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REPORT IN BRIEF

# Science and Decisions

## Advancing Risk Assessment

**Risk assessments evaluate potential adverse health effects posed by harmful chemicals found in the environment and inform a range of decisions from protecting air and water to ensuring food, drug, and consumer product safety. Unfortunately, the risk assessment process is bogged down by challenges to its timeliness and credibility, a lack of adequate resources, and disconnects between the available scientific data and the information needs of decision-makers. This report recommends significant changes to advance the use of risk assessments, including greater attention to planning and problem formulation, improved stakeholder involvement, and a better match of the level of detail needed in a risk assessment to the questions that need to be addressed.**

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 is used by the U.S. Environmental Protection Agency (EPA), other federal and state agencies, industry, and others to evaluate potential health risks posed by harmful chemicals found in the environment. Risk assessments inform a wide range of regulatory and technology decisions from protecting air and water to ensuring the safety of food, drugs, and consumer products such as toys.

EPA uses the risk assessment process that was set forth in the 1983 National Research Council report known as "the Red Book" (see Box 1). Since that report's publication, EPA has greatly advanced risk assessment through the establishment of guidelines and of intra- and cross-agency science-policy panels, and improvements in peer-review standards. Despite this progress, major risk assessments for some chemicals are taking more than 10 years. In the case of trichloroethylene, which has been linked to cancer, the assessment has been under development since the 1980's.

There are several reasons the risk assessment process is bogged down. The credibility of risk assessment is often challenged because of the impacts of regulation, both nationally and internationally. When state and federal lawmakers move forward with risk management decisions in the absence of completed risk assessments, the value and credibility of risk assessments are further threatened. EPA is struggling to meet demands for hazard and dose-response information but is challenged by a lack of resources, including funding and trained staff. Uncertainty, an inherent property of scientific information, continues to lead to multiple interpretations and contribute to decision-making gridlock.

**Box 1. The Risk Assessment Process**

Risk assessment describes what research findings do and do not tell us about threats to human health and to the environment. There are four steps in the process—hazard identification, exposure assessment, dose-response assessment, and risk characterization—which were defined in the 1983 National Research Council report *Risk Assessment in the Federal Government: Managing the Process*, known as the "Red Book." After a risk assessment is complete, decision makers use it to determine how to reduce exposure to toxic substances.

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In addition, the rapid development of large quantities of scientific data, stemming from advancements in fields such as genomics and biomarkers, are increasing the complexity of risk assessments and the decisions that these assessments support. These data have led to questions about how to address, for example, multiple chemical exposures, multiple risks, and susceptibility in sensitive populations. In addition, risk assessment is now being extended to broader environmental questions, such as the "life-cycle analysis" of chemicals from their manufacture through their many uses, and also to issues of costs, benefits, and risk-risk tradeoffs.

In light of these challenges, EPA asked the National Research Council to conduct an independent study on improvements that could be made in the short term (2-5 years) and in the longer term (10-20 years). The report concludes that EPA's overall concept of risk assessment, which is generally based on the National Research Council's 1983 "Red Book" should be retained. However, a number of significant changes are needed to make the process more useful to decision-making.

## MAJOR RECOMMENDATIONS

The report offers the following conclusions and recommendations to enhance the credibility and usefulness of risk assessment.

### Improving the Design of Risk Assessment

This report defines "design" as the process of planning a risk assessment and ensuring that its level and complexity are consistent with the needs to inform decision-making. 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 often more useful and better accepted by decision-makers. However, EPA's incorporation of these stages in risk assessment has been inconsistent to date. The report recommends EPA 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. An important element of planning and scoping is defining of a clear set of options for consideration in decision-making.

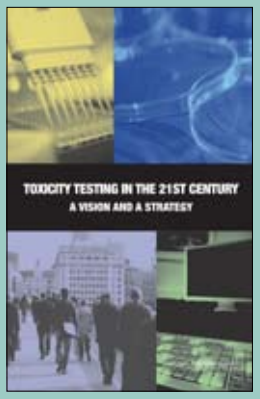
To that end, the report proposes that EPA adopt an expanded risk assessment framework that has the same core as the Red Book model but differs in its preliminary and final steps. The framework begins with a "signal" of potential harm, for example, a suspicious disease cluster, or findings of industrial 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 focus therefore shifts to the risk decisions to be made, more clearly laying out the information needed from the risk assessment.

### Uncertainty and Variability

Addressing uncertainty and variability is critical for the risk-assessment process. Uncertainty stems from lack of knowledge; it can be characterized and reduced by the use of more or better data but not eliminated. 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 better information.

Just as a risk assessment itself should be more closely tied to the questions to be answered, the level of detail for characterizing uncertainty is appropriate only to the extent that it is needed to inform specific risk-management decisions appropriately. The required extent and nature of uncertainty analysis should be decided in the planning and scoping phases of a risk assessment. EPA does not have a consistent approach to determine the level of sophistication or the extent

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



of uncertainty analysis needed to address a particular problem. 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. EPA's 2005 Guidelines for Carcinogen Risk Assessment acknowledges that susceptibility can depend on one's stage in life, but greater attention to susceptibility in practice is needed. EPA should move toward the long-term goal of quantifying population variability more explicitly in exposure assessment and dose-response relationships. An example of progress towards this goal is EPA's draft risk assessment of trichloroethylene, which considers how differences in metabolism, disease, and other factors contribute to human variability in response to exposures.

The report recommends that in the short term, EPA should adopt a "tiered" approach for selecting the level of detail to be used in uncertainty and variability assessments, which should be made explicit in the planning stage. EPA should develop guidance to determine the appropriate level of detail needed to support decision-making.

## A Unified Approach to Dose-Response Assessment

Historically, dose-response assessments at EPA have been conducted differently for cancer and noncancer effects. For cancer, it has generally been assumed that there is no dose threshold of effect—that is, that the smallest exposure has some health effect. For noncancer effects such as asthma or birth defects, risk assessments try to determine a dose threshold—a reference dose--below which effects are not expected to occur or are extremely unlikely in an exposed population. Consequently, noncancer effects have been underemphasized, especially in benefit-cost analyses.

This report recommends a significant departure from current practices to unify the approach to cancer and noncancer effects, which the report concludes is scientifically feasible and should be implemented. The approach for dose-response modeling should include 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.

In this approach, the reference dose would be redefined 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 and determine 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 report acknowledges, however, the widespread application and public-health utility of the reference dose; the redefined reference dose can still be used as it has been to aid risk-management decisions.

## Selection and Use of Defaults

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 the use of a default—an assumption made when chemical-specific data are not available—or an alternative approach that is used in place of a default. The 1983 Red Book recommended the development of guidelines to justify and select from among the available defaults to ensure consistency and to avoid manipulations in the risk-assessment process.

The report concludes that established defaults need to be maintained for the steps in risk assessment when chemical-specific data are not available. 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 that are implicitly 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 or even excluded from risk assessments. This is a problem at Superfund and other risk assessment sites; a relatively short list of chemicals for which there are epidemiologic and toxicologic data tends to drive exposure and risk assessments.

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. 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.

## Cumulative Risk Assessment

There is a need for cumulative risk assessments as defined by EPA—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. Although EPA has used cumulative risk assessment in various contexts, the process should be expanded to include consideration of nonchemical stressors (for example, smoking, diet, and alcohol consumption), 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 is addressed in the National Research Council's *Phthalates and Cumulative Risk Assessment: The Tasks Ahead* (December 2008).

## Stakeholder Involvement

Greater stakeholder involvement is necessary to ensure that the risk assessment process is transparent and that decision-making proceeds effectively, efficiently, and credibly. Although EPA has made great progress in creating programs and guidance documents related to stakeholder involvement, it is important that it adhere to its own guidance. EPA should establish a formal process for stakeholder involvement in the framework for risk-based decision-making. The process should include 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

EPA's current structure and insufficient resources may pose a challenge to implementing the recommendations in this report, which are tantamount to "change-the-culture" transformations in risk assessment and decision-making in the agency. Moving forward will require a commitment to leadership, cross-program coordination and communication, and training to ensure the requisite expertise. EPA should initiate a senior-level strategic examination of its risk-related structures and processes to make sure it has the institutional capacity to carry out these recommendations and develop a capacity building plan that includes budget estimates.

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The National Academies appointed this committee of experts, who volunteered their time to address this specific task and to produce this report. The report is peer-reviewed and the final product signed off by both the committee members and the National Academies.

**This report brief was prepared by the National Research Council based on the committee's report.** For more information, contact the Board on Environmental Studies and Toxicology at (202) 334-3060 or visit http://nationalacademies.org/best. Copies of *Science and Decisions: Advancing Risk Assessment* are available from the National Academies Press, 500 Fifth Street, NW, Washington, D.C. 20001; (800) 624-6242; www.nap.edu.