

Free Executive Summary

Science and Decisions: Advancing Risk Assessment

Committee on Improving Risk Analysis Approaches
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Risk assessment has become a dominant public policy tool for making choices, based on limited resources, to protect public health and the environment. It has been instrumental to the mission of the U.S. Environmental Protection Agency (EPA) as well as other federal agencies in evaluating public health concerns, informing regulatory and technological decisions, prioritizing research needs and funding, and in developing approaches for cost-benefit analysis. However, risk assessment is at a crossroads. Despite advances in the field, risk assessment faces a number of significant challenges including lengthy delays in making complex decisions; lack of data leading to significant uncertainty in risk assessments; and many chemicals in the marketplace that have not been evaluated and emerging agents requiring assessment. Science and Decisions makes practical scientific and technical recommendations to address these challenges. This book is a complement to the widely used 1983 National Academies book, Risk Assessment in the Federal Government (also known as the Red Book). The earlier book established a framework for the concepts and conduct of risk assessment that has been adopted by numerous expert committees, regulatory agencies, and public health institutions. The new book embeds these concepts within a broader framework for risk-based decision-making. Together, these are essential references for those working in the regulatory and public health fields.

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Summary

Virtually every aspect of life involves risk. How we deal with risk depends largely on how well we understand it. The process of risk assessment has been used to help us understand and address a wide variety of hazards and has been instrumental to the U.S. Environmental Protection Agency (EPA), other federal and state agencies, industry, the academic community, and others in evaluating public-health and environmental concerns. From protecting air and water to ensuring the safety of food, drugs, and consumer products such as toys, risk assessment is an important public-policy tool for informing regulatory and technologic decisions, setting priorities among research needs, and developing approaches for considering the costs and benefits of regulatory policies.

Risk assessment, however, is at a crossroads, and its credibility is being challenged (Silbergeld 1993; Montague 2004; Michaels 2008).¹ Because it provides a primary scientific rationale for informing regulations that will have national and global impact, risk assessment is subject to considerable scientific, political, and public scrutiny. The science of risk assessment is increasingly complex; improved analytic techniques have produced more data that lead to questions about how to address issues of, for example, multiple chemical exposures, multiple risks, and susceptibility in populations. In addition, risk assessment is now being extended to address broader environmental questions, such as life-cycle analysis and issues of costs, benefits, and risk-risk tradeoffs.

The regulatory risk assessment process is bogged down; major risk assessments for some chemicals take more than 10 years. In the case of trichloroethylene, which has been linked to cancer, the assessment has been under development since the 1980s, has undergone multiple independent reviews, and is not expected to be final until 2010. Assessments of formaldehyde and dioxin have had similar timelines. EPA is struggling to keep up with demands for hazard and dose-response information but is challenged by a lack of resources, including funding and trained staff.

Decision-making based on risk assessment is also bogged down. Uncertainty, an inherent property of scientific data, continues to lead to multiple interpretations and contribute to decision-making gridlock. Stakeholders—including community groups, environmental organizations, industry, and consumers—are often disengaged from the risk-assessment process at a time when risk assessment is increasingly intertwined with societal concerns. Disconnects between the available scientific data and the information needs of decision-makers hinder the use of risk assessment as a decision-making tool.

Emerging scientific advances hold great promise for improving risk assessment. For example, new toxicity-testing methods are being developed that will probably be quicker, less expensive, and more directly relevant to human exposures, as described in the National Research Council's *Toxicity Testing in*

¹Silbergeld, E.K. 1993. Risk assessment: The perspective and experience of U.S. environmentalists. *Environ. Health Perspect.* 101(2):100-104; Montague, P. 2004. Reducing the harms associated with risk assessment. *Environ. Impact Assess. Rev.* 24:733-748; Michaels, D. 2008. *Doubt Is Their Product: How Industry's Assault on Science Threatens Your Health*. New York: Oxford University Press.

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the 21st Century: A Vision and a Strategy (2007). However, the realization of the promise is at least a decade away.

To address current challenges, EPA asked the National Research Council to perform an independent study on improving risk-analysis approaches, one of a number of studies by the National Research Council that have examined risk assessment in EPA. Specifically, the committee selected by the National Research Council was charged to identify practical improvements that EPA could make in the near term (2-5 years) and in the longer term (10-20 years). The committee focused primarily on human health risk assessment but also considered the implications of its conclusions and recommendations for ecologic risk assessment. The committee conducted its data gathering for this study between fall 2006 and winter 2008, so materials published after this were not considered in the committee's evaluation.

COMMITTEE'S EVALUATION

The committee focused on two broad elements in its evaluation: (1) improving the *technical analysis* that supports risk assessment (addressed in Chapters 4-7) and (2) improving the *utility of risk assessment* (addressed in Chapters 3 and 8). Improving technical analysis entails the development and use of scientific knowledge and information to promote more accurate characterizations of risk. Improving utility entails making risk assessment more relevant to and useful for risk-management decisions.

Regarding improvement in technical analysis, the committee considered such issues as how to improve uncertainty and variability analysis and dose-response assessment to ensure the best use of scientific data, and it concluded that technical improvements are necessary. The committee concluded that EPA's overall concept of risk assessment, which is generally based on the National Research Council's *Risk Assessment in the Federal Government: Managing the Process* (NRC 1983,² also known as the Red Book), should be retained. The four steps of risk assessment (hazard identification, dose-response assessment, exposure assessment, and risk characterization) have been adopted by numerous expert committees, regulatory agencies, public-health institutions, and others.

With respect to improving utility, the committee considered such issues as how risk-related problems are identified and formulated before the development of risk assessments and how a broad set of options might be considered to ensure that risk assessments are most relevant to the problems.

CONCLUSIONS AND RECOMMENDATIONS

A number of improvements are needed to streamline EPA's risk-assessment process to ensure that risk assessments make better use of appropriate available science and are more relevant to decision-making. Implementing improvements will require building on EPA's current practices and developing a long-term strategy that includes greater coordination and communication within the agency, training and building a workforce with the requisite expertise, and a commitment by EPA, the executive branch, and Congress to implement the framework for risk-based decision-making recommended in this report and to fund the needed improvements.

The committee recommends an important extension of the Red Book model to meet today's challenges better—that risk assessment should be viewed as a method for evaluating the relative merits of various options for managing risk rather than as an end in itself. Risk assessment should continue to capture and accurately describe what various research findings do and do not tell us about threats to human health and to the environment, but only *after* the risk-management questions that risk assessment should address have been clearly posed, through careful evaluation of the options available to manage the environmental problems at hand, similar to what is done in ecologic risk assessment. That alteration in the current approach to risk assessment has the potential to increase its influence on decisions because it

²NRC (National Research Council). 1983. *Risk Assessment in the Federal Government: Managing the Process*. Washington DC: National Academy Press.

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requires greater up-front planning to ensure that it is relevant to the specific problems being addressed and that it will cast light on a wider range of decision options than has traditionally been the case.

A second recommended shift in thinking is seen in the technical recommendations in this report that call for improvements in uncertainty and variability analysis and for a unified approach to dose-response assessment that will result in risk estimates for both cancer and noncancer end points. Just as a risk assessment itself should be more closely tied to the questions to be answered, so should the technical analyses supporting it. For example, descriptions of the uncertainty and variability inherent in all risk assessments may be complex or relatively simple; the level of detail in the descriptions should align with what is needed to inform risk-management decisions. Similarly, the results of a dose-response assessment should be relevant to the problem being addressed, whether it is informing risk-risk tradeoffs or a cost-benefit analysis. Ensuring that the technical analyses supporting a risk assessment are both supported by the science and relevant to the problem being addressed will go a long way to improving the value, timeliness, and credibility of the assessment.

The committee's most important conclusions and recommendations are summarized below. The committee believes that implementation of its recommendations will do much to enhance the credibility and usefulness of risk assessment.

Design of Risk Assessment

The process of planning risk assessment and ensuring that its level and complexity are consistent with the needs to inform decision-making can be thought of as the "design" of risk assessment. The committee encourages EPA to focus greater attention on design in the formative stages of risk assessment, specifically on planning and scoping and problem formulation, as articulated in EPA guidance for ecologic and cumulative risk assessment (EPA 1998, 2003).³ Good design involves bringing risk managers, risk assessors, and various stakeholders together early in the process to determine the major factors to be considered, the decision-making context, and the timeline and depth needed to ensure that the right questions are being asked in the context of the assessment.

Increased emphasis on planning and scoping and on problem formulation has been shown to lead to risk assessments that are more useful and better accepted by decision-makers (EPA 2002, 2003, 2004⁴); however, incorporation of these stages in risk assessment has been inconsistent, as noted by their absence from various EPA guidance documents (EPA 2005a,b⁵). An important element of planning and scoping is definition of a clear set of options for consideration in decision-making where appropriate. This should be reinforced by the up-front involvement of decision-makers, stakeholders, and risk assessors, who together can evaluate whether the design of the assessment will address the identified problems.

³EPA (U.S. Environmental Protection Agency). 1998. Guidelines for Ecological Risk Assessment. EPA/630/R-95/002F. Risk Assessment Forum, U.S. Environmental Protection Agency, Washington, DC; EPA (U.S. Environmental Protection Agency). 2003. Framework for Cumulative Risk Assessment. EPA/600/P-02/001F. National Center for Environmental Assessment, Risk Assessment Forum, U.S. Environmental Protection Agency, Washington, DC.

⁴EPA (U.S. Environmental Protection Agency). 2002. A Review of the Reference Dose and Reference Concentration Processes. EPA/630/P-02/002F. Risk Assessment Forum, U.S. Environmental Protection Agency, Washington, DC; EPA (U.S. Environmental Protection Agency). 2003. Framework for Cumulative Risk Assessment. EPA/600/P-02/001F. National Center for Environmental Assessment, Risk Assessment Forum, U.S. Environmental Protection Agency, Washington, DC; EPA (U.S. Environmental Protection Agency). 2004. Risk Assessment Principles and Practices. Staff Paper. EPA/100/B-04/001. Office of the Science Advisor, U.S. Environmental Protection Agency, Washington, DC.

⁵EPA (U.S. Environmental Protection Agency). 2005a. Guidelines for Carcinogen Risk Assessment. EPA/630/P-03/001F. Risk Assessment Forum, U.S. Environmental Protection Agency, Washington, DC; EPA (U.S. Environmental Protection Agency). 2005b. Supplemental Guidance for Assessing Susceptibility for Early-Life Exposures to Carcinogens. EPA/630/R-03/003F. Risk Assessment Forum, U.S. Environmental Protection Agency, Washington, DC.

Recommendation: Increased attention to the design of risk assessment in its formative stages is needed. The committee recommends that planning and scoping and problem formulation, as articulated in EPA guidance documents (EPA 1998, 2003), should be formalized and implemented in EPA risk assessments.

Uncertainty and Variability

Addressing uncertainty and variability is critical for the risk-assessment process. Uncertainty stems from lack of knowledge, so it can be characterized and managed but not eliminated. Uncertainty can be reduced by the use of more or better data. Variability is an inherent characteristic of a population, inasmuch as people vary substantially in their exposures and their susceptibility to potentially harmful effects of the exposures. Variability cannot be reduced, but it can be better characterized with improved information.

There have been substantial differences among EPA's approaches to and guidance for addressing uncertainty in exposure and dose-response assessment. EPA does not have a consistent approach to determine the level of sophistication or the extent of uncertainty analysis needed to address a particular problem. The level of detail for characterizing uncertainty is appropriate only to the extent that it is needed to inform specific risk-management decisions appropriately. It is important to address the required extent and nature of uncertainty analysis in the planning and scoping phases of a risk assessment. Inconsistency in the treatment of uncertainty among components of a risk assessment can make the communication of overall uncertainty difficult and sometimes misleading.

Variability in human susceptibility has not received sufficient or consistent attention in many EPA health risk assessments although there are encouraging exceptions, such as those for lead, ozone, and sulfur oxides. For example, although EPA's 2005 *Guidelines for Carcinogen Risk Assessment* acknowledges that susceptibility can depend on one's stage in life, greater attention to susceptibility in practice is needed, particularly for specific population groups that may have greater susceptibility because of their age, ethnicity, or socioeconomic status. The committee encourages EPA to move toward the long-term goal of quantifying population variability more explicitly in exposure assessment and dose-response relationships. An example of progress that moves towards this goal is EPA's draft risk assessment of trichloroethylene (EPA 2001; NRC 2006), which considers how differences in metabolism, disease, and other factors contribute to human variability in response to exposures.

Recommendation: EPA should encourage risk assessments to characterize and communicate uncertainty and variability in all key computational steps of risk assessment—for example, exposure assessment and dose-response assessment. Uncertainty and variability analysis should be planned and managed to reflect the needs for comparative evaluation of the risk management options. In the short term, EPA should adopt a “tiered” approach for selecting the level of detail to be used in the uncertainty and variability assessments, and this should be made explicit in the planning stage. To facilitate the characterization and interpretation of uncertainty and variability in risk assessments, EPA should develop guidance to determine the appropriate level of detail needed in uncertainty and variability analyses to support decision-making and should provide clear definitions and methods for identifying and addressing different sources of uncertainty and variability.

Selection and Use of Defaults

Uncertainty is inherent in all stages of risk assessment, and EPA typically relies on assumptions when chemical-specific data are not available. The 1983 Red Book recommended the development of guidelines to justify and select from among the available inference options, the assumptions—now called

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defaults—to be used in agency risk assessments to ensure consistency and avoid manipulations in the risk-assessment process. The committee acknowledges EPA’s efforts to examine scientific data related to defaults (EPA 1992, 2004, 2005a),⁶ but recognizes that changes are needed to improve the agency’s use of them. Much of the scientific controversy and delay in completion of some risk assessments has stemmed from the long debates regarding the adequacy of the data to support a default or an alternative approach. The committee concludes that established defaults need to be maintained for the steps in risk assessment that require inferences and that clear criteria should be available for judging whether, in specific cases, data are adequate for direct use or to support an inference in place of a default. EPA, for the most part, has not yet published clear, general guidance on what level of evidence is needed to justify use of agent-specific data and not resort to a default. There are also a number of defaults (missing or implicit defaults) that are engrained in EPA risk-assessment practice but are absent from its risk-assessment guidelines. For example, chemicals that have not been examined sufficiently in epidemiologic or toxicologic studies are often insufficiently considered in or are even excluded from risk assessments; because no description of their risks is included in the risk characterization, they carry no weight in decision-making. That occurs in Superfund-site and other risk assessments, in which a relatively short list of chemicals on which there are epidemiologic and toxicologic data tends to drive the exposure and risk assessments.

Recommendation: EPA should continue and expand use of the best, most current science to support and revise default assumptions. EPA should work toward the development of explicitly stated defaults to take the place of implicit defaults. EPA should develop clear, general standards for the level of evidence needed to justify the use of alternative assumptions in place of defaults. In addition, EPA should describe specific criteria that need to be addressed for the use of alternatives to each particular default assumption. When EPA elects to depart from a default assumption, it should quantify the implications of using an alternative assumption, including how use of the default and the selected alternative influences the risk estimate for risk management options under consideration. EPA needs to more clearly elucidate a policy on defaults and provide guidance on its implementation and on evaluation of its impact on risk decisions and on efforts to protect the environment and public health.

A Unified Approach to Dose-Response Assessment

A challenge to risk assessment is to evaluate risks in ways that are consistent among chemicals, that account adequately for variability and uncertainty, and that provide information that is timely, efficient, and maximally useful for risk characterization and risk management. Historically, dose-response assessments at EPA have been conducted differently for cancer and noncancer effects, and the methods have been criticized for not providing the most useful results. Consequently, noncancer effects have been underemphasized, especially in benefit-cost analyses. A consistent approach to risk assessment for cancer and noncancer effects is scientifically feasible and needs to be implemented.

For cancer, it has generally been assumed that there is no dose threshold of effect, and dose-response assessments have focused on quantifying risk at low doses and estimating a population risk for a given magnitude of exposure. For noncancer effects, a dose threshold (low-dose nonlinearity) has been assumed, below which effects are not expected to occur or are extremely unlikely in an exposed

⁶EPA (U.S. Environmental Protection Agency). 1992. Guidelines for Exposure Assessment. EPA/600/Z-92/001. Risk Assessment Forum, Office of Research and Development, U.S. Environmental Protection Agency, Washington, DC.; EPA (U.S. Environmental Protection Agency). 2004. Risk Assessment Principles and Practices. Staff Paper. EPA/100/B-04/001. Office of the Science Advisor, U.S. Environmental Protection Agency, Washington, DC; EPA (U.S. Environmental Protection Agency). 2005a. Guidelines for Carcinogen Risk Assessment. EPA/630/P-03/001F. Risk Assessment Forum, U.S. Environmental Protection Agency, Washington, DC.

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population; that dose is a reference dose (RfD) or a reference concentration (RfC)—it is thought “likely to be without an appreciable risk of deleterious effects” (EPA 2002).⁷

EPA’s treatment of noncancer and low-dose nonlinear cancer end points is a major step by the agency in an overall strategy to harmonize cancer and noncancer approaches to dose-response assessment; however, the committee finds scientific and operational limitations in the current approaches. Noncancer effects do not necessarily have a threshold, or low-dose nonlinearity, and the mode of action of carcinogens varies. Background exposures and underlying disease processes contribute to population background risk and can lead to linearity at the population doses of concern. Because the RfD and RfC do not quantify risk for different magnitudes of exposure but rather provide a bright line between possible harm and safety, their use in risk-risk and risk-benefit comparisons and in risk-management decision-making is limited. Cancer risk assessments usually do not account for differences among humans in cancer susceptibility other than possible differences in early-life susceptibility.

Scientific and risk-management considerations both support unification of cancer and noncancer dose-response assessment approaches. The committee therefore recommends a consistent, unified approach for dose-response modeling that includes formal, systematic assessment of background disease processes and exposures, possible vulnerable populations, and modes of action that may affect a chemical’s dose-response relationship in humans. That approach redefines the RfD or RfC as a risk-specific dose that provides information on the percentage of the population that can be expected to be above or below a defined acceptable risk with a specific degree of confidence. The risk-specific dose will allow risk managers to weigh alternative risk options with respect to that percentage of the population. It will also permit a quantitative estimate of benefits for different risk-management options. For example, a risk manager could consider various population risks associated with exposures resulting from different control strategies for a pollution source and the benefits associated with each strategy. The committee acknowledges the widespread applications and public-health utility of the RfD; the redefined RfD can still be used as the RfD has been to aid risk-management decisions.

Characteristics of the committee’s recommended unified dose-response approach include use of a spectrum of data from human, animal, mechanistic, and other relevant studies; a probabilistic characterization of risk; explicit consideration of human heterogeneity (including age, sex, and health status) for both cancer and noncancer end points; characterization (through distributions to the extent possible) of the most important uncertainties for cancer and noncancer end points; evaluation of background exposure and susceptibility; use of probabilistic distributions instead of uncertainty factors when possible; and characterization of sensitive populations.

The new unified approach will require implementation and development as new chemicals are assessed or old chemicals are reassessed, including the development of test cases to demonstrate proof of concept.

Recommendation: The committee recommends that EPA implement a phased-in approach to consider chemicals under a unified dose-response assessment framework that includes a systematic evaluation of background exposures and disease processes, possible vulnerable populations, and modes of action that may affect human dose-response relationships. The RfD and RfC should be redefined to take into account the probability of harm. In developing test cases, the committee recommends a flexible approach in which different conceptual models can be applied in the unified approach.

⁷EPA (U.S. Environmental Protection Agency). 2002. A Review of the Reference Dose and Reference Concentration Processes. EPA/630/P-02/002F. Risk Assessment Forum, U.S. Environmental Protection Agency, Washington, DC. December 2002.

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Cumulative Risk Assessment

EPA is increasingly asked to address broader public-health and environmental-health questions involving multiple exposures, complex mixtures, and vulnerability of exposed populations—issues that stakeholder groups (such as communities affected by environmental exposures) often consider to be inadequately captured by current risk assessments. There is a need for cumulative risk assessments as defined by EPA (EPA 2003)⁸—assessments that include combined risks posed by aggregate exposure to multiple agents or stressors; aggregate exposure includes all routes, pathways, and sources of exposure to a given agent or stressor. Chemical, biologic, radiologic, physical, and psychologic stressors are considered in this definition (Callahan and Sexton 2007).⁹

The committee applauds the agency's move toward the broader definition in making risk assessment more informative and relevant to decisions and stakeholders. However, in practice, EPA risk assessments often fall short of what is possible and is supported by agency guidelines in this regard. Although cumulative risk assessment has been used in various contexts, there has been little consideration of nonchemical stressors, vulnerability, and background risk factors. Because of the complexity of considering so many factors simultaneously, there is a need for simplified risk-assessment tools (such as databases, software packages, and other modeling resources) that would allow screening-level risk assessments and could allow communities and stakeholders to conduct assessments and thus increase stakeholder participation. Cumulative human health risk assessment should draw greater insights from ecologic risk assessment and social epidemiology, which have had to grapple with similar issues. (Cumulative risk assessment will be addressed in a forthcoming National Research Council report on phthalates.)

Recommendation: EPA should draw on other approaches, including those from ecologic risk assessment and social epidemiology, to incorporate interactions between chemical and non-chemical stressors in assessments; increase the role of biomonitoring, epidemiologic, and surveillance data in cumulative risk assessments; and develop guidelines and methods for simpler analytical tools to support cumulative risk assessment and to provide for greater involvement of stakeholders. In the short-term, EPA should develop databases and default approaches to allow for incorporation of key non-chemical stressors in cumulative risk assessments in the absence of population-specific data, considering exposure patterns, contributions to relevant background processes, and interactions with chemical stressors. In the long-term, EPA should invest in research programs related to interactions between chemical and non-chemical stressors, including epidemiologic investigations and physiologically-based pharmacokinetic modeling.

Improving the Utility of Risk Assessment

Given the complexities of the current problems and potential decisions faced by EPA, the committee grappled with designing a more coherent, consistent, and transparent process that would provide risk assessments that are relevant to the problems and decisions at hand and that would be sufficiently comprehensive to ensure that the best available options for managing risks were considered. To that end, the committee proposes a framework for risk-based decision-making (see Figure S-1). The framework consists of three phases: I, enhanced problem formulation and scoping, in which the available

⁸EPA (U.S. Environmental Protection Agency). 2003. Framework for Cumulative Risk Assessment. EPA/600/P-02/001F. National Center for Environmental Assessment, Risk Assessment Forum, U.S. Environmental Protection Agency, Washington, DC.

⁹Callahan, M.A., and K. Sexton. 2007. If 'cumulative risk assessment' is the answer, what is the question? *Environ. Health Perspect.* 115(5):799-806.

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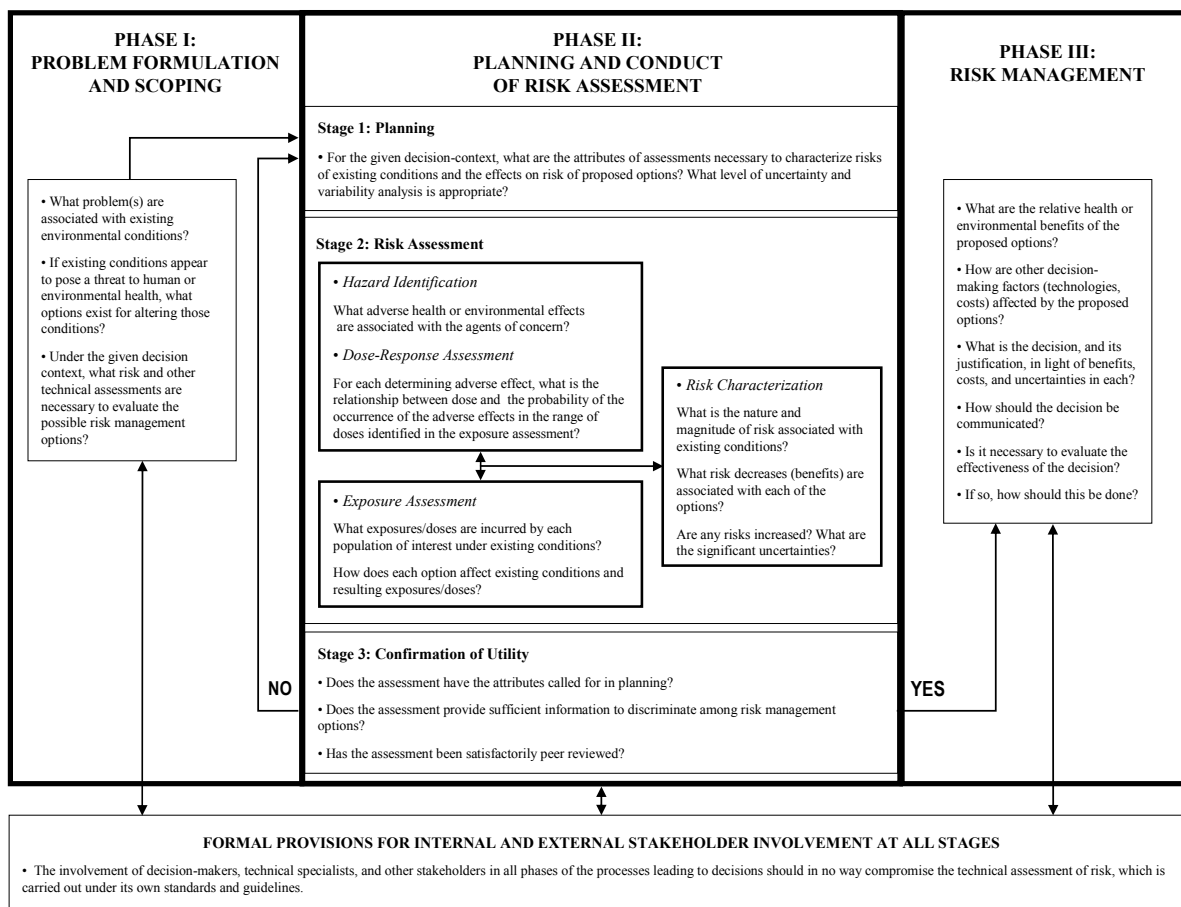


FIGURE S-1 A framework for risk-based decision-making that maximizes the utility of risk assessment.

risk-management options are identified; II, planning and assessment, in which risk-assessment tools are used to determine risks under existing conditions and under potential risk-management options; and III, risk management, in which risk and nonrisk information is integrated to inform choices among options.

The framework has at its core the risk-assessment paradigm (stage 2 of phase II) established in the Red Book (NRC 1983).¹⁰ However, the framework differs from the Red Book paradigm, primarily in its initial and final steps. The framework begins with a “signal” of potential harm (for example, a positive bioassay or epidemiologic study, a suspicious disease cluster, or findings of industrial contamination). Under the traditional paradigm, the question has been, “What are the probability and consequence of an adverse health (or ecologic) effect posed by the signal?” In contrast, the recommended framework asks, implicitly, “What *options* are there to reduce the *hazards* or *exposures* that have been identified, and how can risk assessment be used to evaluate the merits of the various options?” The latter question focuses on the risk-management options (or interventions) designed to provide adequate public-health and environmental protection and to ensure well-supported decision-making. Under this framework, the questions posed arise from early and careful planning of the types of assessments (including risks, costs, and technical feasibility) and the required level of scientific depth that are needed to evaluate the relative

¹⁰NRC (National Research Council). 1983. Risk Assessment in the Federal Government: Managing the Process. Washington DC: National Academy Press.

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merits of the options being considered.¹¹ Risk management involves choosing among the options after the appropriate assessments have been undertaken and evaluated.

The framework begins with enhanced problem formulation and scoping (phase I), in which risk-management options and the types of technical analyses, including risk assessments, needed to evaluate and discriminate among the options are identified. Phase II consists of three stages: planning, risk assessment, and confirmation of utility. Planning (stage 1) is done to ensure that the level and complexity of risk assessment (including uncertainty and variability analysis) are consistent with the goals of decision-making. After risk assessment (stage 2), stage 3 evaluates whether the assessment was appropriate and whether it allows discrimination among the risk-management options. If the assessment is determined not to be adequate, the framework calls for a return to planning (phase II, stage 1). Otherwise, phase III (risk management) is undertaken: the relative health or environmental benefits of the proposed risk-management options are evaluated for the purpose of reaching a decision.

The framework systematically identifies problems and options that risk assessors should evaluate at the earliest stages of decision-making. It expands the array of impacts assessed beyond individual effects (for example, cancer, respiratory problems, and individual species) to include broader questions of health status and ecosystem protection. It provides a formal process for stakeholder involvement throughout all stages but has time constraints to ensure that decisions are made. It increases understanding of the strengths and limitations of risk assessment by decision-makers at all levels, for example, by making uncertainties and choices more transparent.

The committee is mindful of concerns about political interference in the process, and the framework maintains the conceptual distinction between risk assessment and risk management articulated in the Red Book. It is imperative that risk assessments used to evaluate risk-management options not be inappropriately influenced by the preferences of risk managers.

With a focus on early and careful planning and problem formulation and on the options for managing the problem, implementation of the framework can improve the utility of risk assessment for decision-making. Although some aspects of the framework are achievable in the short term, its full implementation will require a substantial transition period. EPA should phase in the framework with a series of demonstration projects that apply it and that determine the degree to which it meets the needs of the agency risk managers, how risk-management conclusions differ as a result of its application, and the effectiveness of measures to ensure that risk managers and policy-makers do not inappropriately influence the scientific conduct of risk assessments.

Recommendations: To make risk assessments most useful for risk management decisions, the committee recommends that EPA adopt a *framework for risk-based decision-making* (see Figure S-1) that embeds the Red Book risk assessment paradigm into a process with initial problem formulation and scoping, upfront identification of risk-management options, and use of risk assessment to discriminate among these options.

Stakeholder Involvement

Many stakeholders believe that the current process for developing and applying risk assessments lacks credibility and transparency. That may be partly because of failure to involve stakeholders adequately as active participants at appropriate points in the risk-assessment and decision-making process rather than as passive recipients of the results. Previous National Research Council and other risk-

¹¹The committee notes that not all decisions require or are amenable to risk assessment and that in most cases one of the options explicitly considered is “no intervention.”

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assessment reports (for example, NRC 1996; PCCRARM 1997)¹² and comments received by the committee (Callahan 2007; Kyle 2007)¹³ echo such concerns.

The committee agrees that greater stakeholder involvement is necessary to ensure that the process is transparent and that risk-based decision-making proceeds effectively, efficiently, and credibly. Stakeholder involvement needs to be an integral part of the risk-based decision-making framework, beginning with problem formulation and scoping.

Although EPA has numerous programs and guidance documents related to stakeholder involvement, it is important that it adhere to its own guidance, particularly in the context of cumulative risk assessment, in which communities often have not been adequately involved.

Recommendation: EPA should establish a formal process for stakeholder involvement in the framework for risk-based decision-making with time limits to ensure that decision-making schedules are met and with incentives to allow for balanced participation of stakeholders, including impacted communities and less advantaged stakeholders.

Capacity-Building

Improving risk-assessment practice and implementing the framework for risk-based decision-making will require a long-term plan and commitment to build the requisite capacity of information, skills, training, and other resources necessary to improve public-health and environmental decision-making. The committee's recommendations call for considerable modification of EPA risk-assessment efforts (for example, implementation of the risk-based decision-making framework, emphasis on problem formulation and scoping as a discrete stage in risk assessment, and greater stakeholder participation) and of technical aspects of risk assessment (for example, unification of cancer and noncancer dose-response assessments, attention to quantitative uncertainty analysis, and development of methods for cumulative risk assessment). The recommendations are tantamount to "change-the-culture" transformations in risk assessment and decision-making in the agency.

EPA's current institutional structure and resources may pose a challenge to implementation of the recommendations, and moving forward with them will require a commitment to leadership, cross-program coordination and communication, and training to ensure the requisite expertise. That will be possible only if leaders are determined to reverse the downward trend in budgeting, staffing, and training and to making high-quality, risk-based decision-making an agencywide goal.

Recommendation: EPA should initiate a senior-level strategic re-examination of its risk-related structures and processes to ensure that it has the institutional capacity to implement the committee's recommendations for improving the conduct and utility of risk assessment for meeting the 21st century environmental challenges. EPA should develop a capacity building plan that includes budget estimates required for implementing the committee's recommendations, including transitioning to and effectively implementing the framework for risk-based decision-making.

¹²NRC (National Research Council). 1996. *Understanding Risk: Informing Decisions in a Democratic Society*. Washington DC: National Academy Press; PCCRARM (Presidential/Congressional Commission on Risk Assessment and Risk Management). 1997. *Framework for Environmental Health Risk Management - Final Report*, Vol. 1.

¹³Callahan, M.A. 2007. *Improving Risk Assessment: A Regional Perspective*. Presentation at the Third Meeting of Improving Risk Analysis Approaches Used by EPA, February 26, 2007, Washington, DC; Kyle, A. 2007. *Community Needs for Assessment of Environmental Problems*. Presentation at the Fourth Meeting of Improving Risk Analysis Approaches Used by EPA, April 17, 2007, Washington, DC.

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CONCLUDING REMARKS

Global impacts are combining with the high financial and political stakes of risk management to place unprecedented pressure on risk assessors in EPA. But risk assessment remains essential to the agency's mission to ensure protection of public health and the environment. Much work is needed to improve the scientific status, utility, and public credibility of risk assessment. The committee's recommendations focus on designing risk assessments to ensure that they make the best possible use of available science, are technically accurate, and address the appropriate risk-management options effectively to inform risk-based decision-making. The committee hopes that the recommendations and the proposed framework for risk-based decision-making will provide a template for the future of risk assessment in EPA and strengthen the scientific basis, credibility, and effectiveness of future risk-management decisions.

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Preface

Risk assessment has become a dominant public-policy tool for informing risk managers and the public about the different policy options for protecting public health and the environment. Risk assessment has been instrumental in fulfilling the missions of the U.S. Environmental Protection Agency (EPA) and other federal and state agencies in evaluating public-health concerns, informing regulatory and technologic decisions, setting priorities for research and funding, and developing approaches for cost-benefit analyses.

However, risk assessment is at a crossroads. Despite advances in the field, it faces a number of substantial challenges, including long delays in completing complex risk assessments, some of which take decades to complete; lack of data, which leads to important uncertainty in risk assessments; and the need for risk assessment of many unevaluated chemicals in the marketplace and emerging agents. To address those challenges, EPA asked the National Academies to develop recommendations for improving the agency's risk-analysis approaches.

In this report, the Committee on Improving Risk Analysis Approaches Used by the U.S. EPA conducts a scientific and technical review of EPA's current risk-analysis concepts and practices and offers recommendations for practical improvements that EPA could make in the near term (2-5 y) and in the longer term (10-20 y). The committee focused on human health risk assessment but considered the implications of its conclusions and recommendations for ecologic risk assessment.

This report has been reviewed in draft form by persons chosen for their diverse perspectives and technical expertise in accordance with procedures approved by the National Research Council's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards of objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following for their review of this report: Lawrence W. Barnhouse, LWB Environmental Services, Inc.; Roger G. Bea, University of California, Berkeley; Allison C. Cullen, University of Washington; William H. Farland, Colorado State University; J. Paul Gilman, Convanta Energy Corporation; Bernard D. Goldstein, University of Pittsburgh; Lynn R. Goldman, Johns Hopkins University; Dale B. Hattis, Clark University; Carol J. Henry, American Chemistry Council (retired); Daniel Krewski, University of Ottawa; Amy D. Kyle, University of California, Berkeley; Ronald L. Melnick, National Institute of Environmental Health Sciences; Gilbert S. Omenn, University of Michigan Medical School; Louis Ryan, Harvard School of Public Health; and Detlof von Winterfeldt, University of Southern California.

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of the report before its release. The review of the report was overseen by the review coordinator William Glaze, Georgetown, TX and the review monitor, John Ahearne, Sigma Xi. Appointed by the National Research Council, they were responsible for making certain that an independent examination of the report was

Preface

carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of the report rests entirely with the committee and the institution.

The committee gratefully acknowledges the following for making presentations to the committee: Nicholas Ashford, Massachusetts Institute of Technology; Robert Brenner, Michael Callahan, George Gray, Jim Jones, Tina Levine, Robert Kavlock, Al McGartland, Peter Preuss, Michael Shapiro, Glenn Suter, and Harold Zenick, EPA; Douglas Crawford-Brown, University of North Carolina; Kenny Crump, ENVIRON International Corporation; Robert Donkers, Delegation of the European Commission to the United States; William Farland, Colorado State University; James A. Fava, Five Winds International; Penny Fenner-Crisp, International Life Sciences Institute Research Foundation; Dale Hattis, Clark University; Amy D. Kyle, University of California, Berkeley; Rebecca Parkin, George Washington University; Chris Portier, National Institute of Environmental Health Sciences; Lorenz Rhomberg, Gradient Corporation; Jennifer Sass, Natural Resources Defense Council; Jay Silkworth, General Electric Company; and Thomas Sinks, Centers for Disease Control and Prevention.

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I would especially like to thank the committee members for their efforts throughout the development of this report.

Thomas Burke, *Chair*
Committee on Improving Risk Analysis Approaches
Used by the U.S. EPA

Abbreviations

ARARs	Applicable or Relevant and Appropriate Requirements
ATSDR	Agency for Toxic Substances and Disease Registry
BMD	benchmark dose
CARE	Community Action for a Renewed Environment
CASAC	Clean Air Scientific Advisory Committee
CBPR	community-based participatory research
CERCLA	Comprehensive Environmental Response Compensation and Liability Act
CTE	central tendency exposure
DBP	dibutyl phthalate
DBPs	disinfection byproducts
EPA	Environmental Protection Agency
EPHT	Environmental Public Health Tracking Program
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FQPA	Food Quality Protection Act
GAO	Government Accountability Office
GIS	geographic information systems
HAPs	hazardous air pollutants
HI	hazard index
IARC	International Agency for Research on Cancer
IPCS	International Program on Chemical Safety
IRIS	Integrated Risk Information System
LNT	linear, no-threshold
MACT	maximum achievable control technology
MCL	maximum contaminant level
MCLG	maximum contaminant level goal
MeCl ₂	methylene chloride
MEI	maximally exposed individual
MOA	mode of action
MOE	margin of exposure
MTD	maximum tolerated dose
NAAQS	National Ambient Air Quality Standards
NCEA	National Center for Environmental Assessment
NEJAC	National Environmental Justice Advisory Council
NER	National Exposure Registry
NHANES	National Health and Nutrition Examination Survey
NOAEL	no-observed-adverse-effect-level
NPL	National Priorities List

Abbreviations

NRC	National Research Council
NTP	National Toxicology Program
OAR	Office of Air and Radiation
OP	organophosphate
OPPTS	Office of Prevention, Pesticides and Toxic Substances
OSWER	Office of Solid Waste and Emergency Response
OW	Office of Water
PBPK	physiologically based pharmacokinetic
PD	pharmacodynamic
PDF	probability density function
PK	pharmacokinetic
POD	point of departure
PPDG	Pesticide Program Dialogue Group
RAGS	Risk Assessment Guidance for Superfund
Red Book	<i>Risk Assessment in the Federal Government: Managing the Process</i>
RfC	reference concentration
RfD	reference dose
RI/FS	remedial investigation and feasibility study
RME	reasonable maximum exposure
ROD	record of decision
RR	relative risk
RRM	relative risk model
SDWA	Safe Drinking Water Act
SEP	socioeconomic position
TCA	1,1,1-trichloroethane
TCE	trichloroethylene
TSCA	Toxic Substances Control Act
UF	uncertainty factor
VOI	value-of-information
WHO	World Health Organization
WOE	weight-of-evidence

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