III discusses various descriptors used in risk characterization.

B. Guiding Principles

- 1. The risk characterization integrates the information from the hazard identification, dose-response, and exposure assessments, using a combination of qualitative information, quantitative information, and information regarding uncertainties.**

Risk assessment is based on a series of questions that the assessor asks about the data and the implications of the data for human risk. Each question calls for analysis and interpretation of the available studies, selection of the data that are most scientifically reliable and most relevant to the problem at hand, and scientific conclusions regarding the question presented. As suggested below, because the questions and analyses are complex, a complete characterization includes several different kinds of information, carefully selected for, reliability and relevance.

- a. Hazard Identification -- What is known about the capacity of an environmental agent for causing cancer (or other adverse effects) in humans and laboratory animals?

Hazard identification is a qualitative description based on factors such as the kind and quality of data on humans or laboratory animals, the availability of ancillary information (e.g., structure-activity analysis, genetic toxicity, pharmacokinetics) from other studies, and the weight-of-the-evidence from all of these data sources. For example, to develop this description, the issues addressed include:

- 1) the nature, reliability, and consistency of the particular studies in humans and in laboratory animals;
- 2) the available information on the mechanistic basis for activity; and
- 3) experimental animal responses and their relevance to human outcomes.

These issues make clear that the task of hazard identification is characterized by describing the full range of available information and the implications of that information for human health.

- b. Dose-Response Assessment* -- What is known about the biological mechanisms and dose-response relationships underlying any effects observed in the laboratory or epidemiology studies providing data for the assessment?

The dose-response assessment examines quantitative relationships between exposure (or dose) and effects in the studies used to identify and define effects of concern. This information is later used along with “real world” exposure information (see below) to develop estimates-of the likelihood of adverse effects in populations potentiality at risk. It should be noted that, in practice, hazard identification for developmental toxicity and other non-cancer health effects is usually done in conjunction with an evaluation of dose-response relationships, since the determination of whether there is a hazard is often dependent on whether a dose response relationship is present. (6) Also, the framework developed by EPA for ecological risk assessment does not distinguish between hazard identification and dose-response assessment, but rather calls for a “characterization of ecological effects.” (7)

Methods for establishing dose-response relationships often depend on various assumptions used in lieu of a complete data base, and the method chosen can strongly influence the overall assessment. The Agency’s risk assessment guidelines often identify so-called “default assumptions” for use in the absence of other information. The risk assessment should pay careful attention to the choice of a high-to-low dose extrapolation procedure. As a result, an assessor who is characterizing a dose-response relationship considers several key issues:

- 1) the relationship between extrapolation models selected and available information on biological mechanisms;

- 2) how appropriate data sets were selected from those that show the range of possible potencies both in laboratory animals and humans;
- 3) the basis for selecting interspecies dose scaling factors to account for scaling doses from experimental animals to humans;
- 4) the correspondence between the expected route(s) of exposure and the exposure route(s) utilized in the studies forming the basis of the dose-response assessment, as well as the interrelationships of potential effects from different exposure routes;
- 5) the correspondence between the expected duration of exposure and the exposure durations in the studies used in forming the basis of the dose-response assessment, e.g., chronic studies would be used to assess long-term, cumulative exposure concentrations, while acute studies would be used in assessing peak levels of exposure; and
- 6) the potential for differing susceptibilities among population subgroups.

The Agency's Integrated Risk Information System (IRIS) is a repository for such information for EPA. EPA program offices also maintain program-specific databases, such as the OSWER Health Effects Assessment Summary Tables (HEAST). IRIS includes data summaries representing Agency consensus on specific chemicals, based on a careful review of the scientific issues listed above. For specific risk assessments based on data from any source, risk assessors should carefully review the information presented, emphasizing confidence in the data and uncertainties (see subsection 2 below). Specifically, when IRIS data are used, the IRIS statement of confidence should be included as an explicit part of the risk characterization for hazard and dose-response information.

- c. Exposure Assessment -- What is known about the principal paths, patterns, and magnitudes of human exposure and numbers of persons who may be exposed?

The exposure assessment examines a wide range of exposure parameters pertaining to the environmental scenarios of people who may be exposed to the agent under study. The information considered for the exposure assessment includes monitoring studies of chemical concentrations in environmental media, food, and other materials; modeling of environmental fate and transport of contaminants; and information on different activity patterns of different population subgroups. An assessor who characterizes exposure should address several issues:

- 1) The basis for the values and input parameters used for each exposure scenario. If the values are based on data, there should be a discussion of the quality, purpose, and representativeness of the database. For monitoring data, there should be a discussion of the data quality objectives as they are relevant to risk

assessment, including the appropriateness of the analytical detection limits. If models are applied, the appropriateness of the models and information on their validation should be presented. When assumptions are made, the source and general logic used to develop the assumptions (e.g., program guidance, analogy, professional judgment) should be described.

- 2) The confidence in the assumptions made about human behavior and the relative likelihood of the different exposure scenarios.
- 3) The major factor or factors (e.g., concentration, body uptake, duration/frequency of exposure) thought to account for the greatest uncertainty in the exposure estimate, due either to sensitivity or lack of data.
- 4) The link between the exposure information and the risk descriptors discussed in Section III of this Appendix. Specifically, the risk assessor needs to discuss the connection between the conservatism or non-conservatism of the data/assumptions used in the scenarios and the choice of descriptors.
- 5) Other information that may be important for the particular risk assessment. For example, for many assessments, other sources and background levels in the environment may contribute significantly to population exposures and should be discussed.

2) The risk characterization includes a discussion of uncertainty and variability.

In the risk characterization, conclusions about hazard and dose response are integrated with those from the exposure assessment. In addition, confidence about these conclusions, including information about the uncertainties associated with each aspect of the assessment in the final risk summary, is highlighted. In the previous assessment steps and in the risk characterization, the risk assessor must distinguish between variability and uncertainty.

Variability arises from true heterogeneity in characteristics such as dose-response differences within a population, or differences in contaminant levels in the environment. The values of some variables used in an assessment change with time and space, or across the population whose exposure is being estimated. Assessments should address the resulting variability in doses received by members of the target population. Individual exposure, dose, and risk can vary widely in a large population. The central tendency and high end individual risk descriptors (discussed in Section III below) are intended to capture the variability in exposure, lifestyles, and other factors that lead to a distribution of risk across a population.

Uncertainty, on the other hand, represents lack of knowledge about factors such as adverse effects or contaminant levels which may be reduced with additional study. Generally, risk assessments carry several categories of uncertainty, and each merits

consideration. Measurement uncertainty refers to the usual error that accompanies scientific measurements--standard statistical techniques can often be used to express measurement uncertainty. A substantial amount of uncertainty is often inherent in environmental sampling, and assessments should address these uncertainties. There are likewise uncertainties associated with the use of scientific models, e.g., dose-response models, models of environmental fate and transport. Evaluation of model uncertainty would consider the scientific basis for the model and available empirical validation.

A different kind of uncertainty stems from data gaps -- that is, estimates or assumptions used in the assessment. Often, the data gap is broad, such as the absence of information on the effects of exposure to a chemical on humans or on the biological mechanism of action of an agent. The risk assessor should include a statement of confidence that reflects the degree to which the risk assessor believes that the estimates or assumptions adequately fill the data gap. For some common and important data gaps, Agency or program-specific risk assessment guidance provides default assumptions or values. Risk assessors should carefully consider all available data before deciding to rely on default assumptions. If defaults are used, the risk assessment should reference the Agency guidance that explains the default assumptions or values.

Often risk assessors and managers simplify discussion of risk issues by speaking only of the numerical components of an assessment. That is, they refer to the alpha-numeric weight-of-the-evidence classification, unit risk, the risk-specific dose or the q_1^* for cancer risk, and the RfD/RfC for health effects other than cancer, to the exclusion of other information bearing on the risk case. However, since every assessment carries uncertainties, a simplified numerical presentation of risk is always incomplete and often misleading. For this reason, the NRC (1) and EPA risk assessment guidelines (2) call for "characterizing" risk to include qualitative information, a related numerical risk estimate and a discussion of uncertainties, limitations, and assumptions--default and otherwise.

Qualitative information on methodology, alternative interpretations, and working assumptions (including defaults) is an important component of risk characterization. For example, specifying that animal studies rather than human studies were used in an assessment tells others that the risk estimate is based on assumptions about human response to a particular chemical rather than human data. Information that human exposure estimates are based in the subjects' presence in the vicinity of a chemical accident rather than tissue measurements defines known and unknown aspects of the exposure component of the study.

Qualitative descriptions of this kind provide crucial information that augments understanding of numerical risk estimates. Uncertainties such as these are expected in scientific studies and in any risk assessment based on these studies. Such

uncertainties do not reduce the validity of the assessment. Rather, they should be highlighted along with other important risk assessment conclusions to inform others fully on the results of the assessment.

In many cases, assessors must choose among available data, models, or assumptions in estimating risks. Examining the impact of selected, plausible alternatives on the conclusions of the assessment is an important part of the uncertainty discussion. The key words are “selected” and “plausible;” listing all alternatives to a particular assumption, regardless of their merits would be superfluous. Generators of the assessment, using best professional judgment, should outline the strengths and weaknesses of the plausible alternative approaches.¹

An adequate description of the process of alternatives selection involves several aspects.

- a. A rationale for the choice.
- b. Discussion of the effects of alternatives selected on the assessment.
- c. Comparison with other plausible alternatives, where appropriate.

The degree to which variability and uncertainty are addressed depends largely on the scope of the assessment and the resources available. For example, the Agency does not expect an assessment to evaluate and assess every conceivable exposure scenario for every possible pollutant, to examine all susceptible populations, potentially at risk, or to characterize every possible environmental scenario to estimate the cause and effect relationships between exposure to pollutants and adverse health effects. Rather, the discussion of uncertainty and variability should reflect the type and complexity of the risk assessment, with the level of effort for analysis and discussion of uncertainty corresponding to the level of effort for the assessment.

3. Well-balanced risk characterizations present risk conclusions and information regarding the strengths and limitations of the assessment for other risk assessors, EPA decision-makers, and the public.

The risk assessment process calls for identifying and highlighting significant risk conclusions and related uncertainties partly to assure full communication among risk assessors and partly to assure that decision-makers are fully informed. Issues are identified by acknowledging noteworthy qualitative and quantitative factors that make a difference in the overall assessment of hazard and risk, and hence in the ultimate regulatory decision. The key word is “noteworthy.” Information that

¹In cases where risk assessments within an Agency program routinely address similar sets of alternatives, program guidance may be developed to streamline and simplify the discussion of these alternatives.

significantly influences the analysis is explicitly noted -- in all future presentations of the risk assessment and in the related decision. Uncertainties and assumptions that strongly influence confidence in the risk estimate also require special attention.

Numerical estimates should not be separated from the descriptive information that is integral to risk characterization. Documents and presentations supporting regulator or site-specific decisions should include both the numerical estimate and descriptive information; in short reports, this information can be abbreviated. Fully visible information assures that important features of the assessment are immediately available at each level of review for evaluating whether risks are acceptable or unreasonable.

III. EXPOSURE ASSESSMENT AND RISK DESCRIPTORS

A. Presentation of Risk Descriptors

The results of a risk assessment are usually communicated to the risk manager in the risk characterization portion of the assessment. This communication is often accomplished through risk descriptors which convey information and answer questions about risk, each descriptor providing different information and insights. Exposure assessment plays a key role in developing these risk descriptors since each descriptor is based in part on the exposure distribution within the population of interest.

The following guidance outlines the different descriptors in a convenient order that should not be construed as a hierarchy of importance. These descriptors should be used to describe risk in a variety of ways for a given assessment, consistent with the assessment's purpose, the data available, and the information the risk manager needs. Use of a range of descriptors instead of a single descriptor enables Agency programs to present a picture of risk that corresponds to the range of different exposure conditions encountered for most environmental chemicals. This analysis, in turn, allows risk managers to identify populations at greater and lesser risk and to shape regulatory solutions accordingly”

Agency risk assessments will be expected to address or ‘provide descriptions of (1) individual risk that include the central tendency and high end portions of the risk distribution, (2) population risk, and (3) important subgroups of the population, such as highly exposed or highly susceptible groups. Assessors may also use additional descriptors of risk as needed when these add to the clarity of the presentation. With the exception of assessments where particular descriptors clearly do not apply, some form of these three types of descriptors should be routinely developed and presented for Agency risk assessments. In other cases, where a descriptor would be relevant, but the program lacks the data or methods to develop it, the program office should design and implement a plan, in coordination with other EPA offices, to meet these assessment needs. While gaps continue to exist, risk assessors should make their best efforts to address each risk descriptor, and at a minimum, should briefly discuss the lack of data or methods. Finally, presenters of risk assessment information “should be prepared to routinely answer questions by risk managers concerning these descriptors.

It is essential that presenters not only communicate the results of the assessment by addressing each of the descriptors where appropriate, but that they also

²Program-specific guidance will need to address these situations. For example, for site-specific assessments, the utility and appropriateness of population risk estimates will be determined based on the available data and program guidance.

communicate their confidence that these results portray a reasonable picture of the actual or projected exposures. This task will usually be accomplished by frankly commenting on the key assumptions and parameters that have the greatest impact on the results, the basis or rationale for choosing these assumptions/parameters, and the consequences of choosing other assumptions.

B. Relationship Between Exposure Descriptors and Risk Descriptors

In the risk assessment process, risk is estimated as a function of exposure, with the risk of adverse affects increasing as exposure increases. Information on the levels of exposure experienced by different members of the population is key to understanding the range of risks that may occur. Risk assessors and risk managers should keep in mind, however, that exposure is not synonymous with risk. Differences among individuals in absorption rates, susceptibility, or other factors mean that individuals with the same level of exposure may be at different levels of risk. In most cases, the state of the science is not yet adequate to define distributions of factors such as population susceptibility. The guidance principles below discuss a variety of risk descriptors that primarily reflect differences in estimated exposure. If a full “description of the range of susceptibility in the population cannot be presented, an effort should be made to identify subgroups that, for various reasons, may be particularly susceptible.

C. Guiding Principles

- 1. Information about the distribution of individual exposures is important to communicating the results of a risk assessment.**

The risk manager is generally interested in answers to questions such as the following:

- Who are the people at the highest risk?
- What risk levels are they subjected to?
- What are they doing, where do they live, etc., that might be putting them at this higher risk?
- What is the average risk for individuals in the population of interest?

Individual exposure and risk descriptors are intended to provide answers to these questions so as to illuminate the risk management decisions that need to be made. In order to describe the range of risks, both high end and central tendency

descriptors are used to convey the variability risk levels experienced by different individuals in the population.

a. High end descriptor

For the Agency's purposes, high end risk descriptors are plausible estimates of the individual risk for those persons at the upper end of the risk distribution. Given limitations in current understanding of variability in individuals' sensitivity to toxins, high end descriptors will usually address high end exposure or dose (herein referred to as exposure for brevity). The intent of these descriptors is to convey estimates of exposure in the upper range of the distribution, but to avoid estimates which are beyond the true distribution. Conceptually, high end exposure means exposure above about the 90th percentile of the population distribution, but not higher than the individual in the population who has the highest exposure. When large populations are assessed, a large number of individuals may be included within the "high end" (e. g., above 90th or 95th percentile) and information on the range of exposures received by these individuals should be presented.

High end descriptors are intended to estimate the exposures that are expected to occur in small, but definable, "high end" segments of the subject population.³ The individuals with these exposures may be members of a special population segment or individual in the general population who are highly exposed because of the inherent stochastic nature of the factors which give rise to exposure. Where differences in sensitivity can be identified within the population, high end estimates addressing sensitive individuals or subgroups can be developed.

In those few cases in which the complete. data on the population distributions of exposures and doses are available, high end exposure or dose estimates can be represented by reporting exposures or doses at a set of selected percentiles of the distributions, such as the 90th, 95th, and 98th percentile. High end exposures or doses, as appropriate, can then be used to calculate high end risk estimates.

In the majority of cases where the complete distributions are not available, several methods help estimate a high end exposure or dose. If sufficient information about the variability in chemical concentrations, activity patterns, or other factors are available, the distribution may be estimated through the use of appropriate modeling (e.g., Monte Carlo simulation or parametric statistical methods). The

³High end estimates focus on estimates of exposure in the exposed populations. Bounding estimates, on the other hand, are constructed to be equal to or greater than the highest actual risk in the population (or the highest risk that could be expected in a future scenario). A "worst case scenario" refers to a combination of events and conditions such that, taken together, produces the highest conceivable risk. Although it is possible that such an exposure, dose, or sensitivity combination might occur in a given population of interest, the probability of an individual receiving this combination of events and conditions is usually small, and often so small that such a combination will not recur in a particular, actual population. "

determination of whether available information is sufficient to support the use of probabilistic estimation methods requires careful review and documentation by the risk assessor. If the input distributions are based on limited data, the resulting distribution should be evaluated carefully to determine whether it is an improvement over more traditional estimation techniques. If a distribution is developed, it should be described with a series of percentiles or population frequency estimates, particularly in the high end range. The assessor and risk manager should be aware, however, that unless a great deal is known about exposures and doses at the high end of the distribution, these estimates will involve considerable uncertainty which the exposure assessor will need to describe. Note that in this context, the probabilistic analysis addresses variability of exposure in the population. Probabilistic techniques may also be applied to evaluate uncertainty in estimates (see section 5, below). However, it is generally inappropriate to combine distributions reflecting both uncertainty and variability to get a single overall distribution. Such a result is not readily interpretable for the concerns of environmental decision-making.

If only limited information on the distribution of the exposure or dose factors is available, the assessor should approach estimating the high end by identifying the most sensitive variables and using high end values for a subset of these variables, leaving others at their central values.⁴ In doing this, the assessor needs to avoid combinations of parameter values that are inconsistent (e.g., low body weight used in combination with high dietary intake rates), and must keep in mind the ultimate objective of being within the distribution of actual expected exposures and doses, and not beyond it.

If very little data are available on the ranges for the various variables, it will be difficult to estimate exposures or doses and associated risks in the high end with much confidence. One method that has been used in such cases is to start with a bounding estimate and “back off” the limits used until the combination of parameter values is, in the judgment of the assessor, within the distribution of expected exposure, and still lies within the upper 10% of persons exposed. Obviously, this method results in a large uncertainty and requires explanation.

b. Central tendency descriptor

Central tendency descriptors generally reflect central estimates of exposure or dose. The descriptor addressing central tendency may be based on either the arithmetic mean exposure (average estimate) or the median exposure (median estimate), either

⁴Maximizing all variables will in virtually all cases result in an estimate that is above the actual values seen in the population. When the principal parameters of the dose equation, e.g., concentration (appropriately integrated over time), intake rate, and duration, are broken out into sub-components, it may be necessary to use maximum values for more than two of these sub-component parameters, depending on a sensitivity analysis.

of which should be clearly labeled. The average estimate, used to approximate the arithmetic mean, can often be derived by using average values for all the exposure factors.⁵ It does not necessarily represent a particular individual on the distribution. Because of the skewness of typical exposure profiles, the arithmetic mean may differ substantially from the median estimate (i.e., 50th percentile estimate, which is equal to the geometric mean for a log normal distribution). The selection of which descriptor(s) to present in the risk characterization will depend on the available data and the goals of the assessment. When data are limited, it may not be possible to construct true median or mean estimates, but it is still possible to construct estimates of central tendency. The discussion of the use of probabilistic techniques in Section I(a) above also applies to estimates of central tendency.

2. Information about population exposure leads to another important way to describe risk.

Population risk refers to an assessment of the extent of harm for the population as a whole. In theory, it can be calculated by summing the individual risks for all individuals within the subject population. This task, of course, requires a great deal more information than is normally, if ever, available.

The kinds of questions addressed by descriptors of population risk include the following:

- How many cases of a particular health effect might be probabilistically estimated in this population for a specific time period?
- For non-carcinogens, what portion of the population is within a specified range of some reference level; e.g., exceedance of the RfD (a dose), the RfC (a concentration), or other health concern level?
- For carcinogens, what portion of the population is above a certain risk level, such as 10^{-6} ?

These questions can lead to two different descriptors of population risk.

a. Probabilistic number of cases

The first descriptor is the probabilistic number of health effect cases estimated in the population of interest over a specified time period. This descriptor can be obtained either by (a) summing the individual risks over all the individuals in the population, e.g. using an estimated distribution of risk in the population, when

⁵This holds true when variables are added (e. g., exposures by different routes) or when independent variables are multiplied (e.g., concentration x intake). However, it would be incorrect for products of correlated variables, variables used as divisors, or for formulas involving exponents.

such information is available, or (b) through the use of a risk model that assumes a linear non-threshold response to exposure, such as many carcinogenic models. In these calculations, data will typically be available to address variability in individual exposures. If risk varies linearly with exposure, multiplying the mean risk by the population size produces an estimate of the number of cases.⁶ At the present time, most cancer potency values represent plausible upper bounds on risk. When such a value is used to estimate numbers of cancer cases, it is important to understand that the result is also an upper bound. As with other risk descriptors, this approach may not adequately address sensitive subgroups for which different dose-response curve or exposure estimates might be needed.

Obviously, the more information one has, the more certain the estimate of this risk descriptor, but inherent uncertainties in risk assessment methodology place limitations on the accuracy of the estimate. The discussion of uncertainty involved in estimating the number of cases should indicate that this descriptor is not to be confused with an actuarial Prediction of cases in the population (which is a statistical prediction based on a great deal of empirical data).

In general, it should be recognized that when small populations are exposed, population risk estimates may be very small. For example, if 100 people are exposed to an individual lifetime cancer risk of 10^{-4} , the expected number of cases is 0.01. In such situations, individual risk estimates will usually be a more meaningful parameter for decision-makers.

b. Estimated percentage of population with risk greater than some level

For non-cancer effects, we generally have not developed the risk assessment techniques to the point of knowing how to add risk probabilities, so a second descriptor is usually more appropriate: An estimate of the percentage of the population, or the number of persons, above a specified level of risk or within a specified range of some reference level, e.g., exceedance of the RfD or the RfC, LOAEL, or other specific level of interest. This descriptor must be obtained through measuring or simulating the population distribution.

3. Information about the distribution of exposure and risk for different subgroups of the population are important components of a risk assessment.

A risk manager might also ask questions about the distribution of the risk burden among various segments of the subject population such as the following: How do exposure and risk impact various subgroups?; and, what is the population risk of a

⁶However, certain important cautions apply (see EPA's Exposure Assessment Guidelines). Also, this is not appropriate for non-carcinogenic effects or for other types of cancer models. For non-linear cancer models, an estimate of population risk must be calculated using the distribution of individual risks.

particular subgroup? Questions about the distribution of exposure and risk among such population segments require additional risk descriptors.

a. Highly exposed

Highly exposed subgroups can be identified, and where possible, characterized and the magnitude of risk quantified. This descriptor is useful when there is (or is expected to be) a subgroup experiencing significantly different exposures or doses from that of the larger population. These sub-populations may be identified by age, sex, lifestyle, economic factors, or other demographic variables. For example, toddlers who play in contaminated soil and high fish consumers represent sub-populations that may have greater exposures to certain agents.

b. Highly susceptible

Highly susceptible subgroups can also be identified, and if possible, characterized and the magnitude of risk quantified. This descriptor is useful when the sensitivity or susceptibility to the effect for specific subgroups is (or is expected to be) significantly different from that of the larger population. In order to calculate risk for these subgroups, it will sometimes be necessary to use a different dose-response relationship; e.g., upon exposure to a chemical, pregnant women, elderly people, children, and people with certain illnesses may each be more sensitive than the population as a whole. For example, children are thought to be both highly exposed and highly susceptible to the effects of environmental lead. A model has been developed that uses data on lead concentrations in different environmental media to predict the resulting blood lead levels in children. Federal agencies are working together to develop "specific guidance on blood lead levels that present risks to children.

It is important to note, however, that the Agency's current methodologies for developing reference doses and reference concentrations (RfDs and RfCs) are designed to protect sensitive populations. If data on sensitive human populations are available (and there is confidence in the quality of the data), then the RfD is set at the dose level at which no adverse effects are observed in the sensitive population (e.g., RfDs for fluoride and nitrate). If no such data are available (for example, if the RfD is developed using data from humans of average or unknown sensitivity) then an additional 10-fold factor is used to account for variability between the average human response and the response of more sensitive individuals.

Generally, selection of the population segments is a matter of either a priori interest in the subgroup (e.g., environmental justice considerations), in which case the risk assessor and risk manager can jointly agree on which subgroups to highlight, or a matter of discovery of a sensitive or highly exposed subgroup during the assessment

process. In either case, once identified, the subgroup can be treated as a population in itself, and characterized in the same way as the larger population using the descriptors for population and individual risk.

4. Situation-specific information adds perspective on possible future events or regulatory options:

“What if...?” questions can be used to examine candidate risk management options. For example, consider the following:

- What if a pesticide applicator applies this pesticide without using protective equipment?
- What if this site becomes residential in the future?
- What risk level will occur if we set the standard at 100 ppb?

Answering these “What if...?” questions involves a calculation of risk based on specific combinations of factors postulated within the assessment⁷. The answers to these “What if...?” questions do not, by themselves, give information about how likely the combination of values might be in the actual population or about how many (if any) persons might be subjected to the potential future risk. However, information on the likelihood of the postulated scenario would also be desirable to include in the assessment.

When addressing projected changes for a population (either expected future developments or consideration of different regulatory options), it is usually appropriate to calculate and consider all the risk descriptors discussed above. When central tendency or high end estimates are developed for a future scenario, these descriptors should reflect reasonable expectations about future activities. For example, in site-specific risk assessments, future scenarios should be evaluated when they are supported by realistic forecasts of future land use, and the risk descriptors should be developed within that context.

5. An evaluation of the uncertainty in the risk descriptor is an important component of the uncertainty discussion in the assessment.

Risk descriptors are intended to address variability of risk within the population and the overall adverse impact on the population. In particular, differences between high end and central tendency estimates reflect variability in the population, but not the scientific uncertainty inherent in the risk estimates. As discussed above, there

⁷ Some programs routinely develop future scenarios as part of developing a risk assessment. Program-specific guidance may address future scenarios in more detail than they are described here.

will be uncertainty in all estimates of risk. These uncertainties can include measurement uncertainties, modeling uncertainties, and assumptions to fill data gaps. Risk assessors should address the impact of each of these factors on the confidence in the estimated risk values.

Both qualitative and quantitative evaluations of uncertainty provide useful information to users of the assessment. The techniques of quantitative uncertainty analysis are evolving rapidly and both the SAB (8) and the NRC (4) have urged the Agency to incorporate these techniques into its risk analyses. However, it should be noted that a probabilistic assessment that uses only the assessor's best estimates for distributions of population variables addresses variability, but not uncertainty. Uncertainties in the estimated risk distribution need to be separately evaluated.

REFERENCES

1. National Research Council. Risk Assessment in the Federal Government: Management the Process, 1983.
2. U.S. EPA. Risk Assessment and Management: Framework for Decision Making, 1984.
3. U.S. EPA. "Risk Assessment Guidelines." 51 Federal Register, 33992-34054, September 24, 1986.
4. National Research Council. Science and Judgement in Risk Assessment. 1994.
5. U.S. EPA "Guidelines for Exposure Assessment." 57 Federal Register, 22888-22938, May 29, 1992.
6. U.S. EPA. "Guidelines for Developmental Toxicity Risk Assessment." 56 Federal Register 67398-63826, December 5, 1991.
7. U.S. EPA. Framework for Ecological Risk Assessment. 1992.
8. Loehr, R. A., and Matanoski, G. M., Letter to Carol M. Browner, EPA Administrator, Re: Quantitative Uncertainty Analysis for Radiological Assessments. EPA Science Advisory Board, July 23, 1993 (EPA-SAB-WC-COM-93-006).