Science Policy Council

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 judgements, 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 export 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 affects 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 affects 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" individuals, "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 affects 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?