UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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THE ADMINISTRATOR

**MEMORANDUM**

**SUBJECT:** Guidance on Risk Characterization for Risk Managers and Risk Assessors

**FROM:** F. Henry Habicht II
Deputy Administrator

**TO:** Assistant Administrators
Regional Administrators



## INTRODUCTION

This memorandum provides guidance for managers and assessors on describing risk assessment results in EPA reports, presentations, and decision packages. The guidance addresses a problem that affects public perception regarding the reliability of EPA's scientific assessments and related regulatory decisions. EPA has talented scientists, and public confidence in the quality of our scientific output will be enhanced by our visible interaction with peer scientists and thorough presentation of risk assessments and underlying scientific data.

Specifically, although a great deal of careful analysis and scientific judgment goes into the development of EPA risk assessments, significant information is often omitted as the results of the assessment are passed along in the decision-making process. Often, when risk information is presented to the ultimate decision-maker and to the public, the results have been boiled down to a point estimate of risk. Such "short hand" approaches to risk assessment do not fully convey the range of information considered and used in developing the assessment. In short, informative risk characterization clarifies the scientific basis for EPA decisions, while numbers alone do not give a true picture of the assessment.

This problem is not EPA's alone. Agency contractors, industry, environmental groups, and other participants in the overall regulatory process use similar "short hand" approaches.

We must do everything we can to ensure that critical information from each stage of the risk assessment is communicated from risk assessors to their managers, from middle

to upper management, from EPA to the public, and from others to EPA. The Risk Assessment Council considered this problem over many months and reached several conclusions: 1) We need to present a full and complete picture of risk, including a statement of confidence about data and methods used to develop the assessment; 2) we need to provide a basis for greater consistency and comparability in risk assessments across Agency programs; and 3) professional scientific judgment plays an important role in the overall statement of risk. The Council also concluded that Agency-wide guidance would be useful.

## BACKGROUND

Principles emphasized during Risk Assessment Council discussions are summarized below and detailed in the attached Appendix.

### Full Characterization of Risk

EPA decisions are based in part on risk assessment, a technical analysis of scientific information on existing and projected risks to human health and the environment. As practiced at EPA, the risk assessment process depends on many different kinds of scientific data (e.g., exposure, toxicity, epidemiology), all of which are used to "characterize" the expected risk to human health or the environment. Informed use of reliable scientific data from many different sources is a central feature of the risk assessment process.

Highly reliable data are available for many aspects of an assessment. However, scientific uncertainty is a fact of life for the risk assessment process as a whole. As a result, agency managers make decisions using scientific assessments that are less certain than the ideal. The issues, then, become when is scientific confidence sufficient to use the assessment for decision-making, and how should the assessment be used? In order to make these decisions, managers need to understand the strengths and the limitations of the assessment.

On this point, the guidance emphasizes that informed EPA risk assessors and managers need to be completely candid about confidence and uncertainties in describing risks and in explaining regulatory decisions. Specifically, the Agency's risk assessment guidelines call for full and open discussion of uncertainties in the body of each EPA risk assessment, including prominent display of critical uncertainties in the risk characterization. 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.

Scientists call for fully characterizing risk not to question the validity of the assessment, but to fully inform others about critical information in the assessment. The emphasis on "full" and "complete" characterization does not refer to an ideal assessment in which risk is completely defined by fully satisfactory scientific data. Rather, the concept of complete risk characterization means that information that is needed for informed evaluation and use of the assessment is carefully highlighted. Thus, even though risk characterization details limitations in an assessment, a balanced discussion of reliable conclusions and related uncertainties enhances, rather than detracts, from the overall credibility of each assessment.

This guidance is not new. Rather, it re-states, clarifies, and expands upon current risk assessment concepts and practices, and emphasizes aspects of the process that are often incompletely developed. It articulates principles that have long guided experienced risk assessors and well-informed risk managers, who recognize that risk is best described not as a classification or single number, but as a composite of information from many different sources, each with varying degrees of scientific certainty.

**Comparability and Consistency**

The Council's second finding, on the need for greater comparability, arose for several reasons. One was confusion -- for example, many people did not understand that a risk estimate of $10^{-6}$ for an "average" individual should not be compared to another $10^{-6}$ 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. Another catalyst for change was the SAB's report, Reducing Risk: Setting Priorities and Strategies for Environmental Protection. In order to implement the SAB's recommendation that we target our efforts to achieve the greatest risk reduction, we need common measures of risk.

EPA's newly revised 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 us to present a more complete picture of risk that corresponds to the range of different exposure conditions encountered by various populations exposed to most environmental chemicals.

**Professional Judgment**

The call for more extensive characterization of risk has obvious limits. For example, the risk characterization includes

only the most significant data and uncertainties from the assessment (those that define and explain the main risk conclusions) so that decision-makers and the public are not overwhelmed by valid but secondary information.

The degree to which confidence and uncertainty are addressed depends largely on the scope of the assessment and available resources. When special circumstances (e.g., lack of data, extremely complex situations, resource limitations, statutory deadlines) preclude a full assessment, such circumstances should be explained. For example, an emergency telephone inquiry does not require a full written risk assessment, but the caller must be told that EPA comments are based on a "back-of-the-envelope" calculation and, like other preliminary or simple calculations, cannot be regarded as a risk assessment.

## GUIDANCE PRINCIPLES

Guidance principles for developing, describing, and using EPA risk assessments are set forth in the Appendix. Some of these principles focus on differences between risk assessment and risk management, with emphasis on differences in the information content of each process. Other principles 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. Comments on each principle appear in the Appendix; more detailed guidance is available in EPA's risk assessment guidelines (e.g., 51 Federal Register 33992-34054, 24 September 1986).

Like EPA's risk assessment guidelines, this guidance applies to the development, evaluation, and description of Agency risk assessments for use in regulatory decision-making. This memorandum does not give guidance on the use of completed risk assessments for risk management decisions, nor does it address the use of non-scientific considerations (e.g., economic or societal factors) that are considered along with the risk assessment in risk management and decision-making. While some aspects of this guidance focus on cancer risk assessment, 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. Guidance specifically for ecological risk assessment is under development.

## IMPLEMENTATION

Effective immediately, it will be Agency policy for each EPA office to provide several kinds of risk assessment information in connection with new Agency reports, presentations, and decision

packages. In general, such information should be presented as carefully selected highlights from the overall assessment. In this regard, common sense regarding information needed to fully inform Agency decision-makers is the best guide for determining the information to be highlighted in decision packages and briefings.

1. Regarding the interface between risk assessment and risk management, risk assessment information must be clearly presented, separate from any non-scientific risk management considerations. Discussion of risk management options should follow, based on consideration of all relevant factors, scientific and non-scientific.

2. Regarding risk characterization, key scientific information on data and methods (e.g., use of animal or human data for extrapolating from high to low doses, use of pharmacokinetics data) must be highlighted. We also expect a statement of confidence in the assessment that identifies all major uncertainties along with comment on their influence on the assessment, consistent with guidance in the attached Appendix.

3. Regarding exposure and risk characterization, it is Agency policy to present information on the range of exposures derived from exposure scenarios and on the use of multiple risk-descriptors (i.e., central tendency, high end of individual risk, population risk, important subgroups, if known) consistent with terminology in the attached Appendix and Agency guidelines.

This guidance applies to all Agency offices. It applies to assessments generated by EPA staff and to those generated by contractors for EPA's use. I believe adherence to this Agency-wide guidance will improve understanding of Agency risk assessments, lead to more informed decisions, and heighten the credibility of both assessments and decisions.

From this time forward, presentations, reports, and decision packages from all Agency offices should characterize risk and related uncertainties as described here. Please be prepared to identify and discuss with me any program-specific modifications that may be appropriate. However, we do not expect risk assessment documents that are close to completion to be rewritten. Although this is internal guidance that applies directly to assessments developed under EPA auspices, I also encourage Agency staff to use these principles as guidance in evaluating assessments submitted to EPA from other sources, and in discussing these submissions with me and with the Administrator.

This guidance is intended for both management and technical staff. Please distribute this document to those who develop or review assessments and to your managers who use them to implement Agency programs. Also, I encourage you to discuss the principles outlined here with your staff, particularly in briefings on particular assessments.

In addition, I expect that the Risk Assessment Council will endorse new guidance on Agency-wide approaches to risk characterization now being developed in the Risk Assessment Forum for EPA's risk assessment guidelines, and that the Agency and the Council will augment that guidance as needed.

The Administrator and I believe that this effort is very important. It furthers our goals of rigor and candor in the preparation, presentation, and use of EPA risk assessments. The tasks outlined above may require extra effort from you, your managers, and your technical staff, but they are critical to full implementation of these principles. We are most grateful for the hard work of your representatives on the RAC and other staff in pulling this document together. I appreciate your cooperation in this important area of science policy, and look forward to our discussions.

Attachment

cc: The Administrator
Risk Assessment Council

# GUIDANCE FOR RISK ASSESSMENT

Section 1. Risk Assessment-Risk Management Interface

Section 2. Risk Characterization

Section 3. Exposure and Risk Descriptors

U.S. Environmental Protection Agency
Risk Assessment Council
November, 1991

## SECTION 1. 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 (hereafter "NRC report") 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).

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.

- Risk Assessment

  One group generates the risk assessment 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 Pesticides and Toxic Substances and other program offices, the Carcinogen Risk Assessment Verification Endeavor (CRAVE), and the RfD/RfC Workgroups.

Others use analyses produced by the first group to generate site- or media-specific exposure assessments and risk characterizations for use in regulation development. These assessors rely on existing databases (e.g., IRIS, ORD Health Assessment Documents, CRAVE and RfD/RfC Workgroup documents) to develop regulations and evaluate alternatives.

Generally, this group includes scientists and analysts in program offices, regional offices, and the Office of Research and Development.

- Risk Management

  A third group integrates the risk characterization with other non-scientific considerations specified in applicable statutes to make and justify regulatory decisions.

  Generally, this group includes Agency managers and decision-makers.

Each group has different responsibilities for observing the distinction between risk assessment and risk management. At the same time, the risk assessment process involves regular interaction between each of the groups, with overlapping responsibilities at various stages in the overall process.

The guidance to follow outlines principles specific 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.

Shared responsibilities of assessors and managers 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.

For the generators of the assessment, distinguishing between risk assessment and risk management means that scientific information is selected, evaluated, and presented without considering non-scientific factors including how the scientific analysis might influence the regulatory decision. Assessors are charged with (1) generating a credible, objective, realistic, and balanced analysis; (2) presenting information on hazard, dose-response, exposure and risk; and (3) explaining confidence in each assessment by clearly delineating 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 decisions, the distinction between risk assessment and risk management means refraining from influencing the risk description through consideration of non-scientific 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 establish 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 regulatory decision-making, but it is only one of several important components in such decisions. Each of the environmental laws administered by EPA calls for consideration of non-scientific 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. That is, the analysis of the overall regulatory problem may not be the same as the picture presented by the risk analysis alone. For example, a pesticide risk assessment may describe moderate risk to some populations but, if the agricultural benefits of its use are important for the nation's food supply, the product may be allowed to remain on the market with certain restrictions on use to reduce possible exposure. 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, 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.

Decision-makers are not "captives of the numbers." On the contrary, the quantitative and qualitative risk characterization is only one of many important factors that must be considered in reaching the final decision -- a difficult and distinctly different task from risk assessment per se. 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.

## SECTION 2. RISK CHARACTERIZATION

EPA risk assessment principles and practices draw on many sources. 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) are obvious sources. 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 must address qualitative and quantitative features of the assessment. Second, it must identify any important uncertainties in the assessment as part of a discussion on 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 <u>risk assessment</u> is often given narrower and broader meanings than we have adopted here. For some observers, the term is synonymous with <u>quantitative</u>

> 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. (Emphasis in original) (1)

More recently, an Ad Hoc Study Group (with represenatives from EPA, HHS, and the private sector) on Risk Presentation reinforced and expanded upon these principles by specifying several "attributes" for risk characterization.

> 1. The major components of risk (hazard identification, dose-response, and exposure assessment) are presented in summary statements, along with quantitative estimates of risk, to give a combined and integrated view of the evidence.
>
> 2. The report clearly identifies key assumptions, their rationale, and the extent of scientific consensus; the uncertainties thus accepted; and the effect of reasonable alternative assumptions on conclusions and estimates.
>
> 3. The report outlines specific ongoing or potential research projects that would probably clarify significantly the extent of uncertainty in the risk estimation. . . . (4)

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 statement is important for several reasons.

- Information from different sources carries different kinds of uncertainty and knowledge of these differences is important when uncertainties are combined for characterizing risk.
- Decisions must be made on expending resources to acquire additional information to reduce the uncertainties.

- A clear and explicit statement of the implications and limitations of a risk assessment requires a clear and explicit statement of related uncertainties.

- Uncertainty analysis gives the decision-maker a better understanding of the implications and limitations of the assessments.

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, 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 that the uncertainties are within reason. This section discusses information content and uncertainty aspects of risk characterization, while Section 3 discusses various descriptors used in risk characterization.

1. The risk assessment process calls for characterizing risk as 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 do we know about the capacity of an environmental agent for causing cancer (or other adverse effects) in laboratory animals and in humans?

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 do we know 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 potentially at risk.

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. This relationship means that careful attention to the choice of a high-to-low dose extrapolation procedure is very important. As a result, an assessor who is characterizing a dose-response relationship considers several key issues:

1. 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. basis for selecting interspecies dose scaling factors to account for scaling doses from experimental animals to humans; and

4. correspondence between the expected route(s) of exposure and the exposure route(s) utilized in the hazard studies, as well as the interrelationships of potential effects from different exposure routes.

EPA's Integrated Risk Information System (IRIS) is a primary source of this information. 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 in IRIS and on other sources, risk assessors should carefully review the information presented, emphasizing confidence in the database and uncertainties (see subsection d below). The IRIS statement of confidence should be included as part of the risk characterization for hazard and dose-response information.

c. Exposure Assessment -- What do we know about the paths, patterns, and magnitudes of human exposure and numbers of persons likely to be exposed?

The exposure assessment examines a wide range of exposure parameters pertaining to the "real world" environmental scenarios of people who may be exposed to the agent under study. The data considered for the exposure assessment range from monitoring studies of chemical concentrations in environmental media, food, and other materials to information on 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 based on data, information on the quality, purpose, and representativeness of the database is needed. If based on assumptions, the source and general logic used to develop the assumption (e.g., monitoring, modeling, analogy, professional judgment) should be described.

2. 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.

3. The link of the exposure information to the risk descriptors discussed in Section 3 of this Appendix. This issue includes the conservatism or non-conservatism of the scenarios, as indicated by the choice of descriptors.

In summary, confidence in the information used to characterize risk is variable, with the result that risk characterization requires a statement regarding the assessor's confidence in each aspect of the assessment.

d. Risk Characterization -- What do other assessors, decision-makers, and the public need to know about the primary conclusions and assumptions, and about the balance between confidence and uncertainty in the assessment?

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 the final risk summary, is highlighted. As summarized below, the characterization integrates all of the preceding information to communicate the overall meaning of, and confidence in, the hazard, exposure, and risk conclusions.

Generally, risk assessments carry two categories of uncertainty, and each merits consideration. Measurement uncertainty refers to the usual variance that accompanies scientific measurements (such as the range around an exposure estimate) and reflects the accumulated variances around the individual measured values used to develop the estimate. A

different kind of uncertainty stems from data gaps -- that is, information needed to complete the data base for 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 degree to which confidence and uncertainty in each of these areas is 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 determine the cause and effect relationships between exposure to pollutants and adverse health effects. Rather, the uncertainty analysis 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. Some sources of confidence and of uncertainty are described below.

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 weight-of-evidence, unit risk, the risk-specific dose or the q1* 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.

Qualitative information on methodology, alternative interpretations, and working assumptions 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 on 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 are highlighted along with other important risk assessment conclusions to inform others fully on the results of the assessment.

2. Well-balanced risk characterization presents information for other risk assessors, EPA decision-makers, and the public regarding the strengths and limitations of the assessment.

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 significantly influences the analysis is retained -- that is, 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 require special attention.

As discussed earlier, two major sources of uncertainty are variability in the factors upon which estimates are based and the existence of fundamental data gaps. This distinction is relevant for some aspects of the risk characterization. For example, the central tendency and high end individual exposure estimates are intended to capture the <u>variability</u> in exposure, lifestyles, and other factors that lead to a distribution of risk across a population. Key considerations underlying these risk estimates should be fully described. In contrast, scientific <u>assumptions</u> are used to bridge knowledge gaps such as the use of scaling or

extrapolation factors and the use of a particular upper confidence limit around a dose-response estimate. Such assumptions need to be discussed separately, along with the implications of using alternative assumptions.

For users of the assessment and others who rely on the assessment, numerical estimates should never be separated from the descriptive information that is integral to risk characterization. All documents and presentations should include both; in short reports, this information is abbreviated but never omitted.

For decision-makers, a complete characterization (key descriptive elements along with numerical estimates) should be retained in all discussions and papers relating to an assessment used in decision-making. Fully visible information assures that important features of the assessment are immediately available at each level of decision-making for evaluating whether risks are acceptable or unreasonable. In short, differences in assumptions and uncertainties, coupled with non-scientific considerations called for in various environmental statutes, can clearly lead to different risk management decisions in cases with ostensibly identical quantitative risks; i.e., the "number" alone does not determine the decision.

Consideration of alternative approaches involves examining selected plausible options for addressing a given uncertainty. The key words are "selected" and "plausible;" listing all options, regardless of their merits would be superfluous.

Generators of the assessment should outline the strengths and weaknesses of each alternative approach and as appropriate, estimates of central tendency and variability (e.g., mean, percentiles, range, variance.)

Describing the option chosen involves several statements.

1. A rationale for the choice.
2. Effects of option selected on the assessment.
3. Comparison with other plausible options.
4. Potential impacts of new research (on-going, potential near-term and/or long-term studies).

For users of the assessment, giving attention to uncertainties in all decisions and discussions involving the assessment, and preserving the statement of confidence in all presentations is important. For decision-makers, understanding the effect of the uncertainties on the overall assessment and explaining the influence of the uncertainties on the regulatory decision.

## SECTION 3. EXPOSURE ASSESSMENT AND 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 Risk Assessment Council (RAC) has been discussing the use of risk descriptors from time to time over the past two years.

The recent RAC efforts have laid the foundation for the discussion to follow. First, as a result of a discussion paper on the comparability of risk assessments across the Agency programs, the RAC discussed how the program presentations of risk led to ambiguity when risk assessments were compared across programs. Because different assessments presented different descriptors of risk without always making clear what was being described, the RAC discussed the advisability of using separate descriptors for population risk, individual risk, and identification of sensitive or highly exposed population segments. The RAC also discussed the need for consistency across programs and the advisability of requiring risk assessments to provide roughly comparable information to risk managers and the public through the use of a consistent set of risk descriptors.

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.

EPA risk assessments will be expected to address or provide descriptions of (1) individual risk to include the central tendency and high end portions of the risk distribution, (2) important subgroups of the population such as highly exposed or highly susceptible groups or individuals, if known, and (3) population risk. 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 EPA risk assessments. Furthermore, 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 they also communicate their confidence that these results portray a reasonable picture of the actual or projected exposures. This task will usually be accomplished by highlighting 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.

In order for the risk assessor to successfully develop and present the various risk descriptors, the exposure assessment must provide exposure and dose information in a form that can be combined with exposure-response or dose-response relationships to estimate risk. Although there will be differences among individuals within a population as to absorption, intake rates, susceptibility, and other variables such that a high exposure does not necessarily result in a high dose or risk, a moderate or highly positive correlation among exposure, dose, and risk is assumed in the following discussion. Since the generation of all descriptors is not appropriate in all risk assessments and the type of descriptor translates fairly directly into the type of analysis that the exposure assessor must perform, the exposure assessor needs to be aware of the ultimate goals of the assessment. The following sections discuss what type of information is necessary.

1. Information about individual exposure and risk is important to communicating the results of a risk assessment.

Individual risk descriptors are intended to address questions dealing with risks borne by individuals within a population. These questions can take the form of:

- 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?

The "high end" of the risk distribution is, conceptually, above the 90th percentile of the actual (either measured or estimated) distribution. This conceptual range is not meant to precisely define the limits of this descriptor, but should be used by the assessor as a target range for characterizing "high end risk". Bounding estimates and worst case scenarios[1] should not be termed high end risk estimates.

> The high end risk descriptor is a plausible estimate of the individual risk for those persons at the upper end of the risk distribution. The intent of this descriptor is to convey an estimate of risk in the upper range of the distribution, but to avoid estimates which are beyond the

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[1] High end estimates focus on estimates of the exposure or dose in the actual populations. "Bounding estimates," on the other hand, purposely overestimate the exposure or dose in an actual population for the purpose of developing a statement that the risk is "not greater than...." 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 occur in a particular, actual population.

> true distribution. Conceptually, high end risk means risks above about the 90th percentile of the population distribution, but not higher than the individual in the population who has the highest risk.

This descriptor is intended to estimate the risks that are expected to occur in small but definable "high end" segments of the subject population. The individuals with these risks may be members of a special population segment or individuals in the general population who are highly exposed because of the inherent stochastic nature of the factors which give rise to exposure. Where no particular difference in sensitivity can be identified within the population, the high end risk will be related to the high end exposure or dose.

In those few cases where 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 selected percentiles of the distributions, such as the 90th, 95th, or 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 lifestyles and other factors are available to simulate the distribution through the use of appropriate modeling, e.g., Monte Carlo simulation, the estimate from the simulated distribution may be used. As in the method above, the risk manager should be told where in the high end range the

estimate is being made by stating the percentile or the number of persons above this estimate. 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.

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 parameters and using maximum or near-maximum values for one or a few of these variables, leaving others at their mean values[2]. In doing this, the exposure assessor needs to avoid combinations of parameter values that are inconsistent, e.g., low body weight used in combination with high 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 almost no data are available on the ranges for the various parameters, it will be difficult to estimate exposures or doses in the high end with much confidence, and to develop the high end risk estimate. One method that has been used in these cases is to start with a bounding estimate and "back off" the limits used until the combination of parameter values is, in the

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[2] Maximizing 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, intake rate, duration) are broken out into subcomponents, it may be necessary to use maximum values for more than two of these subcomponent parameters, depending on a sensitivity analysis.

judgment of the assessor, clearly 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.

> The risk descriptor addressing central tendency may be either the arithmetic mean risk (Average Estimate) or the median risk (Median Estimate), either of which should be clearly labeled. Where both the arithmetic mean and the median are available but they differ substantially, it is helpful to present both.

The Average Estimate, used to approximate the arithmetic mean, can be derived by using average values for all the exposure factors. It does not necessarily represent a particular individual on the distribution. The Average Estimate is not very meaningful when exposure across a population varies by several orders of magnitude or when the population has been truncated, e.g., at some prescribed distance from a point source.

Because of the skewness of typical exposure profiles, the arithmetic mean is not necessarily a good indicator of the midpoint (median, 50th percentile) of a distribution. A Median Estimate, e.g., geometric mean, is usually a valuable descriptor for this type of distribution, since half the population will be above and half below this value.

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.

Some questions addressed by descriptors of population risk include:

- How many cases of a particular health effect might be probabilistically estimated in this population for a specific time period?
- For noncarcinogens, what portion of the population are within a specified range of some benchmark level, e.g., exceedance of the RfD (a dose), the RfC (a concentration), or other health concern level?
- For carcinogens, how many persons are above a certain risk level such as $10^{-6}$ or a series of risk levels such as $10^{-5}$, $10^{-4}$, etc?

Answering these questions requires some knowledge of the exposure frequency distribution in the population. In particular, addressing the second and third questions may require graphing the risk distribution. These questions can lead to two different descriptors of population risk.

> 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 when such information is available, or (b) through the use of a risk model such as carcinogenic models or procedures which assume a

linear non-threshold response to exposure. If risk varies linearly with exposure, knowing the mean risk and the population size can lead to an estimate of the extent of harm for the population as a whole, excluding sensitive subgroups for which a different dose-response curve needs to be used.

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. With the current state of the science, explicit steps should be taken to assure that this descriptor is not confused with an actuarial prediction of cases in the population (which is a statistical prediction based on a great deal of empirical data).

Although estimating population risk by calculating a mean individual risk and multiplying by the population size is sometimes appropriate for carcinogen assessments using linear, non-threshold models[3], 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 by summing individual risks. 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, below, is more appropriate.

> Another descriptor of population risk is an estimate of the percentage of the population, or the number of persons, above a specified level of

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[3] Certain important cautions apply. These cautions are more explicitly spelled out in the Agency's Guidelines for Exposure Assessment, tentatively scheduled to be published in late 1991.

risk or within a specified range of some benchmark 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?
- What is the population risk of a particular subgroup?

Questions about the distribution of exposure and risk among such population segments require additional risk descriptors.

> 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 subpopulations may be identified by age, sex, life-style, economic factors, or other demographic variables. For example, toddlers who play in contaminated soil and certain high fish consumers represent subpopulations that may have greater exposures to certain agents.

> 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.

For example, 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.

Generally, selection of the population segments is a matter of either *a priori* interest in the subgroup, 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 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.

These postulated questions are normally designed to answer "what if" questions, which are either directed at low probability but possibly high consequence events or are intended to examine candidate risk management options. Such questions might take the following form:

- 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?

The assumptions made in answering these postulated questions should not be confused with the assumptions made in developing a baseline estimate of exposure or with the adjustments in parameter values made in performing a sensitivity analysis. The answers to these postulated questions do not 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 calculated exposure or risk in the real world.

> A calculation of risk based on specific hypothetical or actual combinations of factors postulated within the exposure assessment can also be useful as a risk descriptor. It is often valuable to ask and answer specific questions of the "what if" nature to add perspective to the risk assessment.

The only information the answers to these questions convey is that if conditions A, B, and C are assumed, then the resulting exposure or risk will be X, Y, or Z, respectively. The values

for X, Y, and Z are usually fairly straightforward to calculate and can be expressed as point estimates or ranges.

Each assessment may have none, one, or several of these types of descriptors. The answers do not directly give information about how likely that combination of values might be in the actual population, so there are some limits to the applicability of these descriptors.

## References


1. National Research Council. Risk Assessment in the Federal Government: Managing 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. Presentation of Risk Assessment of Carcinogens; Ad Hoc Study Group on Risk Assessment Presentation. American Industrial Health Council. 1989.