United States Government Accountability Office

GAO

Report to the Chairman, Committee on Environment and Public Works, U.S. Senate

May 2006

HUMAN HEALTH RISK ASSESSMENT

EPA Has Taken Steps to Strengthen Its Process, but Improvements Needed in Planning, Data Development, and Training

GAO-06-595

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GAO Accountability·Integrity·Reliability

Highlights

Highlights of GAO-06-595, a report to the Chairman, Committee on Environment and Public Works, U.S. Senate

Why GAO Did This Study

Over 100,000 chemicals, pollutants, and toxic substances are used in the United States and regulated by the Environmental Protection Agency (EPA). EPA uses risk assessment to determine the health risk from exposure to these substances, collectively referred to as contaminants. In the last 12 years, independent reviewers have examined this process and made recommendations for how it could be improved. GAO was asked to (1) identify the significant recommendations that have been made to improve human health risk assessment; (2) describe what EPA has done to modify its human health risk assessment process; (3) determine the effects these past modifications have had on the preparation of risk assessments; and (4) identify any additional actions experts believe EPA could take to improve its process, and the barriers it would face in doing so.

What GAO Recommends

GAO recommends that EPA enhance early planning of each risk assessment, identify and communicate data needs to the public and private research community, and support development and implementation of in-depth training for risk assessors and managers. EPA neither agreed nor disagreed with our findings and recommendations. However, the agency provided specific technical comments, which we incorporated as appropriate.

www.gao.gov/cgi-bin/getrpt?GAO-06-595.

To view the full product, including the scope and methodology, click on the link above. To view the results of GAO's survey of EPA's risk assessors, click www.gao.gov/cgi-bin/getrpt?GAO-06-637SP. For more information, contact John Stephenson at (202) 512-6225 or stephensonj@gao.gov.

What GAO Found

Since 1994, independent reviewers recommended that EPA better plan its risk assessments. In doing so, they said EPA should better utilize scientific data it has and identify other data it needs on the potential adverse effects from exposure to contaminants, and prioritize and support research to meet those needs. Furthermore, reviewers recommended that EPA better evaluate the analytic tools it uses and employ more powerful tools when appropriate. Reviewers also recommended that EPA better analyze and characterize the sources of uncertainty in its risk assessments. Finally, they recommended that EPA enhance its analysis of variability in exposure to contaminants and in susceptibility to harm from exposure, and improve how it considers the effects of exposure to multiple contaminants and through many sources.

EPA has strengthened its risk assessment process since 1994 and improvement efforts are ongoing. For example, EPA has increased planning for assessments and has initiated actions to develop missing or incomplete scientific data. EPA has also begun to embrace new methodologies, such as ones to predict how the body will react to a contaminant. Furthermore, EPA now uses a tiered approach to conducting uncertainty analysis, employing more sophisticated analysis as warranted. Finally, EPA has made progress in characterizing variability due to differences in both exposure and susceptibility of exposed individuals and has begun to take steps to address exposure to multiple contaminants and through multiple sources.

According to EPA's risk assessors, the modifications EPA has made have generally helped improve risk assessments. Many EPA risk assessors believe that agencywide guidance has helped them prepare risk assessments and have resulted in greater consistency across program offices. Furthermore, while most assessors report collaboration with internal and external entities is effective and has improved the quality of risk assessments, some said conflicting priorities and poor communication hindered collaboration among some EPA offices. Finally, while risk assessors said training has helped them gain skills and knowledge, over 70 percent said that more in-depth or relevant training would improve their risk assessment abilities.

Experts identified additional actions EPA could take to further improve its risk assessment process, recognizing that it may face barriers in doing so. Experts said EPA could improve its planning process by better focusing on scientific data needs and involving stakeholders early to obtain their concurrence with EPA's approach. Experts also said EPA could more thoroughly evaluate methods and models, transparently document its analytic choices, and enhance internal review. Finally, experts said EPA could provide additional training for risk assessors, managers, and stakeholders on the risk assessment process. Experts, however, said that the scientific complexity of risk assessment, the difficulty of obtaining and applying data, and a cultural resistance to deviating from established methods could act as obstacles to successfully making such changes.

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Abbreviations

ASPH	Association of Schools of Public Health
ATSDR	Agency for Toxic Substances and Disease Registry
BOSC	Board of Scientific Counselors
Commission	Presidential/Congressional Commission on Risk Assessment and Risk Management
CREM	Council for Regulatory Environmental Modeling
EPA	Environmental Protection Agency
FQPA	Food Quality Protection Act
GIS	Geographic Information System
HEI	Health Effects Institute
HPV	High Production Volume
ILSI-RSI	International Life Sciences Institute—Risk Science Institute
IRIS	Integrated Risk Information System
NAS	National Academy of Sciences
NCCT	National Center for Computational Toxicology
NCEA	National Center for Environmental Assessment
NCER	National Center for Environmental Research
NERL	National Exposure Research Laboratory
NHEERL	National Health and Environmental Effects Research Laboratory
NHEXAS	National Human Exposure Assessment Survey
NIEHS	National Institute for Environmental Health Sciences
NRMRL	National Risk Management Research Laboratory
OAQPS	Office of Air Quality Planning and Standards
OMB	Office of Management and Budget
OP	Office of Pesticides
OPPT	Office of Pollution Prevention and Toxics
ORD	Office of Research and Development
OW	Office of Water
STAR	Science to Achieve Results
TRIM	Total Risk Integrated Methodology
TSCA	Toxic Substances Control Act

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Accountability * Integrity * Reliability

United States Government Accountability Office
Washington, DC 20548

May 31, 2006

The Honorable James M. Inhofe
Chairman
Committee on Environment and Public Works
United States Senate

Dear Mr. Chairman:

Chemicals play an important role in people's everyday lives. Consumers use products containing chemicals, such as cleansers and pesticides, and companies use a variety of toxic substances as solvents or additives to their industrial processes. Although these substances have beneficial uses and are important in producing goods and services, some may adversely affect human health. Over 100,000 chemicals, pollutants, and toxic substances are used in the United States and regulated by the Environmental Protection Agency (EPA). These substances, whether produced in the United States or imported, include 187 hazardous air pollutants, nearly 20,000 pesticide products on the market, and a growing number of substances used in industrial processes—over 82,000 as of December 2005. EPA uses a process known as risk assessment to estimate the health risk from exposure to these substances, collectively referred to in this report as contaminants.[1] While highly technical by nature, risk assessments, along with other relevant information, serve as a basis for regulatory decisions that protect human health. EPA's risk assessments are shaped by available scientific information and by provisions in major environmental statutes, such as the Clean Air Act, and they affect a range of stakeholders, including regulated industries, federal agencies, environmental advocacy groups, academic and other researchers, and the public.[2]

[1]Although other regulatory agencies, such as the Food and Drug Administration, also use risk assessments as part of regulatory decision making, this report discusses only the risk assessment process used by EPA.

[2]EPA's mission is to protect human health and to safeguard the natural environment—air, water, and land—upon which life depends. This report focuses only on EPA's efforts to protect human health.

In 1994, as part of a congressionally mandated review of the methods used by EPA to estimate the risk of developing cancer from exposure to hazardous air pollutants, the National Academy of Sciences (NAS) issued a report entitled *Science and Judgment in Risk Assessment*. This report focused primarily on hazardous air pollutants and provided an overview assessment of EPA's risk assessment methods.[3] In providing this overview, the NAS committee identified several themes, largely focusing on the quality and availability of essential information, that serve as a useful framework for discussing the risk assessment process:

- *Implementation*. EPA faces certain overarching, institutional issues that affect its implementation of the risk assessment process.
- *Data needs*. Data necessary to complete scientifically plausible risk assessments are often unavailable on such topics as the actual levels of exposure to contaminants and how those exposures affect human health.
- *Default options*. In the absence of convincing scientific knowledge or data, EPA relies on assumptions, often conservative in nature, about such questions as how exposure to low doses of a contaminant affects human health.
- *Method and model evaluation*. The predictive accuracy of methods and models, such as those used to predict how a contaminant will be processed once it enters the body, is not always known.
- *Uncertainty*. The lack of precise knowledge about the type, likelihood, and extent of adverse effects from exposure to a contaminant results in uncertainty in risk assessment that can be reduced only by advances in scientific understanding or the collection of better data.
- *Variability*. Variability, in exposure or in the biological differences among humans that determine how exposure to contaminants affects health, can be better characterized with more data but cannot be reduced or eliminated.

[3]Pollutants are generally categorized as hazardous air pollutants under the Clean Air Act if they cause or may cause cancer or other serious health effects, such as reproductive effects or birth defects, or adverse environmental and ecological effects. Currently, the Clean Air Act regulates 187 chemicals and chemical categories as hazardous air pollutants.

- *Aggregate and cumulative effects*. Aggregate effects are the results from exposure to a single contaminant by any combination of means—including inhalation, contact with the skin, and ingestion; cumulative effects are the results from exposure to multiple contaminants by any combination of means.

Science and Judgment in Risk Assessment was one of several reports by NAS that discussed risk assessment in general and made recommendations for ways to improve it.[4] In addition, the Presidential/Congressional Commission on Risk Assessment and Risk Management issued a report in 1997 that reviewed risk assessment, as well as risk management, in regulatory programs.[5] Furthermore, the Office of Management and Budget (OMB) issued guidance related to peer review and ensuring the quality, objectivity, utility, and integrity of information released to the public.[6] More recently, in January 2006, OMB issued a proposed bulletin that advocates minimum standards for the scientific quality of risk assessments to enhance their technical quality and objectivity.

In the context of these prior reviews, you asked us to (1) identify the significant recommendations to improve human health risk assessment that have been made since 1994; (2) describe what EPA has done to modify its human health risk assessment process over the same period; (3) determine the effects these past modifications have had on the preparation of risk assessments; and (4) identify any additional actions experts believe EPA could take to improve its risk assessment process in the future, and the barriers EPA would face in doing so.

To identify significant recommendations to improve human health risk assessment since 1994, we reviewed EPA documents, including those produced by EPA's Risk Assessment Forum, Science Policy Council,

[4]National Academy of Sciences, *Risk Assessment in the Federal Government: Managing the Process* (Washington, D.C., 1983).

[5]The Presidential/Congressional Commission was created by Pub. L. No. 101-549 (1990).

[6]Peer review is a documented critical review of a specific scientific or technical work product, conducted by qualified individuals who are independent of those who performed the work, but who are collectively equivalent in technical expertise—for example, EPA's Science Advisory Board or the National Academy of Sciences. According to EPA's 2006 Peer Review Policy, peer review can be internal, in which the reviewers are independent experts from inside EPA, or external, in which the reviewers are independent experts from outside EPA.

Council for Regulatory Environmental Modeling, and Science Advisory Board, as well as each of EPA's program offices. We also reviewed our own reports and documents produced by NAS and the Presidential/ Congressional Commission on Risk Assessment and Risk Management. We also spoke with experts in the risk assessment field, who identified many of these documents in the course of our discussions and provided insight into some of the recommendations made therein. To describe what EPA has done to modify its human health risk assessment process, we interviewed program office managers from EPA's Office of Air and Radiation, Office of Pesticide Programs, Office of Pollution Prevention and Toxics, Office of Water, and Office of Research and Development (ORD). While we recognize that EPA's regional offices and the Office of Solid Waste and Emergency Response conduct risk assessments, for the most part their work focuses on site-specific assessments and thus was not included in this effort. Within ORD, we interviewed managers in two of EPA's laboratories (the National Health and Environmental Effects Laboratory and the National Exposure Research Laboratory) and three of EPA's research centers (the National Center for Environmental Assessment, National Center for Environmental Research, and National Center for Computational Toxicology). Furthermore, we attended various EPA and stakeholder group training sessions and meetings.

To determine the effects these modifications have had on the preparation of risk assessments, we surveyed risk assessors from the program offices mentioned above. We sought their views on the usefulness of many of these modifications, as well as on aspects of EPA's risk assessment process, including guidance documents, training, organizational structure, and collaboration. The survey and results can be viewed at http://www.gao.gov/cgi-bin/getrpt?GAO-06-637SP. In addition, we interviewed experts in the risk assessment field and obtained their perspectives on the extent to which these modifications were helpful to EPA's risk assessment process. To identify additional actions experts believe EPA could take to improve its process and to identify barriers to such actions, we contacted experts representing a range of stakeholders in the process. Specifically, we contacted risk assessment scientists; toxicologists; scientific advisers to EPA; state officials; and representatives from regulated industries, government agencies, and environmental advocacy groups who have an expertise in risk assessment. We used an iterative process (often referred to as the "snowball sampling" technique) to identify these knowledgeable experts and selected for interviews those who would provide us with a broad and balanced range of perspectives on EPA risk assessment practices. We used a standard set of questions to interview each of these experts to ensure we consistently

discussed each aspect of EPA risk assessment policies and practices. (See app. I for a more detailed description of the methodology we employed.) In addition, we consulted with NAS's Board on Environmental Studies and Toxicology at its June 2005 meeting to obtain input on the areas in which EPA has made the most progress in improving its risk assessment practices and areas EPA will need to focus on in the future. We used the experts present at this meeting as a starting point for our snowball sampling technique used to identify subsequent experts. We conducted our work from February 2005 through March 2006 in accordance with generally accepted government auditing standards.

Results in Brief

Independent reviewers, including NAS, have made a number of significant recommendations to improve EPA's human health risk assessment process since 1994 that can be grouped and discussed in terms of the seven themes originally identified by NAS in 1994. First, reviewers have said that EPA should improve its overall implementation of the process with such steps as more thorough planning of its risk assessments and greater use of independent reviews by scientists (called peer reviews). Second, to improve the quantity and quality of the data upon which risk assessments are based, reviewers have recommended that EPA better utilize the scientific data it has and identify additional data needs on the potential adverse effects from exposure to contaminants, and prioritize and support research to meet the data needs identified. Third, because EPA lacks data to fully assess the health risk from exposures, reviewers have recommended that when the agency relies on assumptions—known as default options—it should, among other things, more clearly indicate when it relies on default options and how it chooses them. Fourth, to improve the accuracy of EPA's risk assessments, reviewers have stated that EPA should better evaluate the methods and models used in its analysis and incorporate newer, more powerful tools when appropriate. Fifth, to address the inevitable uncertainties associated with gaps in scientific knowledge and general unknowns about model and data accuracy, EPA should, according to reviewers, more explicitly analyze and characterize the sources of uncertainty in its risk assessments and, when possible, discuss the uncertainties both descriptively (qualitatively) and numerically (quantitatively). Sixth, reviewers have also recommended that EPA enhance its analysis of variability in levels of exposures to contaminants, as well as differences in individual reactions to exposure. Finally, because people are typically exposed to a mixture of contaminants through a variety of means, such as contact with skin and breathing air, reviewers have recommended that EPA improve how it considers the

effects of combinations of contaminants and all possible means of exposure.

EPA has strengthened many aspects of its risk assessment process since 1994, and improvement efforts are ongoing. First, EPA has improved implementation of its risk assessment process by, for example, beginning to improve risk assessment planning and creating scientific leadership positions, such as the Office of the Science Advisor. Second, EPA has initiated actions to develop missing or incomplete scientific data on the potential adverse effects from exposure to contaminants. For example, EPA officials told us they have begun to use the planning and review processes to determine what data are needed and communicate these needs to both EPA and outside researchers. Third, EPA has cited the need for risk assessments to be more transparent about their use of default options. For example, EPA has recently issued guidance describing default options that are appropriate for certain purposes and directing risk assessments to disclose the default options used in a particular risk assessment. Fourth, EPA is enhancing its use of models and embracing new methodologies. For example, EPA has established a group—the Council for Environmental Regulatory Modeling—to review models and provide guidance in model selection. Furthermore, some program offices now use more advanced models to predict how a contaminant will be processed once it enters the body. Fifth, EPA generally characterizes uncertainty descriptively, but has begun to incorporate quantitative techniques into its uncertainty analyses. For example, EPA typically uses a tiered approach to conducting uncertainty analysis, starting as simply as possible, describing uncertainty qualitatively, and sequentially employing more sophisticated analysis, such as probabilistic analysis, as warranted. Sixth, EPA has made progress in describing variability due to differences in both the exposure and the susceptibility of exposed individuals to contaminants. For example, when determining a level of exposure that is unlikely to be harmful, EPA includes adverse effects for people who might be at increased risk because of their age or the state of their health. Finally, EPA has begun to take steps to consider the combined effects of exposure to multiple contaminants through multiple means of exposure. For example, EPA has developed a framework to assess the combined, or cumulative, risk and has directed its program offices to include cumulative risks when planning major risk assessments.

EPA risk assessors believe the modifications EPA has made over the past 10 years—particularly issuing additional guidance—have generally helped them improve risk assessments, but collaboration and training could be improved. Most EPA risk assessors believe that agencywide guidelines and

policy and reference documents have helped them prepare risk assessments by, for example, providing useful frameworks for evaluating potential harm from chemicals, and have resulted in greater consistency among risk assessments prepared by different offices within EPA. Furthermore, EPA's collaboration with external researchers, including other federal research entities, academia, and industry, has improved EPA's ability to conduct risk assessments by providing expertise and research not always available within the agency, according to risk assessors. In addition, risk assessors reported that internal collaboration among EPA offices is moderately to very effective, but could be improved. For example, a few risk assessors commented that the program offices' knowledge of the regulatory context in which research will be used helps the researchers structure their work. However, risk assessors also reported that collaboration is hindered within EPA by, for example, conflicting priorities among the various offices and the poor communication between some of them. Finally, while risk assessors said improved training has also helped them gain relevant skills and knowledge, over 70 percent of the risk assessors responding to our survey stated that more in-depth or relevant training would improve their ability to prepare risk assessments. In addition, they believe training for risk assessors and managers in specific technical and scientific areas, such as emerging scientific issues and the use of newer models, is lacking.

While the experts we spoke with said the modifications EPA has made over the past 10 years have been beneficial overall, they identified additional actions EPA could take to improve its risk assessment process, recognizing that EPA may face barriers to doing so. Specifically, experts said EPA could improve the planning it undertakes prior to starting a risk assessment by better focusing on what data are needed for the assessment and by involving stakeholders early in this planning process. For example, several experts said that increased involvement with a broad range of stakeholders early in the planning process would help identify alternative methods and models and obtain stakeholder concurrence with the agency's approach. In addition, experts said EPA could more thoroughly evaluate methods and models, transparently document its analytic choices, and enhance internal review. For example, several experts said that EPA should more transparently communicate which default assumptions were used in risk assessments, why the defaults were chosen, and what judgments EPA was making when it employed certain methods. Finally, experts said EPA could provide additional training for risk assessors, managers, and stakeholders on all elements of the risk assessment process, such as how to use and apply models and how to interpret data from emerging scientific fields. While these efforts would

further improve the risk assessment process, experts pointed out inherent barriers that EPA may face in carrying them out, such as the scientific complexity of risk assessment, the difficulty of obtaining and applying data, and a cultural resistance to deviating from established methods. For example, several experts said that EPA's risk assessments have grown more technically challenging and require risk assessors and managers to have different skills from what they had in the past.

To further improve the risk assessment process, GAO recommends that EPA enhance early planning of each risk assessment, identify and communicate data needs to the research community, and support development and implementation of in-depth training for risk assessors and managers.

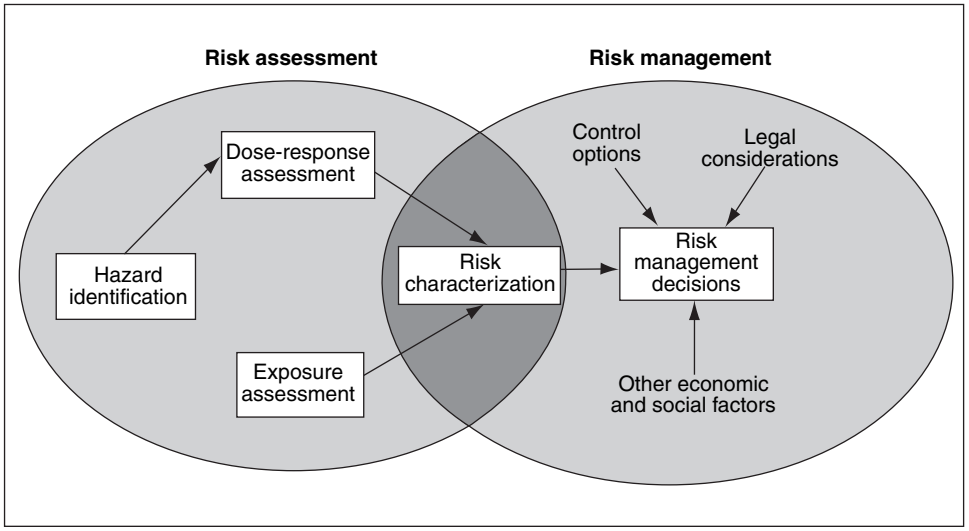
We provided EPA with a draft of this report for review and comment. EPA neither agreed nor disagreed with our findings and recommendations. However, the agency provided specific comments to improve the report's technical accuracy, which we incorporated as appropriate.

Background

Risk assessment, as used in public health and environmental settings, is inherently a complex and highly technical process that provides a systematic scientific description of potential adverse effects from exposure to contaminants. Risk assessments are conducted to estimate whether and how much harm can be expected from exposure to a given contaminant or mixture of contaminants and to help determine whether the harm is significant enough to require regulatory or other corrective action. The adverse effects from exposure can be acute, such as respiratory illnesses or poisonings, or chronic, such as cancer or reproductive or genetic abnormalities. The result of a risk assessment is a statement of the likelihood that an exposed population will be harmed and to what extent. EPA's human health risk assessment process generally consists of the four stages recommended in 1983 by the National Academy of Sciences (NAS): (1) hazard identification (determining whether a substance could cause adverse affects and what those adverse affects would be), (2) dose-response assessment (determining the relationship between the magnitude of exposure to a contaminant and the probability and severity of adverse effects), (3) exposure assessment (identifying the extent to which exposure is predicted to occur), and (4) risk characterization (combining the information from the preceding analyses into a conclusion about the nature and magnitude of risk).

Risk assessment plays a critical role in EPA's regulatory decisions, but the characterization of risk that results from a risk assessment is only one piece of information used to inform decisions on regulatory standards for protecting human health. This analysis is integrated with other information, such as economic information on the costs and benefits of mitigating the risk, technological information on the feasibility of managing the risk, and the concerns of various stakeholders. The combined analysis informs agency officials who ultimately make regulatory decisions. This overall process is generally called risk management. (See fig. 1.) According to NAS, the risk assessment process should be conceptually distinguished from how the results of that process are used in the risk management process. However, in practice, maintaining this separation is difficult because the two processes are fundamentally linked by the complementary needs of the risk assessors and the risk managers. Specifically, risk assessors need to be aware of the context in which the assessment will be used and to communicate their key findings, as well as their confidence in them, in a way that risk managers can understand and apply. Risk managers need to ensure that the risk assessment has been properly performed and can be integrated with other information to make and justify a sound regulatory decision.

Figure 1: Typical Sequence of Risk Assessment and Risk Management Processes



Source: EPA.

EPA's human health risk assessment process is limited to a great extent by the amount of scientific data available on contaminants and by the level of scientific understanding about how contaminants act in the body to produce adverse effects. Data are often unavailable, and science cannot always provide definitive answers. The complex and sophisticated analytic tools used in risk assessment cannot overcome basic scientific unknowns. As a result, EPA's risk assessments almost always include assumptions about potential adverse effects. Some assumptions are conservative—that is, they are intended to help ensure that the agency does not underestimate health risks. Some critics of EPA's risk assessment practices believe EPA uses assumptions that are unjustifiably conservative, given new scientific data and methods, and thereby produces estimates that overstate actual risks. Other stakeholders, however, criticize some agency assumptions for not being conservative enough in the face of scientific uncertainties. These criticisms often result in legal challenges to EPA's decisions.

EPA's human health risk assessment process is also greatly dependent on its degree of knowledge about the population's level of exposure to contaminants. This knowledge includes the extent to which people are exposed to potentially harmful contaminants in their daily lives, the chemicals to which they are most often exposed, the levels of such exposures, how exposures change over time, and the sources of exposure. Risk assessors, researchers, and policymakers must often rely on estimates of human exposure that are often derived from data showing the extent the chemicals are found in the air, water, food, or other environmental media and assumptions about how and at what rate the body absorbs the chemicals it contacts. In addition to estimates from models, extrapolations from experiments involving animals, and measurements of chemicals in the environment, EPA also relies on more direct methods to measure exposure and more accurately assess exactly how much of a contaminant has been absorbed in the body. For example, EPA uses population activity models—models based on actual human behavior, such as the time spent outdoors or, for children, the amount of time spent on the floor—to better estimate an individual's true exposure.

Risk assessment activities at EPA are carried out by both the agency's Office of Research and Development (ORD)—its principal scientific and research arm—and its program and regional offices, including the Office of Air and Radiation, Office of Pesticide Programs, Office of Pollution Prevention and Toxics, Office of Solid Waste and Emergency Response, and Office of Water. ORD carries out all steps of highly complex, precedent-setting risk assessments for specific contaminants, such as

dioxin. In addition, ORD often has responsibility for the first two steps of the risk assessment process—hazard identification and dose-response assessment—in support of the program offices. In such cases, the last two steps—exposure assessment and risk characterization—are the responsibility of the various program offices. Three notable exceptions exist to this division of responsibility. The Office of Pesticide Programs and the Office of Pollution Prevention and Toxics often conduct all steps of risk assessments independently, in part, because the relevant statutes for these program offices place strict time frames on decision making and the confidential nature of data provided to the agency under these programs. Furthermore, the Office of Water also does all of the stages for some of the assessments for purposes of the Safe Drinking Water Act.

EPA's approach to risk assessment varies across program offices, often as a result of different regulatory and legal requirements. For example, a branch of the Office of Pollution Prevention and Toxics assesses data submitted by industry applicants on approximately 2000 new chemicals annually under the Toxic Substances Control Act (TSCA) of 1976. TSCA generally requires EPA to evaluate the chemicals within 90 days, but does not require all applicants to conduct laboratory tests on the potential hazards and risks of the chemicals. In contrast, the Clean Air Act requires EPA to establish National Ambient Air Quality Standards, to review the scientific basis for those standards at least every five years, and to revise the standards as appropriate. As part of this process, ORD summarizes the most current scientific information on the pollutant in question. ORD's findings and conclusions are then combined with other exposure and risk analyses to determine what, if any, revisions should be made to the standards.

Risk assessment has been the center of numerous reports, analyses, and regulations over the years. One of the earliest was the National Academy of Sciences' 1983 report *Risk Assessment in the Federal Government: Managing the Process*, often referred to as the "Red Book" because of the color of its cover. Subsequently, NAS released several related reports, including *Science and Judgment in Risk Assessment* (1994), *Understanding Risk: Informing Decisions in a Democratic Society* (1996), and *Strengthening Science at the U.S. Environmental Protection Agency* (2000). In addition, Congress, via the Clean Air Act Amendments of 1990, created the Presidential/Congressional Commission on Risk Assessment and Risk Management (Commission) and required it to investigate the policy implications and appropriate uses of risk assessment and risk management in various regulatory programs designed to protect people from cancer and other chronic health effects that may result from

exposure to hazardous substances. The Commission published its two-volume final report in 1997.

In addition, the Office of Management and Budget (OMB) has issued guidelines, reports, and bulletins that have affected the practice of risk assessment. For example, in October 2001, OMB issued its *Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies*, which required agencies to issue their own guidelines to ensure the quality of information being disseminated. Furthermore, in September 2003, OMB issued a report to Congress on the costs and benefits of federal regulation. As part of this effort, OMB sought public comment on the practice of risk assessment, many of which were directed at, and passed along to, EPA. OMB also issued the *Final Information Quality Bulletin for Peer Review* in December 2004 that provided guidance to federal agencies on what information is subject to peer review and defined a planning process for peer review. Most recently, on January 9, 2006, OMB released a draft bulletin on procedures agencies should use to conduct risk assessments and information that should be included. Public comment on this draft will be accepted until June 15, 2006.

Independent Reviewers Have Recommended Improvements to EPA's Risk Assessment Process Since 1994

Independent reviewers, including the National Academy of Sciences (NAS) and the Presidential/Congressional Commission on Risk Assessment and Risk Management have made a number of significant recommendations to improve EPA's human health risk assessment process since 1994. These recommendations cover a range of actions, including improving planning of what will be required to complete a particular risk assessment and what key stakeholders need to be involved, supporting development of new scientific data on the potential adverse effects from exposure to the contaminant under review, and enhancing analysis of the potential risk and its uncertainties. All of them can be summarized and discussed in terms of the seven themes—implementation, data needs, default options, method and model evaluation, uncertainty, variability, and exposure to multiple contaminants and routes of exposure—reported in NAS's report *Science and Judgment in Risk Assessment*.[7]

[7]National Academy of Sciences, *Science and Judgment in Risk Assessment* (Washington, D.C., 1994).

Improve Planning and Review Process and Ensure an Appropriately Skilled Workforce to Conduct Risk Assessment

Independent reviewers made a number of recommendations to EPA to improve the overall implementation of its risk assessment process. The reviewers recommended that EPA improve its planning of risk assessments before beginning the process and adopt an iterative risk assessment approach. Reviewers also stressed that EPA should increase its use of risk assessment reviews by independent scientists, known as peer reviews; increase stakeholder involvement in the risk assessment process; and ensure it has the workforce needed to conduct quality risk assessments. Finally, the reviewers recommended that EPA improve the way it characterizes the risk it finds and strengthen the link between risk assessment and risk management.

Improve Planning and Adopt an Iterative Risk Assessment Approach

In 1996, NAS reviewers stressed the importance of planning from the beginning of a risk assessment to incorporate the perspectives and knowledge of interested and affected parties.[8] Because of the large number of stakeholders interested in the results of a risk assessment, it is important to ensure that the risk assessment addresses all of the stakeholders' needs. NAS pointed out that one way to do this is to be aware of the stakeholders' concerns from the outset and incorporate them into the analysis and characterization of risk. By involving stakeholders early, risk assessors can ensure that they ask the right questions, make appropriate assumptions, and determine the best way to summarize information, thereby potentially making the resulting message more credible to these parties.

In addition to improved planning, NAS suggested in 1994, and the Commission concurred, that EPA develop the ability to conduct risk assessments iteratively—that is, begin with a screening analysis to ascertain the potential risk and refine that analysis as appropriate. Such an approach would start with relatively inexpensive screening techniques and move to more resource-intensive data gathering and modeling as the particular situation warranted. To guard against the possibility of underestimating risk, these screening techniques should be constructed to err on the side of caution where there is uncertainty.

Increase Peer Review and Stakeholder Involvement in the Risk Assessment Process

Each of the NAS reports we reviewed, as well as the report by the Commission, recommended ways EPA could improve its peer review process and better involve stakeholders in risk assessment. These

[8]National Academy of Sciences, *Understanding Risk: Informing Decision in a Democratic Society* (Washington, D.C., 1996).

independent reviewers said peer review is critical to evaluate the accuracy and appropriateness of technical information, scientific observations, and interpretations used in regulatory decision making. The Commission observed that peer review can also help in the planning stages of a risk assessment to put a problem in context and draw on the knowledge of experienced researchers, public health officials, and scientists.

In particular, NAS recommended in 2000 that EPA change its peer review policy to ensure greater independence of these reviews from the control, or appearance of control, of the program managers.[9] EPA's Science Advisory Board had expressed concern about potential conflicts of interest because agency policy allowed the same individual to serve as both project manager for a particular work product and peer review leader.[10] The NAS committee concurred with this concern.

In addition, NAS's 1994 report recommended that EPA collaborate more with outside parties to improve the overall risk assessment process. For example, EPA could use external advisory groups, such as its Science Advisory Board, to help ensure that risk assessment decisions use the best science and incorporate full public discussion and participation from the scientific community. Such collaboration could also include a process for public review and comment. The Commission also said that agencies should use advisory groups, composed of stakeholders, to periodically evaluate the use of technical information. In addition, the Commission recommended that agencies establish clear, written guidelines for peer review and match the use of peer review to the importance of the decision to be made.

In 1996, NAS commented on the importance of stakeholder involvement in the risk assessment process. NAS suggested that the risk assessment process involve the spectrum of interested and affected parties, including decision makers and specialists in risk analysis, at each step of the process. According to NAS, such involvement will help ensure that as much important, relevant knowledge as possible enters the process and

[9]National Academy of Sciences, *Strengthening Science at the U.S. Environmental Protection Agency* (Washington, D.C., 2000).

[10]EPA's Science Advisory Board provides independent advice and peer review on scientific and technical aspects of environmental problems and issues. Experts, including scientists, engineers, and economists, provide independent, balanced, and scientifically sound advice to EPA.

that the process remains open and inclusive. NAS also mentioned another benefit of involving these stakeholders in the process: the participation of a spectrum of people helps ensure that the process will be framed correctly and the resulting risk characterization will be accurate, balanced, and informative.

Ensure EPA Has the Skilled Workforce Needed to Conduct Quality Risk Assessments

Each of the NAS reports we reviewed contained recommendations stressing the importance of an organization's ability to ensure that it has the expertise and leadership needed to conduct risk analyses. In addition, according to current workforce models, agencies need to ensure that they have effective training and the capability to identify what skills and competencies the employees and the organization need. In 1994, NAS recommended that EPA acquire additional expertise, as needed, to better interpret data and reach sound conclusions about the risks to human health from a contaminant. For example, many of the conclusions regarding the potential risks from a particular contaminant rely upon risk assessment models based on animal data or, when available, human evidence from epidemiological studies. The quality of the risk assessment will depend upon how well these data are interpreted to predict health effects in human populations. NAS recommended that EPA acquire staff with specialized skills in fields such as toxicology to successfully complete this type of analysis.

NAS also recommended in 2000 that EPA continue to place high priority on ORD's graduate fellowship and postdoctoral program. The report stated that to achieve scientific and technical excellence, EPA must first attract, retain, and properly support a dedicated professional staff. NAS also noted that while EPA has many outstanding scientists and engineers, ORD's workforce is aging and many staff may retire in the relatively near future. Periodic hiring freezes, combined with high competition from the private sector, had made it difficult for ORD to recruit the new talent needed to sustain and enhance the research workforce. NAS concluded that ORD's graduate fellowships and postdoctoral programs brought a stream of fresh scientific and technical talent into EPA's research program and helped train future researchers in environmental science, engineering, and other disciplines. NAS urged EPA to continue to place a high priority on these programs.

In 2000, NAS made a series of recommendations related to scientific leadership and talent at EPA. Specifically, NAS recommended that EPA establish a new position—deputy administrator for science and technology—to address concerns that science at EPA was not perceived to be strong and that many EPA scientists believed their scientific knowledge

and resources were not effectively used. Traditionally, EPA's most senior science official had been the assistant administrator for research and development, but that official lacked agencywide responsibility or authority to oversee the scientific and technical basis for regulatory and policy decision making. In addition, EPA's program offices were not required to follow scientific advice from ORD. Consequently, the NAS panel concluded that EPA needed an appropriately qualified science official at a sufficiently high level with both the authority and responsibility for agencywide scientific performance.

Improve Characterization of Risk and More Closely Link Risk Assessment with the Needs of Risk Managers

Finally, reviewers recommended ways EPA could improve its characterization of risk and better link its risk assessment and risk management processes to harmonize the scientific aspects of risk assessment and the broader policy objectives of risk management. NAS's 1996 report, which primarily focused on risk characterization and the role it plays in risk assessment, stressed that successful risk characterization can result in better and more widely accepted risk assessment and risk management decisions. The Commission echoed NAS's position and recommended that risk characterizations should include information useful to everyone in the risk management process, such as information on who is at risk, how they might be affected, what the severity of an adverse effect might be, and how confident the risk assessors are about their predictions.

Reviewers also suggested that EPA better link its risk assessment and risk management processes. EPA had tried to separate these processes entirely to avoid the possible perception that EPA made scientific judgments on the risk posed by a contaminant on the basis of its willingness to regulate the substance rather than on the science. However, NAS pointed out that while some degree of judgment is necessary, the science-policy judgments EPA makes in the course of risk assessment should more clearly be informed by the agency's risk management priorities and goals. According to NAS, better linkage between risk assessment and risk management will help ensure that the risk assessments will be more accurate and relevant to risk managers. The Commission concurred, stating that risk assessment should be guided by an understanding of the issues important to risk managers' decisions about how to protect public health and the environment.

Review Existing Data, Identify Data Gaps, Prioritize Research Needs, Foster Development of New Data, and Improve Strategic Research Planning and Collaboration

In 1994, NAS found, in general, that EPA did not have the full range of data needed to conduct adequate risk assessments to estimate the health risks associated with most contaminants—for example, data related to the effect a contaminant has on the body and the extent of exposure to the contaminant. These data are essential to ensure the accuracy and precision of the risk assessment. In addition, NAS recommended that EPA increase its collaboration with researchers and improve the transparency of its research priorities.

To help address EPA's dearth of data, NAS recommended, among other things, that EPA review its existing databases, such as the Integrated Risk Information System (IRIS), and identify data gaps.[11] As part of its database review, NAS recommended that EPA compile an inventory of the chemical, toxicological, and epidemiological literature in the databases to determine what gaps exist. NAS further suggested that EPA prioritize its future research on the basis of the significance of the missing data to risk assessments, convey its data needs to other public and private researchers, such as the Agency for Toxic Substances and Disease Registry,[12] and develop incentives to expedite the generation of needed data by these entities.

Furthermore, in 2000, NAS recommended, among other things, that EPA expand the multiyear research planning by its Office of Research and Development (ORD). For example, ORD had developed plans for research on topics such as particulate matter, endocrine disruptors,[13] and drinking water. The NAS committee pointed out that these planning efforts will contribute to research program continuity and the achievement of strategic goals. In addition, NAS recommended that the plans be both continued for problem-driven research—research targeted at a particular environmental problem—and expanded to include core research—

[11]IRIS contains information on the human health effects that may result from exposure to various chemicals in the environment and helps provide consistent information on chemical substances for use in risk assessments.

[12]The Agency for Toxic Substances and Disease Registry is the primary public health agency involved with hazardous waste issues and works to prevent or reduce the harmful effects of exposure to hazardous substances on human health by, for example, supporting research that assists with risk assessment.

[13]Endocrine disrupting chemicals are thought to mimic natural human hormones that influence important regulatory and development mechanisms such as blood pressure, metabolism, and reproduction. Important endocrine glands include the thyroid, pancreas, and male and female gonads (testes and ovaries).

broader, more generic research that will help improve current and future understanding of a scientific issue. Research should be balanced between these two types, since core research will help ORD better understand and anticipate environmental risks and will enable ORD to provide better problem-specific research and technical assistance to the agency.

NAS has also made recommendations to EPA in the area of research accountability. Specifically, NAS recommended that EPA improve the documentation and transparency of the decision-making process ORD uses to set research and technical assistance priorities and allocate funds. For example, NAS pointed to an EPA Science Advisory Board finding that ORD's lack of transparency in its process for setting research priorities made it difficult to evaluate the adequacy of proposed budgets. NAS also recommended that EPA expand on its efforts to create an inventory of science projects and programs across EPA by documenting and publishing a comprehensive and detailed inventory. The inventory should include information such as goals and objectives of each project, milestones, schedules, and staff allocations and should be used to ensure that science activities are properly coordinated through the agencywide science planning and budgeting process and are appropriately peer reviewed.

Once the research strategy has been established, research collaborations can help execute it. NAS suggested that EPA should recognize the limits of its own research capabilities and develop a strategy to obtain outside support in research areas where ORD is not pre-eminent. Specifically, NAS recommended EPA enhance its research collaborations by developing and implementing a strategy to stimulate, acquire, and apply the results of research conducted or sponsored by other federal agencies, state agencies, universities, and industry in this country and abroad. NAS said such collaboration is especially important given the budget constraints EPA and the federal government face and the breadth of knowledge required to conduct the full range of risk assessments. In addition, NAS recommended that EPA develop additional mechanisms to promote and facilitate research interactions among grantees in EPA's Science to Achieve Results (STAR) grant program and ORD research staff.[14] For example, NAS suggested that grant applicants could identify in their proposals how their research might complement or supplement ongoing or planned research in the ORD laboratories. NAS also recommended that

[14]The STAR program funds peer reviewed competitive grants on research topics selected by ORD and postgraduate training for scientists in environmental fields.

EPA increase its efforts to disseminate ORD's research products, explain their significance, and assist others inside and outside the agency in applying the research. NAS noted that while EPA's policy and regulatory work receives a great deal of public attention, the agency's science research typically receives a similar degree of attention only when the scientific basis for a decision is questioned. They also pointed out that even internal EPA offices may be unaware of important benefits from ORD's research program.

More Clearly Indicate Use of Default Options and How They Were Chosen

When EPA needs to rely on assumptions—known as default options—because it lacks data to fully assess the potential health risks from exposure to a contaminant, reviewers said EPA should, among other things, more clearly indicate that it relied on these defaults and how they were chosen. EPA's defaults, which are based on general scientific knowledge and policy judgment, are, for the most part, conservative.[15] One example of a commonly used default option is that laboratory animals are a surrogate for humans in assessing health risks: An adverse effect in the animals is taken as evidence of a chemical's potential to harm humans.

Independent reviewers agreed with EPA's use of default options as a reasonable way to cope with the lack of available data. However, NAS recommended that EPA be clearer about the scientific and policy basis for each default option and when it uses a default. Furthermore, reviewers said that EPA should fully explain under what conditions they would depart from these default options. According to NAS, giving greater formality to the criteria for a departure would result in greater guidance for the public and lessen the possibility of undocumented departures that would undercut the scientific credibility of a risk assessment. The Commission concurred, stressing that the defaults used in risk assessments and the uncertainty associated with their results should be clearly identified and justified.

[15]EPA's defaults represent a choice that, although scientifically plausible given the existing uncertainty, is more likely to result in overestimating than underestimating human health risk.

Better Evaluate Available Methods and Models and Incorporate More Advanced Tools When Appropriate

The overall accuracy of a risk assessment largely depends on the validity of the various analytic methods and models EPA uses to assess the toxicity of, and exposure to, a particular contaminant. However, according to NAS, EPA often does not clearly understand the extent to which the methods or models it chooses accurately predict the toxicity or exposure to a contaminant. For example, because of limited scientific information on how contaminants actually work in the body to produce adverse effects in humans, EPA frequently uses a method that relies on studies involving laboratory animals to understand the toxicity of a substance. The concentrations of the contaminant introduced into the animals as part of these studies are higher and administered for shorter periods of time than humans would normally experience. Consequently, to determine the expected response in people, EPA extrapolates the response from laboratory animals to humans. While such extrapolations are useful to predict potential harmful effects of a contaminant, different analytic methods may better predict the effect.

In 1994, NAS recommended, among other things, that EPA evaluate the accuracy of its methods and models for assessing toxicity and, when appropriate, incorporate more advanced tools. For example, models that are based on the underlying mechanisms at the cellular or molecular level can more accurately estimate the dose of the contaminant that would have an adverse biological effect on a specific part of the body. Regarding the risk of cancer from a particular contaminant, NAS recommended that EPA continue to both use methods involving animal studies to evaluate the possibility of adverse effects in humans and explore, when appropriate, mechanistic models. Furthermore, to better convey the cancer risk associated with a particular substance, NAS recommended that EPA develop a classification scheme that provides narrative statements regarding the hazards posed by carcinogens and a descriptive evaluation of the strength and nature of the evidence used to estimate the substance's potential for causing cancer.

Regarding exposure, NAS noted that EPA had traditionally characterized exposure according to two criteria: exposure of the total population and exposure of a specified highly exposed subpopulation. While these two criteria can help assess whether any particular exposure might occur above a regulatory threshold, only considering the highly exposed subpopulation is likely to overestimate the exposures of most of the population. Consequently, NAS recommended, and the Commission concurred, that EPA consider the entire range of a population's exposure, rather than just the exposures of a highly exposed subpopulation. The Commission also recommended that EPA identify and evaluate highly

exposed populations separately. Moreover, NAS recommended that EPA use population-activity models—models based on actual human activity patterns—to better estimate an individual's true exposure and expand efforts to use personal monitoring data to better understand actual exposures and variances across the population.

More Explicitly Analyze and Characterize the Sources of Uncertainty in Risk Assessments

To address the inevitable uncertainties associated with gaps in scientific knowledge and general unknowns about model and data accuracy, reviewers recommended that EPA more explicitly analyze and characterize the sources of uncertainty in its risk assessments. Numerous gaps in scientific knowledge exist regarding the health effects of various contaminants, such as the exact amount of exposure to a particular contaminant that can cause an adverse effect or the biological effect of a contaminant on the body. In addition, knowledge is often lacking about which model or method might be most appropriate to estimate risks to human health from a particular contaminant. NAS recommended that EPA develop guidelines for how to analyze and report the different types of uncertainty, both for the overall assessment and for the different stages of the risk assessment, such as hazard identification and exposure assessment. For example, during hazard identification, uncertainty can be related to the quality, type, and results of scientific studies; however, during exposure assessment, uncertainty can be related to model choice or available data.

NAS also recommended in 1994 that EPA conduct uncertainty analysis of the risk estimate and present the identified uncertainties as explicitly, accurately, and fully as feasible. Analysis of the effects of uncertainties can help inform EPA decision makers and the public about the extent of uncertainty associated with the risk assessment. The analysis can also show where additional research might resolve major uncertainties and where it might not. NAS recommended that the uncertainty analysis be presented both descriptively (qualitatively) and, where possible, numerically (quantitatively). For example, some sources of uncertainty, such as those related to estimating exposures, can be reduced through the use of more advanced statistical methods. Other types of uncertainty, such as those associated with extrapolating data from animal testing to predict the effect on humans, are more difficult to quantify. The Commission concurred and recommended that risk characterizations include narrative descriptions of the primary reasons for uncertainty, as this information is likely to be more understandable and useful than quantitative estimates or model results.

Enhance Analysis of Variability in Exposure Levels and Health Risks to Exposed Individuals

Variability, which refers to the natural diversity in a population, can be better understood or described, but not reduced. To address the two main categories of variability—one related to differences in levels of individual exposures to contaminants and the other related to differences in individual reactions to exposure—reviewers recommended that EPA enhance its analysis of both types and carefully state in each risk assessment what assumptions it made about what is and is not accounted for. Specifically, variability related to different exposures depends on the various concentrations of a contaminant as it disperses in the environment, different breathing rates, and different food consumption and personal activity patterns. For example, infants and children generally consume more fruits, vegetables, and fruit juices per body weight than adults, and some people, such as agricultural workers, are more exposed to pesticides through breathing and skin contact. The Commission recommended that risk assessments identify groups of people who are likely to have higher exposures to contaminants and consult these groups in the early stages of an assessment to obtain information about all known sources of exposure.

Reviewers also recommended that EPA revise the way it estimates how long a person is exposed to a contaminant. NAS and the Commission recommended that EPA move away from estimates of exposure based on a hypothetical "maximally exposed individual," who was assumed to be the person at greatest risk in a worst-case scenario, because these estimates do not account for a number of other factors that may affect exposure patterns and rates, such as the time the person spends indoors or going to work. Furthermore, estimates based on the hypothetical maximally exposed individual likely overestimate the exposures of most of the population and underestimate the exposures of subpopulations, such as agricultural workers, who may be more highly exposed than the general population. While EPA's 1992 exposure assessment guidelines suggest the use of ranges and high-end exposure estimates chosen from the high end of those ranges, according to NAS, EPA had not sufficiently documented the reliability of such estimates when data are limited.

The second type of variability—differences in human susceptibility—is related to inherent differences among people, such as age, physiologic characteristics, lifestyle, genetics, sex, and ethnicity. Reviewers found that EPA's approach for reducing risks associated with chemical exposures generally did not include information on differences in individual susceptibility or encourage gathering evidence to identify these differences. The reviewers recommended, among other things, that EPA consider this "interindividual" variability and adopt a default option for

differences in susceptibility among humans. In addition, NAS recommended that EPA assess risks to infants and children whenever it appears that their risks might be greater than those of adults. For example, the developing brains of infants and young children have an increased susceptibility to contaminants that harm the nervous system, such as lead. NAS specifically recommended that EPA sponsor research to examine the causes and extent of interindividual variability in susceptibility to cancer and the possible connection between susceptibility and age, race, ethnicity, and sex. The Commission generally concurred, adding that risk assessments should also identify especially susceptible subpopulations, such as people with asthma who may have an increased responsiveness to allergens and respiratory irritants. The Commission also stated that, where possible, available information about the range of the population's susceptibility should be considered and used in place of default assumptions.

Better Consider the Human Health Effects of Exposure to Multiple Contaminants and Routes of Exposure

Reviewers recommended that EPA improve how it considers the effects of combinations of contaminants (cumulative exposure) and all possible paths of exposure to a single contaminant (aggregate exposure). People are typically exposed to a mixture of contaminants through a variety of pathways, such as contact with skin or eating food, each of which might be associated with an increased probability of one or more health effects. However, most risk assessments address a single contaminant and often focus on a single pathway of exposure, such as inhalation. As a result, NAS recommended that EPA should consider all possible exposure pathways. For example, when assessing risk from mercury, EPA should consider the risk to residents from inhaling mercury emitted from a nearby industrial smoke stack, as well as the possibly greater health risk of consuming mercury that has accumulated in the tissue of fish that are caught and eaten locally after mercury from the smoke stack was deposited into water.[16]

When assessing the risks of exposure to chemical mixtures, most risk assessments estimate the risks from individual contaminants, then calculate the combined risk by simple addition. However, this method ignores potentially synergistic interactions that may make the effects more

[16]Contaminants can progressively accumulate in the tissues of an organism, such as a human or a fish, as a result of uptake by the body from all routes of exposure. This process, called bioaccumulation, occurs because the rate of intake exceeds the organism's ability to eliminate the substance from the body.

damaging to human health than anticipated or antagonistic interactions that may make the effects less damaging than anticipated. Consequently, this method could either under- or overestimate the total risk. NAS said that simple addition of the risks from multiple contaminants may be appropriate for screening-level risk estimates. However if a more refined quantitative estimate is needed, EPA should consider using statistical procedures to combine the risks from exposures to multiple contaminants, which would help produce a more comprehensive estimate of risk. The Commission concurred but stressed that combining risks may not always be feasible; the risk analyses for exposure to each contaminant may not be compatible because the risk assessments may differ in accuracy. Further, the Commission recommended that for risk assessments involving exposures to low concentrations of multiple chemicals, the risks from each exposure should be added in the absence of information on exactly how the chemicals affect the body. However, if the multiple chemicals affect the body in different ways—for example, if one chemical affected development while another affected the nervous system—the impact of each chemical on the body should be considered independently and not added together.

EPA Has Strengthened Many Facets of Its Risk Assessment Process Since 1994, and Efforts Are Ongoing

EPA has modified its human health risk assessment process since 1994 in several ways. First, the agency enhanced implementation of its risk assessment process by, for example, issuing guidance and realigning staff resources. In addition, EPA has taken steps to identify the scientific data it has on the potential adverse effects from exposure to various contaminants and has established collaborative relationships with external researchers to foster the development of needed additional data. Furthermore, EPA has begun to improve its use of default options, enhance its modeling capabilities, and explore new methodologies. EPA has also begun to characterize uncertainty quantitatively and analyze and communicate variability more thoroughly. Finally, EPA is more often considering the combined effects of exposure to multiple contaminants through multiple pathways. Most of these efforts are ongoing and can be discussed in terms of the themes presented in the previous section.

EPA Has Enhanced Implementation of Key Aspects of Its Risk Assessment Process

EPA has taken a number of steps to improve implementation of its risk assessment process. Specifically, EPA has developed guidance and policy documents at the agency and program office levels; built scientific capacity; modified components of its approach to risk assessment; and refined its peer review and quality-assurance practices.

EPA Has Issued Many Agencywide and Program Office-Specific Guidance and Policy Documents to Improve Risk Assessment Practices

The guidance and policy documents EPA has issued over the past decade were intended to help staff develop and use risk assessments and to provide basic information to the public about EPA's risk assessment methods. While some of these documents have remained unchanged over time, many have been revised, or will be revised, as science, knowledge, and analytic methods have improved. Among these documents are the guidelines issued by EPA's Risk Assessment Forum, a committee of senior EPA scientists established to promote agencywide consensus on risk assessment issues, which cover such topics as neurotoxicity,[17] exposure assessment, and carcinogenic risk assessment. Each of the original five guideline documents created in 1986 has been updated at least once, and some are slated to be revised again. For example, the exposure guidelines were revised in 1992 and revisions are currently being planned. In addition, the forum has issued two entirely new sets of guidelines since 1994—*Guidelines for Reproductive Toxicity Risk Assessment* and *Guidelines for Neurotoxicity Risk Assessment*—and has developed a number of policies on, among other things, risk characterization, peer review, and evaluating risk to children. EPA has also issued interim policy memorandums and position papers on scientific issues such as genomics and endocrine disruption.

Similarly, much of EPA's agencywide guidance issued since 1994 has undergone revision and has its origins in earlier policy documents. For example, EPA's *Risk Characterization Handbook*, issued in 2000, has its roots in the 1995 *Policy for Risk Characterization*. The handbook stresses that risk characterization should be transparent, clear, consistent, and reasonable. EPA's policy on the use of peer review was originally issued in 1994 and was followed up by issuance of peer review handbooks in 1998 and again in 2000.[18] The peer review policy was recently updated in January 2006. EPA has also issued technical guidance, such as its review of the processes to estimate a daily or continuous exposure to humans that is likely to be without appreciable adverse effects during a lifetime.

In addition to the EPA-wide guidance, many of the program offices have also issued guidance documents that support their particular risk assessment efforts. In general, the office-specific guidance documents provide risk assessors with analytic tools and exposure scenarios

[17]Neurotoxicity is an adverse change in the structure or function of the central or peripheral nervous system following exposure to a chemical, physical, or biological agent.

[18]U.S. Environmental Protection Agency, *Peer Review Handbook* (Washington, D.C., 2000).

pertinent to the statutory responsibilities of the office. For example, the Office of Pollution Prevention and Toxics created guidance in the form of an analytic tool to screen chemicals in the absence of data, which frequently occurs because of the lack of a requirement for industry to develop extensive data on new chemicals or new uses of existing chemicals. In addition, the Office of Pesticide Programs has issued pesticide-specific guidance documents. For example, to help ensure consistency in pesticide chemical risk assessments, the Office of Pesticide Programs issued guidance for developing residential exposure assessments and developed a template for making and documenting registration eligibility decisions.

EPA Has Built Scientific Capacity through Increased Focus on Scientific Leadership, Greater Reliance on Research Advisory Groups, and Development of Future Scientific Talent

EPA enhanced its scientific leadership through the creation of the position of science advisor in 2002 and the Office of the Science Advisor in 2003, the increased reliance on research advisory groups composed of senior EPA scientists and external experts, and the continuation of its research fellowship programs. The overarching responsibility of the science advisor is to coordinate and oversee the scientific activities of the program offices at EPA to ensure the best use of science. The Office of the Science Advisor provides further leadership by establishing specific mechanisms to ensure that scientific results, combined with technical evaluation and peer review, play a prominent role in regulatory decisions and that EPA staff interpret and enforce regulations consistent with the science supporting them.

In addition to enhancing its scientific leadership, EPA has also increased its reliance on research advisory groups since 1994. The Science Policy Council and the Risk Assessment Forum play key roles in advancing the practice of risk assessment at EPA. The council reviews the adequacy of existing policies, establishes science policy as needed, and coordinates EPA efforts related to methods, modeling, risk assessment, and environmental technology. The Science Policy Council staff facilitate ad hoc work groups, encourage communication and consensus building within the agency, and participate in technical work-group activities and deliberations.

The Risk Assessment Forum is a standing committee of senior EPA scientists established to promote agencywide consensus on difficult and controversial risk assessment issues and to ensure that this consensus is incorporated into guidance. According to an agency official, the forum is designed as a venue where staff can meet and discuss common risk assessment issues across program offices. One of the forum's main contributions to risk assessment at EPA has been the issuance of a series

of risk assessment guidelines. The forum is currently working on new guidelines, such as one related to adverse effects on the immune system. When more specificity is needed on an existing guideline, the forum issues companion pieces, known as "purple books" because of the color of their cover, that provide additional or updated information.

The Board of Scientific Counselors (BOSC) provides objective and independent advice, information, and recommendations about ORD's research program to ORD's assistant administrator. BOSC is composed of scientists and engineers from academia, industry, and environmental organizations who are recognized as experts in their fields. In 1998, BOSC completed a peer review of ORD's laboratories and centers.[19] BOSC completed a second review of the laboratories and centers in 2002 and 2003 that identified key accomplishments of the laboratories and centers, as well as areas for future improvement. In addition, after EPA's Office of the Science Advisor issued its 2004 staff paper,[20] it asked BOSC to host a workshop for EPA staff and other interested stakeholders, such as industry, environmental groups, and researchers, to provide feedback to refine EPA's current practices and to suggest alternative approaches for specific aspects of risk assessment.

EPA has also worked to foster scientific excellence and enhance the skills of its existing workforce through its graduate and postdoctoral fellowship programs. One such program, the EPA/ORD Postdoctoral Fellowship Program, began in 1998, and, as of May 2003, 205 individuals had participated in the program. One benefit of the program is that it helps provide a ready pool of talented candidates for EPA vacancies. In fact, according to a study of the program conducted by the National Council for Science and the Environment, nearly half of the former postdoctoral participants had taken permanent positions at EPA. The Science to Achieve Results (STAR) fellowship program is designed to encourage masters and doctoral students to pursue careers in an environmental field. The STAR fellowship program has provided new environmental research in the biological and health sciences, two fields related to the development

[19]ORD's laboratories and centers are the National Center for Environmental Assessment (NCEA), National Health and Environmental Effects Research Laboratory (NHEERL), National Exposure Research Laboratory (NERL), National Center for Environmental Research (NCER), National Risk Management Research Laboratory (NRMRL), and National Homeland Security Research Center.

[20]U.S. Environmental Protection Agency, *Risk Assessment Principles and Practice* (Washington, D.C., 2004).

of human health risk assessment. EPA has also partnered with the Association of Schools of Public Health (ASPH) to offer 1-year placements of graduates in EPA laboratories, centers, and program offices to work on public health issues. In the announcement of opportunities for the 2006 ASPH Fellows Program, a dozen fellowships are being offered in areas related to human health risk assessment. For example, the National Center for Environmental Assessment is offering a fellowship to develop health assessments for various chemicals, and the National Center for Environmental Research is offering a position for someone interested in working on developing models or analyzing uncertainty in risk assessments.

EPA Has Begun to Incorporate Planning Activities and Stakeholder Input into Its Risk Assessment Approach

To improve planning, which is a part of all risk assessments to some degree, EPA has issued various guidance documents and held workshops for staff. One of EPA's earliest related guidance documents,[21] released in 1997, was designed to help risk assessors and risk managers plan and document the scope of risk assessments and to consider input from appropriate stakeholders and experts, especially in those assessments involving the effects of combinations of contaminants.[22] EPA followed up this guidance with workshops to help staff apply it in risk assessments. In January 2002, EPA issued a handbook to reflect some of the lessons learned from implementation of the 1997 guidance to make risk assessments more useful to decision makers and other stakeholders. These lessons, conveyed through case studies, include that planning can be particularly valuable when the assessment is complex, controversial, or precedent setting, and that explaining uncertainty to stakeholders can help develop trust, credibility, and support for the decision-making process.

The 2000 *Risk Characterization Handbook* also strongly advocates the use of planning and presents a number of topics for both risk managers and risk assessors to consider, such as identifying the stakeholders in the process; scope of the effort; relevant management goals, issues, and policies; available data; and data needs. For example, during planning, risk assessors, risk managers, and stakeholders need to identify the key data gaps and discuss how best to fill them, such as whether to use existing data or conduct additional short- or long-term tests to evaluate exposure

[21]U.S. Environmental Protection Agency, *Guidance on Cumulative Risk Assessment—Part 1: Planning and Scoping* (Washington, D.C., 1997).

[22]U.S. Environmental Protection Agency, *Lessons Learned on Planning and Scoping for Environmental Risk Assessments* (Washington, D.C., 2002).

and effects. The Office of Air and Radiation recognized the need for planning and developed planning guidance as part of its Air Toxics Risk Assessment Reference Library, issued in 2004. EPA acknowledged in its 2004 staff paper that it needs to continue to stress the importance of concerted and conscious planning with risk assessors and risk managers before a risk assessment is started. According to EPA, risk assessors need to outline early in the development of a risk assessment what will and will not be addressed and how they will develop the risk assessment.

Stakeholders and the public play a key role in the planning, as well as at later stages in the development of a risk assessment. Stakeholders, at various levels and in various forms, can help ensure better understanding of the risk assessment results and may promote support for the selected risk reduction strategies. Program offices involve stakeholders in various ways. For example, the branch of the Office of Air Quality Planning and Standards (OAQPS) responsible for setting certain air quality standards for six principal pollutants solicits input from stakeholders in the planning phase of its periodic updates to the standards it sets.[23] In addition, the public may officially comment on draft air quality standards once they are publicly released. The Office of Water pursues stakeholder and public involvement that includes working with the environmental community, industry, trade associations, risk assessor organizations, states, and bordering countries. In addition, the office's periodic reviews of water quality standards and other nonregulatory actions, such as health advisories, are all open processes that allow for public input on various stages of the analysis.

For risk assessments involving the reregistration of pesticides, the Office of Pesticide Programs (OPP) established a process that provides several opportunities for public participation.[24] Depending on the potential health risks posed by a pesticide product, the public has anywhere from one to

[23]These six principal pollutants, known as "criteria pollutants," are carbon monoxide, lead, nitrogen dioxide, ozone, particulate matter, and sulfur dioxide.

[24]EPA is reviewing older pesticides (those initially registered prior to November 1984) under the Federal Insecticide, Fungicide, and Rodenticide Act to ensure they meet current scientific and regulatory standards. EPA is also reassessing tolerances (pesticide residue limits in food) to ensure they meet safety standards established under the Food Quality Protection Act (FQPA) of 1996. Under FQPA, EPA must reassess all tolerances established before August 3, 1996, within 10 years. The Office of Pesticide Programs reviews the registrations of all pesticide products every 15 years to determine whether they still meet safety standards as part of its registration review process.

four separate opportunities to comment. For example, if risk assessors estimate that the product poses little risk to human health, the public will have one opportunity to comment before OPP decides whether to approve the pesticide product. For higher-risk products, the public will have as many as four opportunities to comment. The first opportunity to comment occurs after OPP has completed a preliminary risk assessment. This preliminary assessment contains all of the elements of a risk assessment and has undergone internal review, but is not yet finalized. Notice of the opportunity to comment is distributed to people who have elected to sign up for such notifications, as well as through a "notice of availability" published in the *Federal Register*. The public can also comment on risk assessments prepared by the Office of Pesticide Programs through the office's Science Advisory Panel—which holds periodic public meetings on pesticide-related risk assessment issues, such as methods to assess skin sensitivity to exposure to pesticides or models used to estimate dietary exposures.

EPA has also adopted an iterative approach to many of its risk assessments. An iterative approach begins with a screening assessment and progressively grows in depth and scope in relation to the estimated risks to human health. When a screening assessment identifies a potential for a nontrivial risk, EPA decides if pursuing that risk is appropriate based on its current priorities and available resources. If EPA decides to pursue the risk, a more detailed, refined risk assessment is performed. The degree of refinement is based on the type of decision, the available resources, and the needs of the risk manager. After refinement of the estimate, EPA reviews it to see if it will be sufficient to answer the questions posed. Refinements proceed iteratively until the assessment provides an adequate answer for the decision maker within the resources available. Both the revised cancer guidelines and EPA's 1995 *Policy for Risk Characterization* support an iterative approach to risk assessment. Some program offices have also adopted an iterative—or tiered—approach to risk assessment. For example, the air toxics program follows a tiered approach, beginning with an analysis that includes few data and many conservative assumptions. If this analysis indicates that the risk may be relatively high, assessors pursue more intensive analysis to determine if the risk is realistic or an artifact of the lower tier's conservative assumptions. Despite this move toward greater use of an iterative approach, EPA acknowledges it could be clearer about when it is taking such an approach. For example, EPA could be more transparent about when and why it makes a risk management decision based on a screening-level assessment rather than a more detailed assessment.

EPA Has Refined Its Peer Review and Quality-Assurance Practices

In the years since the issuance of *Science and Judgment in Risk Assessment*, EPA has made strides to improve its peer review practices. EPA uses peer review to help ensure the quality of its risk assessments and keep them as objective and consistent as possible. EPA's *Peer Review Policy* states that scientifically and technically based work products related to agency decisions should be peer reviewed. In 2000, EPA issued its revised *Peer Review Handbook*, an update of the original 1998 edition. In the intervening 3 years, EPA's Science Advisory Board, EPA's Office of Inspector General, the National Research Council, and GAO scrutinized the peer review process. In response, in part, to recommendations made by many of these groups, EPA issued the current edition of the handbook. Among other things, it instructs EPA to balance peer review panels in terms of expertise and biases to help ensure a reasonable and scientific review.

In addition to issuing the *Peer Review Handbook*, EPA has undertaken a number of actions to help ensure the quality of its data and information. In May 2000, EPA established an agencywide quality-assurance system and issued the *EPA Quality Manual for Environmental Programs.* Key components of this system include assigning a quality-assurance manager to conduct independent oversight of data quality, developing a management plan, and conducting an annual assessment of the quality system. In addition, the system calls for an assessment of the data EPA used to support agency decisions to verify that they were of sufficient quantity and quality for their intended use. In 2002, EPA developed its information-quality guidelines in response to those issued by OMB, which stated that agencies must ensure the quality, objectivity, utility, and integrity of information released to the public.[25] EPA's guidelines outline its policy and procedures to ensure and maximize the quality of the information it disseminates and describe the mechanisms by which EPA reviews information prior to dissemination. EPA issued a complement to these guidelines in 2003 to raise awareness among the public about EPA's ongoing interest in high-quality data and to serve as an additional resource for staff as they evaluate the quality and relevance of information.[26]

[25]Office of Management and Budget, *Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies* (Washington, D.C., 2002).

[26]U.S. Environmental Protection Agency, *A Summary of General Assessment Factors for Evaluating the Quality of Scientific and Technical Information* (Washington, D.C., 2003).

EPA Has Enhanced Its Strategic Planning and Refocused Staff Resources to Initiate Review of Existing Data and Development of Needed Data

Since 1994, EPA has initiated a number of actions to develop missing or incomplete scientific data on the potential adverse effects from exposure to contaminants, including refocusing and expanding the Office of Research and Development human health risk assessment program, improving strategic research planning, increasing collaboration with outside researchers, and enhancing databases.

EPA Restructured and Augmented Its Research Office

In 1995, EPA restructured ORD to more effectively generate and gather information needed for the risk assessment process, combining 12 existing laboratories into 3 national laboratories and 2 national centers—the National Health and Environmental Effects Research Laboratory (NHEERL), National Exposure Research Laboratory (NERL), National Risk Management Research Laboratory (NRMRL), National Center for Environmental Research (NCER), and National Center for Environmental Assessment (NCEA).[27] Specifically, one laboratory, NHEERL, conducts research on the effects of various exposure routes and rates, dose levels and duration, and cumulative doses on health outcomes. Its main research areas, all of which help improve risk assessments, target (1) the use of mechanistic information—how a substance causes an effect at a biological level—to reduce uncertainties in risk assessment; (2) the cumulative risks posed by exposure to contaminant mixtures; (3) the health risks to particularly susceptible populations; and (4) the evaluation of public health outcomes to determine the effectiveness of actions designed to reduce health risks. This research is developed in coordination with the program offices to target issues in risk assessment for air pollutants, safe foods and pesticides, water, and contaminated lands.

A second laboratory, NERL, researches and develops improved methods and models to assess and predict human exposures to harmful contaminants in air, water, soil, and food. For example, it developed methods to better characterize pollution sources, and models to quantify the effects on exposure from various individual behaviors. NERL works closely with the program offices to set research priorities and help ensure that its results are useful to the program offices. For example, NERL coordinated with OAQPS to format data from several studies on airborne

[27]In September 2002, EPA formed the National Homeland Security Research Center to, among other things, provide appropriate, affordable, effective, and validated technologies and methods for assessing risks posed by chemical, biological, and radiological terror attacks.

particulate matter in a comparable manner that allowed NERL and OAQPS staff to develop more powerful analytic results than would have been possible from the individual studies alone. NERL also developed tools to enhance the exposure assessment portion of the risk assessment, such as a database of human activities by age, sex, and location, to better characterize exposure risk based on personal activities. The third laboratory, NRMRL, focuses its research more on ways to minimize exposure to contaminants that cause health risks than on ways to improve the preparation of risk assessments. For example, NRMRL researches sources of chemicals that disrupt the endocrine system and strategies to minimize exposure to such chemicals.

The two centers, NCER and NCEA, serve as focal points for external researchers and risk assessors, respectively. NCER funds innovative environmental research by academic scientists to reduce uncertainty in risk assessment. Specifically, NCER has sponsored research to develop data for use in models, thereby helping to reduce the model's uncertainties. NCER also coordinates with EPA's laboratories and program offices to develop its research topics. The Science to Achieve Results (STAR) program, one of NCER's grant programs, funds competitive research proposals and graduate fellowships in environmental science and engineering fields to complement ORD's research in its strategic and research plans, such as the health effects of contaminants on airborne particulate matter and in drinking water, and, more generally, on children's health. For example, the STAR program has funded research to generate data on human exposures that will improve risk estimates. NCER has also established academic research centers in such areas as children's health. NCEA, EPA's national resource center for human health risk assessment, supports EPA's work in three main ways. First, NCEA conducts risk assessments of national significance—for example, assessments of dioxin and diesel emissions—and prepares the air quality criteria documents that reflect the state of the science for six principal air pollutants. Second, it develops scientifically sound, defensible risk assessment methods to improve the use of science in risk assessment, such as software to estimate a benchmark dose—the dose that produces change in the risk of an adverse effect. Third, it provides guidance and support to risk assessors and risk managers through such means as its management of the Integrated Risk Information Systems (IRIS), a database of the potential human health effects of exposure to various chemicals in the environment.

In addition to the six labs and centers, EPA in 2005 established the National Center for Computational Toxicology (NCCT) to coordinate and

implement EPA's research on computational toxicology, a cutting-edge field that uses mathematical models to predict adverse effects and to better understand the mechanisms through which a given contaminant causes harm. Given advances in such newly emerging disciplines as the study of genes and their functions, computational toxicology offers the potential for scientists to develop a more detailed understanding of the risks posed by a much larger number of chemicals than is currently possible. NCCT research is designed to develop tools to conduct quantitative risk assessments more rapidly and to improve the identification of chemicals that may pose substantial health risks. NCCT staff have begun to collaborate with other ORD laboratories and centers to effectively target their research efforts.

EPA Has Enhanced Strategic Research Planning

Since 1994, EPA has undertaken a number of strategic activities to more closely link the data needs of program offices to research agendas of EPA and ORD.[28] In connection with the goals presented in EPA's and ORD's strategic plans, ORD defined 16 high-priority research areas such as human health, endocrine disruption, airborne particulate matter and other air pollutants, and safe pesticides. Research strategies for each area are either in place or under development. For example, EPA's *Human Health Research Strategy* identifies four broad, overarching research areas to guide ORD's human health research over the next 5 to 10 years.[29]

To carry out its 16 research strategies, ORD began in 2000 to develop a multiyear implementation plan for each. The first plans emerged in 2001, with most finalized by 2003 following widespread participation and input from many stakeholders as well as review by senior ORD managers. ORD invites input on the plans from ORD and program office staff, federal research partners, and outside peer groups, such as EPA's Science Advisory Board, the Board of Scientific Counselors, and the National Research Council. These plans establish the short- and long-term goals and timelines required for ORD's laboratories or centers to implement each of the strategies. The National Program Director, a newly established

[28]To comply with the Government Performance and Results Act (GPRA), EPA every 3 years generates an agencywide 5-year strategic plan that highlights high-level environmental issues. The most recent plan for fiscal years 2003-2008 identified key research needs related to EPA's mission.

[29]The four strategic research directions are harmonizing cancer and noncancer risk assessments, assessing aggregate and cumulative risk, determining risk to susceptible human subpopulations, and conducting research to enable evaluation of public health outcomes from risk management decisions.

position for each major ORD research area including human health, helps ensure that ORD's time and staff resources are used strategically and that the overall planning effort links to the needs of the program offices.

Program offices use various planning and review approaches to determine data needs. For example, the Office of Air Quality Planning and Standards develops a research-needs paper at the conclusion of each periodic review of the air quality standards it establishes to inform the research agenda for the next review, which occurs about every 5 years. Each paper helps ensure that research in key areas will be available for the next review. In contrast, the data needs of the Office of Pesticide Programs are defined by law.[30] Applicants who wish to register a pesticide product must submit the data defined in the statute and regulations, and OPP staff determine whether the data are of sufficient quality and quantity to assess the risk from the pesticide product.[31] This list of required data is currently undergoing revision and additional data requirements may be added.

EPA Program Offices Have Established Collaborative Relationships with External Researchers

Since 1994, EPA has strengthened and formalized collaboration with a range of other federal researchers to better leverage its limited research dollars and foster the development of data to improve human health risk assessments. Specifically, EPA has developed relationships with agencies such as the National Institute for Environmental Health Sciences (NIEHS) and the Agency for Toxic Substances and Disease Registry (ATSDR). For example, in 1998, EPA established a cooperative agreement with NIEHS to develop a body of research on the relationship between exposures and children's health. This collaboration jointly funded Children's Environmental Health Research Centers at seven U.S. universities and one medical center to research children's asthma and other respiratory diseases, as well as ways to reduce farm children's exposure to pesticides. In addition, EPA works closely with ATSDR to help fill research gaps and develop chemical-specific toxicological assessments used in risk assessments. In 2004, EPA and ATSDR entered into a formal agreement to ensure close collaboration to avoid duplicating efforts to fill data gaps. Under the agreement, the two agencies formed a work group to coordinate their efforts to develop toxicological assessments for ATSDR's work at

[30]The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. §§ 136-136y.

[31]Applicants must submit data on the acute and chronic toxicity of the pesticide product under different conditions, such as how and at what rate it can be applied. See 40 C.F.R. Part 158 (2005).

specific highly contaminated locations and for EPA's Integrated Risk Information System (IRIS) database.

EPA, NIEHS, and ATSDR also jointly develop and annually review a list of approximately 275 hazardous substances commonly found at the nation's highly contaminated sites and for which ATSDR will prepare toxicological assessments. At each annual review, agency staff may add chemicals to the list and identify priority research to fill gaps in knowledge. Of these 275 chemicals, approximately 150 have been identified by EPA as high-priority needs. Each toxicological assessment contains almost everything that is known about the chemical, including its potential to harm human health or the environment. A key difference between these toxicological assessments and the ones in EPA's IRIS database is that ATSDR includes chronic cancer and noncancer effects, as well as acute effects, while IRIS generally includes only chronic cancer and noncancer effects.

In addition, EPA has begun to establish collaborative relationships with scientific and industry-related researchers. For example, EPA has cooperative agreements with the International Life Sciences Institute's Risk Science Institute (ILSI-RSI), an organization that researches critical scientific issues in risk assessment, such as the development of risk assessment methodologies.[32] These cooperative agreements were specifically designed to engage the scientific community and bring together scientists from different affiliations (including academia, other parts of government, and the private sector including industry) to address risk assessment issues. Under one agreement, ILSI-RSI is to research risk assessment approaches for cumulative and aggregate exposures. In addition, EPA has used research provided by CIIT Centers for Health Research, a chemical research laboratory funded by EPA, industry, and other federal agencies, to provide information for its formaldehyde IRIS assessment. Furthermore, EPA and industry jointly fund the Health Effects Institute (HEI)—an organization that researches the health effects of various air pollutants, including airborne particulate matter and ozone. HEI has provided data for risk assessments and convened panels of experts to review and issue reports related to risk assessment, recently on diesel exhaust. In its 2004 staff paper, EPA noted that it needs to continue to encourage development of the specific data necessary to more

[32]ILSI-RSI is primarily funded through cooperative agreements with regulatory agencies such as EPA and Health Canada, but also receives financial support from the European Commission, the National Institute of Environmental Health Sciences, and industry trade groups.

accurately assess potential risks, particularly with researchers responsible for generating appropriate data, such as those seeking approval to manufacture or use a chemical.

The Office of Pollution Prevention and Toxics has two programs to work with industry to develop data on contaminants that can be used to better understand risks. The first is the High Production Volume (HPV) Challenge Program. This program was officially launched in late 1998 to ensure that a baseline set of data would be made available to the public on approximately 2,800 chemicals that are manufactured or imported in amounts greater than 1 million pounds per year. Diverse stakeholders, including the American Chemistry Council, Environmental Defense, and the American Petroleum Institute participate in the program. The HPV Challenge Program provides an opportunity for all stakeholders, including the public, to comment on the tests and data summaries from the chemical sponsors—companies and consortia that volunteered to make publicly available screening-level data that allow EPA, industry, and other stakeholders to more effectively gauge the potential hazards of HPV chemicals. All comments are publicly available on the World Wide Web. As of January 2006, EPA had commitments from industry sponsors to provide data for 2,247 of the chemicals. The second program, the Voluntary Children's Chemical Evaluation Program, is designed to provide data that will allow the public to better understand the potential health risks to children associated with certain chemical exposures. EPA asked companies that manufacture or import 23 chemicals that have been found in human tissues in various biological monitoring programs to voluntarily sponsor the evaluation of specific chemicals in a pilot program. Thirty-five companies and 10 consortia volunteered to sponsor 20 chemicals. This program was developed only after considering comments and concerns from stakeholders. Of the 23 chemicals chosen for this pilot, data gathering has been completed for 9 and is under way for another 11. The remaining 3 chemicals in the pilot program have no sponsors.

EPA Maintains Databases of Information Related to Risk Assessment

EPA maintains both an agencywide and several program-specific databases of information to help in the development of risk assessments. The primary database used by risk assessors in the program offices is the Integrated Risk Information System (IRIS), an electronic database of descriptive and quantitative information on human health effects that may result from exposure to various chemicals in the environment. Program office staff combine the IRIS data with exposure information they develop to characterize the health risks of a given chemical in a given situation.

Since 1994, EPA has changed the IRIS assessment process in several ways. For example, each IRIS file now contains a discussion of the key studies, as well as a description of the decisions and default assumptions used in the assessment. EPA has also expanded the review that IRIS assessments undergo. For example, internal peer reviewers, including EPA senior health scientists representing program offices and regions, review the IRIS summary and accompanying detailed technical information. After this review, ORD releases the document for external peer review. EPA makes draft assessments available to the public at this time and, following peer review, the IRIS assessment discusses the key issues reviewers raised and EPA's response. In addition, EPA has added a tracking system that allows IRIS users to readily determine where an individual assessment is in its development.

In September 2003, EPA completed a congressionally requested review to assess the need to update information in IRIS, based on concerns that EPA and state regulators rely on potentially outdated scientific information. Input from EPA program and regional offices, the public, and other stakeholders indicated that EPA should, among other things, increase the number of new or updated assessments completed each year to 50. To date, EPA has fallen considerably short of this goal. According to a program official, EPA completed 8 IRIS assessments in 2005, plans to complete 16 in 2006, and has approximately 75 assessments under way. EPA officials said a number of factors, such as the complexity of the assessment process, resource limitations, and extensive peer review, had limited EPA's ability to complete more assessments last year. EPA has increased the number of staff working on IRIS assessments from 6 to 23 and may ultimately increase the number to 29. The review also indicated that EPA needs to assign staff to develop health assessments for IRIS, and provide funding for extramural research and contracts to develop IRIS files and subject them to external peer review.

EPA also changed how it sets priorities for which chemicals need new or updated IRIS assessments.[33] Annually, EPA asks its program offices, regions, and the public to identify contaminants for which it should

[33]EPA uses four criteria to prioritize chemicals for IRIS reviews: (1) EPA statutory, regulatory, or program needs; (2) availability of new scientific information that might significantly change the current information; (3) interest from state and local government or the public; and (4) the amount of additional information that would be needed to complete the review. Ultimately, the decision to assess any given substance hinges on available agency resources.

develop or revise IRIS assessments. EPA publishes the list in the *Federal Register* and requests the public and scientific community to submit any relevant data on substances undergoing review. EPA is currently reviewing ways to increase coordination with other governmental agencies that develop chemical assessments, outreach to stakeholders earlier in the development of IRIS assessments, and consultation with independent external reviewers. In 2004, the IRIS program also initiated a review of available scientific literature for the 460 chemicals in the database that are not under active reassessment to determine whether a reassessment based on new literature could significantly change existing toxicity information. For 63 percent of the chemicals reviewed, no major new health effects studies were found. Such literature reviews will be conducted annually and the findings noted in the IRIS database.

In addition, some program offices maintain databases to enhance their risk assessments. For example, the Office of Air Quality Planning and Standards (OAQPS) maintains a database of dose-response values developed by various sources, including IRIS, ATSDR, and the California Environmental Protection Agency, as an aide for its risk assessors. OAQPS staff update this database as better data become available. As part of its National Air Toxics Assessment—an ongoing comprehensive evaluation of hazardous air pollutants in the United States—EPA assessed 32 air pollutants plus particulate matter in diesel exhaust in 1996. The national assessment is designed to identify air pollutants with the greatest potential to harm human health, and the results will help set priorities for collecting additional data. As part of its assessment, EPA compiled a national emissions inventory of hazardous air pollutants from outdoor sources, estimated population exposures to the pollutants, and characterized the potential cancer and noncancer health risks from breathing the pollutants.

ORD also maintains personal monitoring data on the chemicals in the air, foods and beverages, water, and dust in an individual's personal indoor and outdoor environments. For example, in its National Human Exposure Assessment Survey (NHEXAS) program, which was completed in 1998, ORD collected human exposure data from hundreds of subjects from several areas of the country. NHEXAS provided data on background levels of total exposure to environmental contaminants that can be used as a baseline in exposure and risk assessments to estimate whether specific populations are exposed to increased levels of environmental contaminants.

EPA Has Improved Its Choice and Communication of Default Options

EPA has explicitly stated the need for risk assessors to identify when they relied on a default option, why they chose it, and when they departed from using a standard default option, but the agency acknowledges more could be done. To carry out its mission to protect human health, EPA's risk assessment procedures, including its default options, are protective of human health. In three recent guidance documents—the 2004 staff paper, the 2005 cancer guidelines, and the risk characterization handbook—EPA advocated more transparency in the choice of default options. These documents summarize a significant change in EPA's approach. Specifically, EPA first critically examines all relevant and available data to assess health risks, then uses the default options only in the absence of adequate contaminant-specific data. EPA also states in its staff paper that it bases its default assumptions on peer reviewed published studies, empirical observations, extrapolation from related observations, and scientific theory. Moreover, the cancer guidelines include an appendix that defines the basis for each of the default options that may be used in a cancer risk assessment. The *Risk Characterization Handbook* notes that risk assessments should describe the full range of default options that were used, including ones to address uncertainty. Moreover, the handbook states that when defaults are used, the risk assessment should reference the relevant EPA guidance that explains them.

EPA program offices also advocate greater transparency when using default options. Specifically, the majority of IRIS assessments completed since 1997 describe the defaults used in the analysis and any departures from those defaults. The Office of Air Quality Planning and Standard's *Air Toxics Risk Assessment Reference Library* contains a number of references to defaults that should be used in the course of preparing a human health risk assessment.[34] For example, to estimate an individual's exposure to an air pollutant, the guidance presents the default option to use for exposure in a screening-level assessment, namely that the individual remains at a single location and continuously breathes polluted air.

Despite the increased focus on more transparency in the use of defaults, EPA acknowledges it could more consistently describe how the default was developed and explain why it is a reasonable assumption. In its staff

[34]The *Air Toxics Risk Assessment Reference Library* is a multivolume technical resource manual that provides information on the fundamental principles of risk-based assessment for hazardous air pollutants and how to apply those principles in different settings.

paper, EPA acknowledges it needs to ensure that the defaults are supported by the best available data and should look for opportunities to increase certainty and confidence in the defaults and extrapolations used. EPA also acknowledges it may need to re-examine older risk assessments that relied on defaults that can now be replaced with relevant data. To a large degree, the use of defaults is intertwined with EPA's ability to get the data it needs. As was discussed previously, EPA has targeted research, both within EPA and through its grant programs, to understand variability and uncertainty in the data derived from studies of laboratory animals, and this research may further reduce EPA's need to rely on default options.

EPA Has Taken Steps to Enhance Its Modeling Capabilities and Embrace New Methodologies

Since 1994, EPA has taken several steps to enhance its modeling capabilities and embrace new methodologies for risk assessment through improved guidance and workshops. To help improve its models, EPA's Agency Task Force on Environmental Regulatory Modeling published a report that concluded a need existed for, among other things, training and technical support, agency guidance on external peer review of environmental regulatory modeling, and creation of a Committee on Regulatory Environmental Modeling.[35] Also in 1994, EPA's Risk Assessment Forum developed a draft protocol to evaluate models for exposure assessments.[36] In 1997, ORD and program offices conducted an agencywide conference, called the Models 2000 Workshop, to facilitate adherence to existing guidance on modeling, to define and implement improvements in how the agency developed and used models, and to recommend an implementation plan for improving modeling within the agency.

EPA followed up these activities in 2000 by creating the Committee on Regulatory Environmental Modeling (CREM) to promote consistency and consensus within the agency on modeling issues (including modeling guidance, development, and application) and to enhance internal and external communications on modeling activities. CREM supports and enhances the existing modeling activities in the program offices and provides EPA with tools to support environmental decision making. CREM

[35]U.S. Environmental Protection Agency, *Report of the Agency Task Force on Environmental Regulatory Modeling—Guidance, Support Needs, Draft Criteria and Charter* (Washington, D.C., 1994).

[36]U.S. Environmental Protection Agency, *Model Validation for Predictive Exposure Assessments* (Washington, D.C., 1994).

also provides the public and EPA staff with a central point of inquiry about EPA's use of models. In 2000, CREM launched agencywide activities designed to enhance the development, use, and selection of regulatory environmental models at EPA. One such activity—a workshop to facilitate discussion of good modeling practices—resulted in the development of modeling guidance.

In 2003, CREM developed guidance and created a database—called the Models Knowledge Base—of the models most frequently used in EPA.[37] The guidance recommends best practices to help determine when a model, despite its uncertainties, can be appropriately used to inform a decision. Specifically, it recommends that model developers and users subject their model to credible, objective peer review, assess the quality of the data they use as inputs, and perform sensitivity and uncertainty analysis to determine which of the model inputs has the greatest impact on the modeled results.

EPA has also incorporated efforts to improve models in its research strategies and implementation plans. For example, in its plan for research on hazardous air pollutants, EPA established a long-term goal to reduce uncertainties in risk assessments through methods, data, and models of acute and chronic exposures and exposures through multiple pathways at both the national and regional levels. In addition, one of ORD's laboratories established an exposure modeling research branch and develops population exposure models, such as the Stochastic Human Exposure and Dose Simulation model for inhalation and exposures of general and sensitive subpopulations through multiple pathways. EPA has also begun to use geographic information systems (GIS) to present risk information spatially. For example, a GIS system is being developed that maps all of the drinking water intakes in the United States and their associated watersheds, so that the agency can better assess risks to drinking water supplies stemming from activities in the related watershed. For risk assessments of hazardous air pollutants, GIS can display and analyze data during planning, scoping, and problem formulation, during the exposure assessment, and during the characterization of risks. GIS can also help communicate information to risk managers and other stakeholders.

[37]U.S. Environmental Protection Agency, *Draft Guidance on the Development, Evaluation, and Application of Regulatory Environmental Models* (Washington, D.C., 2003).

In addition to models, EPA is beginning to embrace such new risk assessment methodologies as probabilistic risk assessment and mode of action analysis. Probabilistic risk assessment characterizes the variability or uncertainty in risk estimates as the range or distribution of the number of times each possible outcome will occur. In probabilistic risk assessment, one or more variables in the risk equation, such as the exposure rate, is defined as a distribution rather than as a single number. A primary advantage of probabilistic risk assessment is that it provides a quantitative description of the degree of variability or uncertainty. EPA's 1997 policy states that probabilistic techniques, such as Monte Carlo analysis, can be viable statistical tools to analyze variability in risk assessments, when they are based on adequate supporting data and credible assumptions.[38] The guidance presents a general framework and broad set of principles to ensure the use of good scientific practices when conducting probabilistic analyses of variability and uncertainty. EPA currently uses a number of models that include probabilistic analyses and is developing a new modeling framework, known as the Multimedia Integrated Modeling System, that will further enhance the agency's ability to probabilistically model uncertainty.

EPA's recently revised cancer guidelines advocate the use of a mode of action analysis—based on the sequence of biological events that must occur to produce a harmful effect—to improve the accuracy of risk assessments. As a general rule, EPA assumes that toxic responses observed in laboratory animals indicate that the same responses are likely to occur in people even though differences in such areas as metabolic rates can result in different sensitivities between laboratory animals and humans. Mode of action analysis will more clearly indicate whether a difference exists between animals and humans in their response to contaminants. In addition, the guidelines present a new cancer characterization system consisting of five summary descriptors, to be used in conjunction with narrative, to describe the extent to which available data support the conclusion that a contaminant causes cancer in humans and to justify the summary descriptor selected. For noncancer risk assessments, EPA has used, and continues to refine, the benchmark dose methodology, which identifies the dose or concentration of a contaminant that slightly increases the likelihood of an adverse effect.

[38]U.S. Environmental Protection Agency, *Policy for Use of Probabilistic Analysis in Risk Assessment* (Washington, D.C., 2003).

EPA Is Introducing More Quantitative Characterization of Uncertainty into Its Risk Assessments

Uncertainty is inherent in all phases of risk assessment, from hazard identification through risk characterization. Over the years, EPA has relied more on qualitative, or descriptive, characterizations of uncertainty and less on quantitative, or numeric, characterizations. EPA's practice now is to use a tiered approach to analyze uncertainty. That is, EPA starts with a simple description of uncertainty and sequentially employs more sophisticated quantitative analysis, such as sensitivity analysis, provided the additional analysis reduces the uncertainty. To characterize risk quantitatively, EPA has typically used approaches that produce a single number to characterize the risk in terms of the level of a contaminant that does not cause harm, as opposed to presenting a range of possible values.

Although EPA is beginning to use probabilistic approaches in exposure assessments, and has done so for six principal air pollutants, it does not typically do so to analyze uncertainty in its dose-response analyses, though its Science Advisory Board encouraged development of such approaches in 2000. EPA acknowledged in its 2004 staff paper that probabilistic risk assessment could be used more frequently and could provide useful information beyond screening-level assessments. However, the staff paper said probabilistic analysis may not be appropriate in all situations and the accuracy of the analysis will depend largely on the availability and quality of the data used in the analysis.

Another quantitative approach to uncertainty is the use of uncertainty factors to account for such unknowns as variation in sensitivity among members of the human population or the appropriateness of extrapolating animal data to humans. EPA routinely uses uncertainty factors when it estimates the daily exposure to the human population that is likely to be without appreciable risk of adverse effects during a lifetime. This daily exposure estimate is called a reference dose for contaminants that are consumed and a reference concentration for inhaled contaminants. EPA states in its 2004 staff paper that it applies uncertainty factors in health assessments based on available data and the scientific judgment of EPA risk assessors and peer reviewers. According to EPA, most IRIS toxicological assessments, which contain a chemical's reference dose and reference concentration, provide justifications for the uncertainty factors applied to a particular chemical. Moreover, the factors undergo rigorous internal, and independent, external scientific peer review before being used in IRIS assessments.

EPA has issued a number of documents that delineate the need to clearly and consistently characterize uncertainty in risk assessments. In 1995, EPA issued a risk characterization policy that stated that the risk

assessment should fully, openly, and clearly characterize risks, and should disclose the scientific analyses, uncertainties, assumptions, and policies underlying the decisions. This policy was followed in December 2000 by the *Risk Characterization Handbook*, which includes guidance on how to address, among other things, uncertainty in risk assessment and describes the need and methods to present the sources and magnitude of uncertainty to the risk manager. More recently, the 2005 revised cancer guidelines discuss each of the major uncertainties, such as model uncertainty or uncertainty related to human variation, and stress that assessments should discuss the significant uncertainties encountered in the analysis. For example, the guidance calls for the assessments of hazard, dose-response, and exposure to have accompanying technical characterizations covering the strengths and limitations of data and a discussion of uncertainty.

EPA Better Analyzes and Communicates Variability in both Exposure and Susceptibility

EPA has made progress in describing variability due to differences in both the exposure individuals receive and the susceptibility of exposed individuals to adverse effects. A key document EPA risk assessors use to account for variation in exposure is its *Exposure Factors Handbook*, originally issued in 1989 and revised in 1997. The handbook summarizes data on human behaviors and characteristics that influence exposure to environmental contaminants and recommends values to account for those factors in assessing risk. Specifically, the handbook contains a series of over 150 data tables that provide information on how much time individuals spend at various activities and in various environments. Assessors can use these data to develop exposure duration estimates for exposure scenarios. For example, the tables contain statistics—broken down by age, gender, race, education, and some medical conditions, such as asthma or emphysema—for time spent in various outdoor locations. The handbook also provides general guidance to risk assessors on the types of variability relevant to a risk assessment and ways variability can be analyzed and addressed.

All program offices address exposure variability in their risk assessments, although they do so in different ways. For example, risk assessors in the Office of Air Quality Planning and Standards who set certain air quality standards for six principal pollutants said they consider individual activity patterns for sensitive populations like children or asthmatics in exposure modeling by including a distribution of breathing rates to reflect variability inherent in the population. Furthermore, by modeling to protect the most sensitive or at-risks groups, they are assured of protecting the rest of the population. Variability in exposure to the six principal pollutants is generally described qualitatively in scientific summaries for each

pollutant. The Office of Water includes an analysis of risks to various subpopulations and a narrative discussion of the strengths and weaknesses of the studies it used to estimate exposure, but generally does not include a quantitative analysis. The Office of Pesticide Programs considers 24 different population subgroups in its exposure estimates, including differences in age, gender, ethnicity, and geographic dispersion. When data allow, the Office of Pesticide Programs develops a distribution of exposures and risks for its more refined risk assessments.

To further its understanding of variability in exposure, EPA has undertaken a number of research projects. For example, one of ORD's laboratories conducted the National Human Activity Pattern Survey to provide detailed human exposure information for specific populations and allow EPA to better understand actual human exposure to pollutants in real-world situations. The survey results are stored in the Consolidated Human Activity Database to help risk assessors estimate the time that exposed people spend in various environments and their inhalation, ingestion, and dermal absorption rates while in those environments. This laboratory also conducts research to define, quantify, and reduce the uncertainty associated with the exposure and risk assessments, to develop improved methods to more accurately measure exposure and dose, and to develop technical information and quantitative tools to predict the nature and magnitude of human exposures to environmental contaminants. A recent EPA study was designed to identify chemicals commonly used in homes or day care centers, and whether children in these environments encountered the chemicals in the course of their daily activities.[39] The research sought to identify the major routes (i.e., breathing and ingestion) and sources (i.e., dust, food, air, soil, and water) through which children come into contact with chemicals.

Variability also exists with regard to susceptibility to adverse affects because of inherent differences among humans. EPA most recently addressed variability in susceptibility in the 2005 revision of its cancer guidelines, which describe the importance of separate risk assessments for all potentially sensitive life stages, including adults and children. The supplementary cancer guidelines for children address issues pertaining to cancer risks associated with early-life exposures. Legislation can also require EPA to consider potentially susceptible populations and life

[39]U.S. Environmental Protection Agency, *Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants* (Washington, D.C., 1999).

stages. For example, the Safe Drinking Water Act Amendments mandate that EPA consider risks to groups within the general population that are at greater risk of adverse health effects, including children, the elderly, and people with serious illnesses. In addition, the Food Quality Protection Act contains special provisions for the consideration of risks to children from pesticides. In 1995, EPA's Science Policy Council called for EPA to consider the risks to infants and children consistently and explicitly as part of its risk assessments. In 1997, the White House issued an executive order that required EPA and other federal agencies to identify and assess environmental health and safety risks that may disproportionately affect children and to ensure that policies, programs, activities, and standards address such disproportionate risks.[40]

In its 2004 staff paper, EPA acknowledges that characterizing variability for susceptible populations and life stages is an area where it could improve, although the absence of data limits its efforts. In 2002, EPA pointed out that data are limited to identify susceptible populations and life stages for many contaminants.[41] In these situations, EPA typically relies on default options, such as the use of uncertainty factors to account for variations in susceptibility. Many of the exposure assumptions and default values used to assess plausible current and future exposure scenarios can be found in EPA's 1997 *Exposure Factors Handbook*, and recent updates to the handbook are available online.

Another way EPA addresses variability is through research. One of ORD's four strategic research directions in its *Human Health Research Strategy* is designed to improve the understanding of why some people and groups are more susceptible and highly exposed than others. According to this strategy, ORD's research on subpopulations will focus on three factors—life stage, genetic factors, and pre-existing diseases—that have been identified by a program office and the scientific community as having a high priority for risk assessment. In 2000, ORD released its *Strategy for Research on Environmental Risks to Children* to strengthen the scientific foundation of risk assessment and management decisions that affect children and guide EPA's research needs and priorities over the following 5 to 10 years. Approximately 75 percent of the funding for this strategy will

[40]Exec. Order No. 13045, 62 Fed. Reg. 19885 (Apr. 21, 1997).

[41]U.S. Environmental Protection Agency, *Review of the Reference Dose and Reference Concentration Processes* (Washington, D.C., 2002).

be dedicated to research grants under the STAR program, such as those designed to evaluate children's exposure to pesticides.

EPA Has Begun to Consider the Combined Effects of Exposure to Multiple Contaminants through Multiple Pathways

To help risk assessors analyze the health effects of exposure to multiple contaminants (cumulative exposure) and through multiple routes (aggregate exposure), EPA has issued guidance, developed methods and models, and supported research. In 1997, EPA's Science Policy Council issued guidance on cumulative risk assessment. This guidance directs each office to consider cumulative risk in planning major risk assessments and, where relevant data are available, to broaden the scope of the assessment to integrate multiple sources, effects, pathways, stressors, and populations for cumulative risk analyses. The guidance also highlights the need to ensure that the public and other stakeholders have an opportunity to help define the way EPA assesses an environmental or public health problem and calls for ongoing communication and coordination among EPA's risk assessors, risk managers, economists, engineers, and other technical experts.

In 2000, EPA updated its 1986 guidance on chemical mixtures, to generate a consistent agencywide approach to assess health risks from exposures to multiple chemicals.[42] The guidance is organized according to the type of data available to risk assessors, ranging from data-rich to data-poor situations, to help risk assessors select an appropriate methodology. For example, if data are of poor quality or quantitative data are very limited on chemical mixtures, the risk assessor may choose to perform a qualitative analysis of the potential human health impacts from exposure to the mixture. The guidance also contains procedures to develop toxicity equivalency factors, based on the toxicity of components of the mixture, to assess the risk from mixtures in the absence of data on the specific mixture.

In 2003, EPA's Risk Assessment Forum developed a simple, flexible framework to help risk assessors consistently conduct and evaluate cumulative risk assessments.[43] The framework is conceptually similar to the one used in human health assessments of a single contaminant in that

[42]U.S. Environmental Protection Agency, *Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures* (Washington, D.C., 2000).

[43]U.S. Environmental Protection Agency, *Framework for Cumulative Risk Assessment* (Washington, D.C., 2003).

it follows a three-stage approach of (1) planning, scoping, and problem formulation; (2) analysis; and (3) risk characterization. In addition, the document also highlights needed areas of research and methods development that may be important to the evaluation of cumulative risks, such as understanding how the sequence and timing of exposure may influence the ultimate risk for effects.

EPA risk assessors use a number of models and methodologies to analyze multiple routes of exposure. For example, the branch of the Office of Air Quality Planning and Standards that regulates hazardous air pollutants employs the Multiple Pathways of Exposure model to assess and predict the movement and behavior of chemicals in the environment. For example, the Multiple Pathways of Exposure model includes procedures to estimate human exposures and health risks that result from the transfer of pollutants from the air to soil and surface water bodies and the subsequent uptake of the pollutant by plants, animals, and humans. The model specifically addresses exposures from breathing; consuming food, water, and soil; and contact with skin. More recently, EPA developed the Total Risk Integrated Methodology (TRIM) and created the TRIM Fate, Transport, and Ecological Exposure model that describes the movement of air pollutants emitted from any type of stationary source as well as their transformation over time in water, air and soil.

Some program offices have also taken steps to explicitly consider the risks associated with more than one route of exposure or more than one chemical. Specifically, the Office of Pesticide Programs issued guidance in 2001 and 2002 in response to statutory requirements to assess the risk of aggregate exposure—exposure to a single chemical by multiple pathways and routes.[44] The first set of guidance focuses on how to assess aggregate risk in those cases where more extensive data and more sophisticated exposure assessment methods and tools are available; this guidance also emphasizes, when data are available, the use of distributional data—aggregate exposures of many individuals in the population of interest—for all pathways of exposure.[45] This approach allows the risk assessor to more fully evaluate exposure and resulting risk across the entire population, rather than the exposure of a single highly exposed individual. The second

[44]See § 405 of the Food Quality Protection Act of 1996, amending 21 U.S.C. § 346a(b)(2)(D)(vi).

[45]U.S. Environmental Protection Agency, *General Principles for Performing Aggregate Exposure and Risk Assessments* (Washington, D.C., 2001).

set of guidance describes a framework to assess potential human health risks from all pathways of exposure to multiple pesticides that share a common mechanism of toxicity—that is, the pesticides produce a similar toxic effect on the same organ or tissue.[46]

In addition, the branch of the Office of Air Quality Planning and Standards that regulates hazardous air pollutants developed the Integrated Urban Air Toxics Strategy, which is used to consider cumulative risks presented by exposures to hazardous air pollutants emitted from various sources. Staff can assess risk at both a national and an urban or a neighborhood scale. Furthermore, the hazardous air pollutant office developed guidance on multipathway risk assessments that are particularly important for hazardous air pollutants, such as mercury and dioxins, because human exposure occurs both from breathing air containing the toxins and from consuming plants, water, and soil where the pollutants were deposited. Moreover, these pollutants persist in the environment for long periods of time and may also accumulate in the tissues of commonly consumed plants and animals to levels that are harmful to humans.[47] The guidance, maintained in the *Air Toxics Risk Assessment Reference Library*, describes how to plan, scope, and formulate the problem, conduct the analysis, and characterize the risk for such cases.

The extent to which program offices assess the effects of cumulative and aggregate exposures is related to the regulatory responsibilities of each office and by the availability of data. For example, the hazardous air pollutant office routinely analyzes a mix of chemicals from various emitting sources, such as petroleum refineries, to regulate hazardous air pollutants.[48] Similarly, as mentioned above, the Office of Pesticide Programs is required to consider exposure to pesticides from various pathways, such as food, drinking water, and residential uses, and various routes, such as eating, breathing, and contact with skin. In contrast, the Toxic Substances Control Act does not require the Office of Pollution

[46]U.S. Environmental Protection Agency, *Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity* (Washington, D.C., 2002).

[47]For example, metals released into the air may be deposited on the ground, where they remain in surface soils for long periods of time. The chemicals in the soil may be taken up into plants through the roots and accumulate in the tissues of foraging animals.

[48]By statute, hazardous air pollutants are regulated not as individual pollutants but by emission sources that consist of a group of similar industrial processes or industries that release multiple pollutants.

Prevention and Toxics to assess the risks of a new chemical that may occur through its interaction with other chemicals. The office also assesses the risks of existing chemicals but cannot conduct cumulative risk assessment for classes of chemical that share a common mode of action because no data exist. Program managers hope such data will become available in the future.

In its 2004 staff paper, EPA commented that while it has increased its emphasis on evaluating cumulative risks, it needs to expand on approaches to do so, and it needs to produce a rigorous scientific base to support such evaluations. To that end, one of ORD's four strategic research directions in its Human Health Research Strategy is to improve assessments of aggregate and cumulative risks. Specific research objectives are to develop exposure models and methods, provide a scientific basis to predict interactive effects of contaminants in mixtures, and determine the most appropriate approaches to combine effects and risks from mixtures.

EPA Risk Assessors Responding to Our Survey Reported That Process Modifications Have Helped Them Prepare Better Risk Assessments but That Collaboration and Training Limitations Hamper Further Progress

EPA risk assessors responding to our survey reported that some modifications to its risk assessment processes, such as new or updated EPA guidance issued over the last 10 years, have been helpful. They also said that although collaboration among internal and external researchers has improved, problems remain with communication and coordination. Finally, risk assessors said that the training they've taken in the last 5 years has been beneficial, but they need additional training on analytic tools, such as modeling, and on other scientific disciplines related to risk assessment.

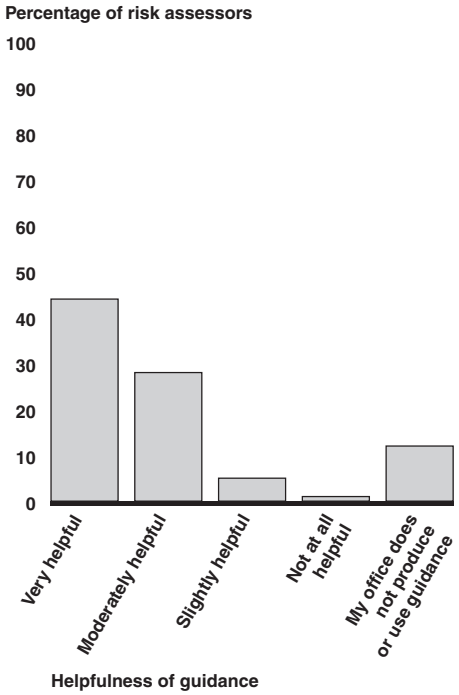
EPA Has Issued Numerous Guidance Documents That Have Been Generally Helpful to Risk Assessors

At least two-thirds of risk assessors responding to our survey who reported using guidelines or reference documents indicated that these documents were moderately to very helpful in preparing risk assessments.[49] In addition, between one-third and two-thirds of respondents who reported using policy documents said these documents were moderately to very helpful in preparing risk assessments. More specifically, many risk assessors said agencywide guidelines and reference documents provide a framework to assess risks to human health that help make risk assessments more consistent. For example, some risk assessors noted the usefulness of agency reviewed or approved procedures to support their assessments. In addition, some risk assessors said the guidelines and reference documents helped clarify issues, and several assessors said they were a good source for data needed to conduct assessments. Risk assessors responding to our survey cited the *Guidelines for Carcinogen Risk Assessment* as the document most frequently used when preparing human health risk assessments. More specifically, several risk assessors noted that the carcinogen guidelines provide a useful framework for preparing risk assessments. Many risk assessors commented that agencywide guidelines and reference documents are helpful or provide useful examples. For example, a few risk assessors stated that the *Exposure Factors Handbook* helps provide consistency among EPA offices that conduct exposure assessments because it defines standard values for exposure, and the rationale behind those values. Another assessor said that the *Review of the Reference Dose and Reference Concentration Processes* provides comprehensive guidance on setting reference values and contains a case study that serves as a model for concise and well-written hazard identification. Although risk assessors responding to our survey reported that guidance documents are generally helpful, many expressed concerns about them. For example, some risk assessors consider the documents too general or too difficult to decipher.

[49]Guidelines refer to the *Guidelines for Carcinogen Risk Assessment*, *Guidelines for Neurotoxicity Risk Assessment*, *Guidelines for Reproductive Toxicity Risk Assessment*, and *Supplemental Guidelines for Chemical Mixtures*. Reference documents refer to the *Assessment Factors Handbook*, *Exposure Factors Handbook*, *Framework for Cumulative Risk Assessment*, *Guiding Principles for Monte Carlo Analysis*, *Peer Review Handbook*, *Review of Reference Dose and Reference Concentration Processes*, *Risk Assessment Principles and Practices*, and *Risk Characterization Handbook*. Policy documents refer to the *Policy on Evaluating Health Risks to Children*, *Policy for Use of Probabilistic Analysis in Risk Assessment*, *Interim Genomics Policy*, and *Interim Position on Environmental Endocrine Disruption*.

In addition, 82 percent of the risk assessors whose offices have office-specific guidance said that the guidance is very or moderately helpful with regard to preparing risk assessments. (See fig. 2.) According to many risk assessors, office-specific guidance provides information in a format relevant to each office's specific needs. For example, the Office of Pesticide Programs periodically issues "hot sheets" that describe how to apply general guidance to pesticide product risk assessments. In addition, the Office of Air and Radiation created the *Air Toxics Risk Assessment Reference Library* that provides information on how to analyze the risks from hazardous air pollutants. Over 65 percent of risk assessors reported that EPA and program offices were moderately to very effective at disseminating guidance.

Figure 2: Helpfulness of Office-Specific Guidance



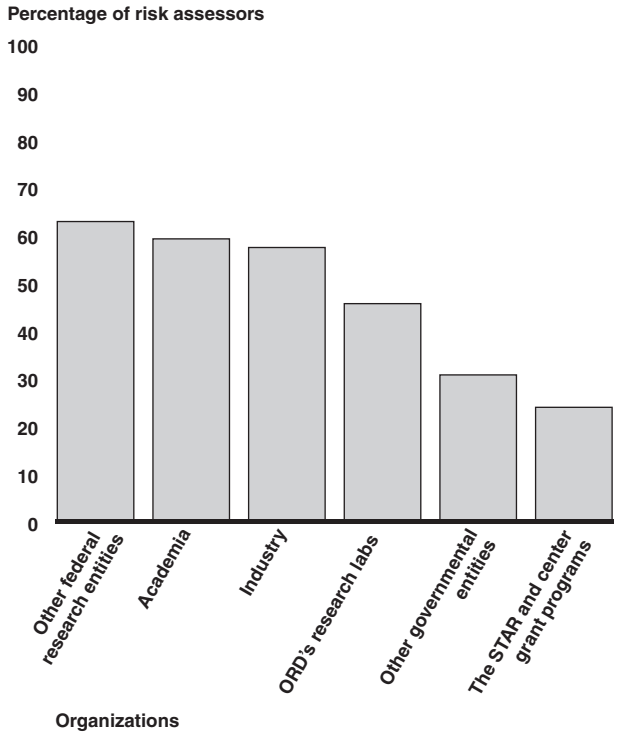
Source: GAO analysis of survey data.

Note: Percentages do not total to 100 because of some risk assessors did not respond to this question.

Collaboration Has Improved EPA's Ability to Conduct Risk Assessment, but Problems Remain

To prepare risk assessments, EPA relies on external peer review and scientific data from a variety of sources on the potential health risks from exposure to contaminants. Collectively, this collaboration has improved EPA's ability to conduct those assessments. For example, 35 percent of risk assessors responding to our survey reported that external peer review, which is often conducted by independent researchers, has definitely helped improve the overall quality of EPA's risk assessments, with an additional 48 percent noting that it has probably helped improve the overall quality. Furthermore, at least 32 percent noted that peer review has definitely helped ensure that the science used in risk assessments is appropriately characterized, helped advance the use of new scientific methods or models, and helped EPA produce risk assessments that are more defensible. Another 38 percent said that peer review has probably helped with these improvements. In addition, responding EPA risk assessors rely primarily on other federal research entities, academia, and industry, and to a slightly lesser extent, ORD's research laboratories, to meet their offices' research needs. (See fig. 3.)

Figure 3: Risk Assessors That Generally or Strongly Agree That Organizations Help Fill Data Needs



Source: GAO analysis of survey data.

More specifically, 63 percent of risk assessors generally or strongly agreed that they relied on other federal research entities, such as the National Toxicology Program; [50] the National Institute for Environmental Health Sciences (NIEHS) and the National Cancer Institute—both within the National Institutes of Health; and the Agency for Toxic Substances and Disease Registry (ATSDR) to help fill their offices' needs for scientific data. EPA has established formal collaborative agreements with both NIEHS and ATSDR to research children's health and to develop toxicological data useful to both agencies, respectively. In addition, EPA

[50]The National Toxicology Program is an interagency program established by the Department of Health and Human Services that provides information about potentially toxic chemicals to health, regulatory, and research agencies, scientific and medical communities, and the public.

has also collaborated with the U.S. Geological Service to identify contaminants in ground and surface waters.

In addition to federal research entities, over 57 percent of respondents generally or strongly agreed that their offices rely on research from academia and industry to meet their research needs. For example, EPA has formal agreements with the International Life Sciences Institute's Risk Science Institute and the Health Effects Institute to develop research on approaches to analyze cumulative and aggregate exposures and the health effects of various air pollutants, respectively. EPA also relies heavily on industry-generated research on specific chemical substances. For example, under the laws that govern registration of pesticide products and new chemicals, applicants must supply specific data for relevant EPA offices to review when deciding whether to approve the pesticide products or chemicals in question.

Furthermore, 46 percent of risk assessors said they relied on ORD's laboratories to generate research that helps fill scientific data needs. For example, some risk assessors said scientists from ORD's laboratories provide useful technical guidance on scientific issues or the risk assessment process. Another risk assessor commented that ORD's expertise is very useful to help interpret unusual findings or to advise on emerging issues. One risk assessor stated that ORD helped develop a specific model to use in probabilistic risk assessments. Other types of collaboration with ORD's laboratories include help to develop models for assessing dose and response relationships, to interpret toxicity data, to conduct epidemiological studies, and to develop scientific summaries for risk assessments of priority air pollutants.

Overall, of the risk assessors who said they often or always collaborate with other EPA offices, at least 46 percent said that the collaboration was very effective. A few risk assessors commented that collaboration has become more effective in recent years, in part because staff in the various offices have more contact with one other, established scientist-to-scientist relationships, or learned whom to contact to address a particular question. For example, one risk assessor pointed out that cross-agency workgroups help to facilitate agencywide collaboration. Furthermore, a few risk assessors commented that the program offices' knowledge of the regulatory context in which research will be used helps ORD's researchers structure their work. For example, NERL collaborated with the Office of Air to fund studies that coordinated the format of data produced by different researchers to enhance the consistency of research approaches, which created more powerful results and made the data more useful to

program offices. Finally, because some chemicals may be assessed by more than one office, collaboration across program offices helps ensure the consistency of risk assessments across EPA. For example, the Office of Pesticide Programs and the Office of Water may both prepare risk assessments for certain contaminants that may be found on food and in drinking water.

Despite the improvements to collaboration at EPA, some risk assessors pointed out two barriers that limit collaboration. Specifically, assessors noted that conflicting priorities or goals among EPA offices and poor communication between some offices hinder the effectiveness of collaboration. For example, although some chemicals are studied by more than one office within EPA, the approaches and timelines differ among offices because the laws and responsibilities for each program office can differ significantly. As a result, what may be a priority chemical in one program office may not be a priority in another, thereby hindering timely collaboration. Furthermore, a couple of risk assessors found collaboration challenging because they could not find the right person in another office to communicate with on a specific issue.

Several risk assessors suggested ways to improve and increase communication among program offices, ORD, and non-EPA organizations. For example, some risk assessors suggested more interagency work groups or meetings as a way to address research needs and foster information exchange on the development of methods. A few risk assessors suggested that a central library of risk assessment information would facilitate collaboration and avoid duplicating work already done by others. Specifically, one risk assessor said EPA could provide centralized databases of work conducted by different agencies and organizations, such as chemical-specific toxicity data, specific exposure or other values, and points of contact at each office.

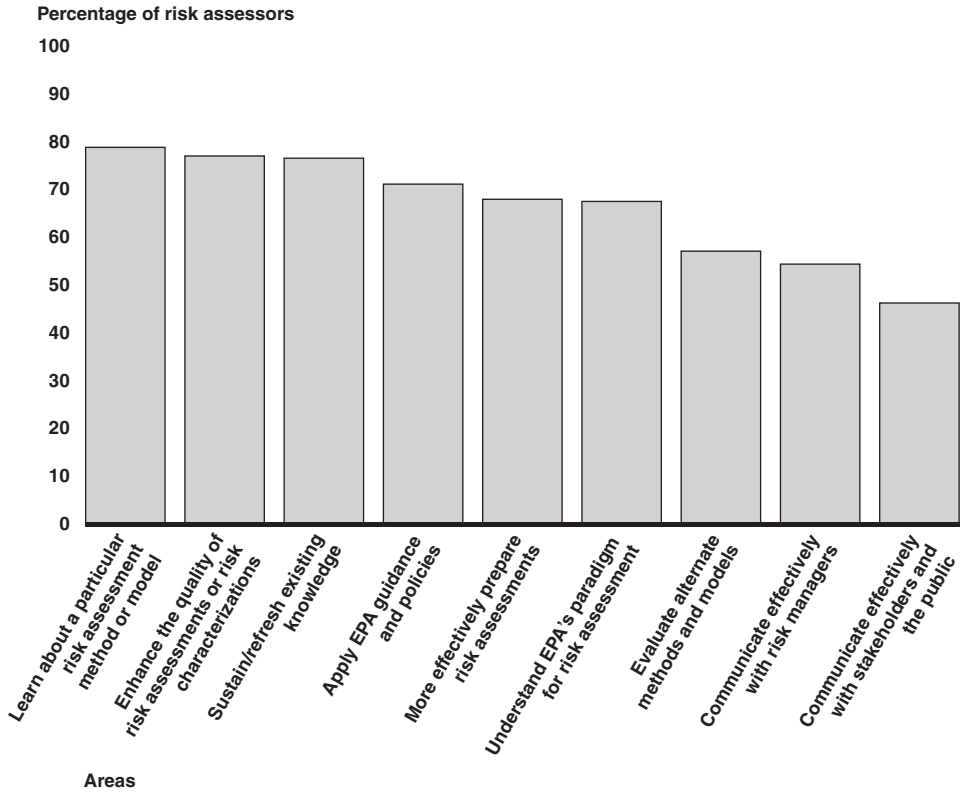
EPA's Training Has Been Helpful, but Risk Assessors and Managers Lack Sufficient Training on Analytic Tools and Emerging Issues

At least 80 percent of risk assessors responding to our survey said that the training they received, whether on the job, self-directed, office specific, or agencywide, was moderately to very useful. Moreover, over half of these risk assessors said that training improved their ability to prepare risk assessments. Nevertheless, risk assessors surveyed and agency officials interviewed reported that both risk assessors and managers would benefit from more in-depth training on subjects such as analytic tools and emerging scientific issues.

Risk Assessors Have Enhanced Their Skills through Training in Various Areas

Over half of the risk assessors reported that training had moderately or greatly improved their abilities in at least seven different risk assessment skill and knowledge areas. More specifically, over 75 percent of risk assessors reported that training has helped them learn about a particular risk assessment method or model, enhance the quality of risk assessments or risk characterizations they prepare, and maintain or refresh their existing knowledge (see fig. 4). To a slightly lesser extent, training also helped risk assessors apply EPA guidance and policies, more effectively prepare risk assessments, and understand EPA's four-stage paradigm for risk assessment.

Figure 4: Areas in Which Training Has Moderately or Greatly Improved Risk Assessor Knowledge and Skills

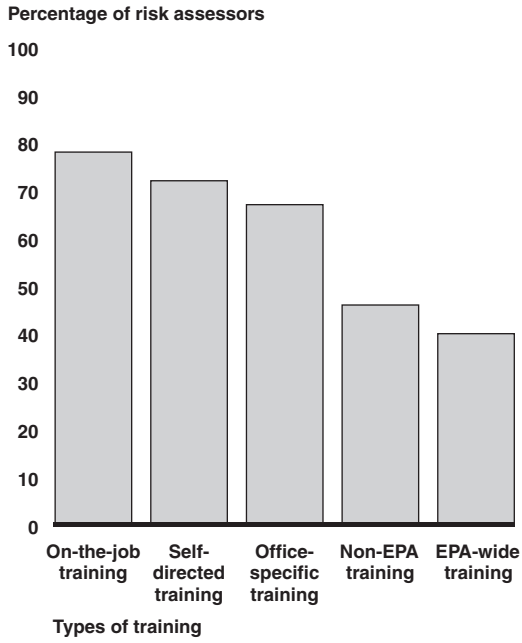


Source: GAO analysis of survey data.

Over three-quarters of risk assessors reported that they participated in on-the-job (82 percent) or self-directed (77 percent) training to enhance their skills. (See fig. 5.) According to risk assessors in the office that reviews

new chemical applications, training is primarily on the job, largely because the office makes risk assessment decisions under tight time frames, which limits the time available for formal training, according to program officials. Similarly, workload constraints affect opportunities for formal training at the Office of Water, which instead relies primarily on self-directed or on-the-job training. Some on-the-job training takes the form of mentoring, such as in the Office of Research and Development, where senior staff are expected to mentor newer staff.

Figure 5: Types of Training Taken by Risk Assessors



Source: GAO analysis of survey data.

In addition, over 70 percent of risk assessors who responded to our survey reported that they participated in office-specific training to enhance their risk assessment skills. For example, the Office of Pesticide Programs (OPP) has a comprehensive risk assessment training program focusing mostly on scientific issues, but also on other issues to improve the overall quality of risk assessments. This training features speakers, including some from outside OPP, such as from other EPA offices, academia, and industry. These biweekly sessions are broadcast live over the office's internal computer system and taped for future use as well as broader distribution, so that staff can access them as needed. Moreover, OPP's

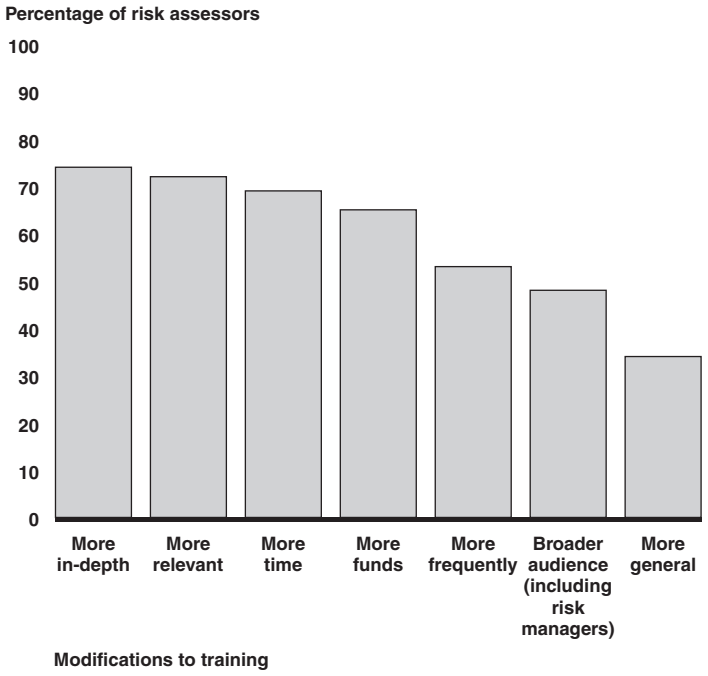
training program includes having experienced risk assessors nearing retirement share their knowledge with other staff. Of the risk assessors responding to our survey that work in OPP, over 90 percent took advantage of its office-specific training. A similarly high percentage of staff in the hazardous air pollutant branch of the Office of Air and Radiation reported that they took that office's training on preparing risk assessments.

In addition, 50 percent of risk assessors said they attended external training, such as professional society meetings sponsored by the Society for Risk Analysis, Health Effects Institute, and the Society of Toxicology and university courses related to scientific methods and disciplines. Finally, 46 percent of risk assessors said they participated in agencywide training. According to an EPA official, the agency offers a broad array of agencywide risk assessment training. For example, EPA's Risk Assessment Forum develops training to accompany the agency's risk assessment guidelines. More specifically, forum staff conducted briefings and orientation sessions on the 2005 cancer risk assessment guidelines. In addition, the forum sponsors colloquia approximately twice a year for staff to exchange information on risk assessment issues. Recent colloquia dealt with dermal exposure assessment and whether additional guidance is needed on the use of Monte Carlo analysis. Colloquia usually result in reports that summarize the findings and may inform future guidance documents.

Additional Training Is Needed

While risk assessors reported taking advantage of and benefiting from various forms of training, they also said additional training would improve their ability to prepare risk assessments, a belief echoed by agency officials we spoke with. Over 70 percent of risk assessors stated that more in-depth or relevant training would improve their ability to prepare risk assessments. More specifically, some risk assessors expressed the need for training on analytic tools, such as modeling the dose-response relationship and statistical analysis and software. Several risk assessors also expressed a strong interest in training on scientific topics, including toxicology and such emerging issues as genomics, as well as nonscientific topics, such as public communications and public relations. Some risk assessors suggested EPA provide formal, comprehensive training for new risk assessors to educate them on how to use the guidance documents and more advanced courses for experienced risk assessors. Furthermore, many risk assessors reported that more time (69 percent) and more funds (65 percent) for training would moderately or greatly improve their ability to prepare risk assessments. (See fig. 6.)

Figure 6: Modifications in Training That Would Moderately or Greatly Improve the Preparation of Risk Assessments



Source: GAO analysis of survey data.

In addition to our survey respondents, some program officials we interviewed pointed out the need for additional training for both risk assessors and risk managers. For example, risk assessors need training in emerging issues, such as genomics, so that they can use these types of data in risk assessments, according to one agency official. In contrast, risk managers need training on the elements of risk assessment, so that they will be better able to interpret the information provided and apply it to risk management decisions. According to one program manager, risk managers often want the "bottom line" (numerical) results of a risk assessment without understanding the nature of the uncertainties in the assessment, or the potential value of obtaining more information to help clarify those uncertainties.

Finally, the changing nature of the workforce may have implications for training at EPA. According to an agency official, many experienced risk assessors who possess years of institutional knowledge are retiring or nearing retirement age. Consequently, the agency needs to educate newer

risk assessment staff as quickly and thoroughly as possible to help ensure that the agency's ability to accurately and effectively produce risk assessments does not decline. While recently hired risk assessors come to EPA with specialized knowledge in fields related to risk assessment, they may not understand the broader context of risk assessment. For example, a new employee with degrees in biology and toxicology may not know how to integrate that knowledge with other scientific information to prepare a risk assessment. Furthermore, one EPA official noted that the agency has no formal training course, or set of courses, to help develop staff's ability to prepare risk assessments.

Enhanced Risk Assessment Planning, Improved Analysis and Review, and Added Training Could Further Improve EPA's Process, but Barriers Could Limit Progress

The experts we spoke with, including representatives of federal and state agencies, regulated industry, environmental advocacy groups, and outside researchers and consultants, said the modifications EPA has made over the past 10 years have been beneficial overall. However, they identified additional actions EPA could take to improve its risk assessment process, recognizing that EPA would face barriers to doing so. Specifically, EPA could improve its planning process of what will be required to complete a risk assessment by better identifying the scientific data it has and data it needs on the potential adverse effects from exposure to a contaminant and by seeking stakeholder input early in this planning process. In addition, EPA could more thoroughly evaluate methods and models, transparently document its analytic choices, and enhance internal review. Finally, experts believe EPA could provide additional training for risk assessors, managers, and stakeholders. While these efforts would further improve the risk assessment process, EPA could face barriers in carrying them out, such as the scientific complexity of risk assessment, the difficulty of obtaining and applying data, and a cultural resistance to deviating from established methods.

Enhance Planning by Increasing Focus on Data Needs and Involving a Broad Range of Stakeholders

In order to ensure that EPA has the data needed for risk assessment, it needs to better identify data that are available, prioritize its data needs, and collaborate with the external research community during the planning phase. For example, several experts said EPA should generate a searchable database of studies conducted by different agencies and organizations related to the chemicals being evaluated, so that researchers and risk assessors could more easily identify what studies are available and what additional research is needed. Experts also suggested several ways for EPA to prioritize its data needs. For example, sensitivity analysis can be used within individual risk assessments to determine which data gaps are the most critical to the risk assessment result. Some experts also

said EPA could better prioritize its data needs by increasing its use of data on the amounts of contaminants in people's bodies to help concentrate its research on the chemicals to which humans are actually exposed. Finally, several experts suggested that EPA increase its collaboration with external researchers, in part because the agency lacks the resources to independently generate all of the data that are needed. If EPA more effectively collaborated with other federal research organizations, such as the National Toxicology Program and the National Institute of Environmental Health Sciences, federal research dollars could be better harnessed to help EPA protect the public from exposure to contaminants. For example, the National Toxicology Program has the technology to assist the Office of Pesticide Programs with its screening of inert ingredients, which are all of the "other" chemicals in a pesticide product. In addition, experts said EPA should use all relevant data, including data from industry research laboratories, provided EPA takes steps to ensure the data are generated in an unbiased and scientifically defensible way. For example, experts suggested that EPA could subject studies to independent peer review and evaluate the sufficiency of data produced by these organizations to increase confidence about using these data in EPA risk assessments.

Experts also said that EPA could improve the quality of risk assessments if the agency enhanced its planning by more consistently involving stakeholders, especially early in the process. Several experts said that increased involvement with a broad range of stakeholders early in the planning process would help identify alternate methods and models to use and obtain stakeholder concurrence with the agency's approach. Although all stakeholders might not agree on the methods chosen, some experts believe that by seeking stakeholder input on these issues early in the process, EPA may minimize arguments later. In addition to stakeholder involvement with early planning, several experts recommended that EPA increase coordination with stakeholders throughout the process. For example, one expert said EPA could more transparently acknowledge and address comments from the public and other stakeholders, regardless of whether the agency planned to implement their suggestions.

More Thoroughly Evaluate and Transparently Document Analytic Choices, and Increase Internal Review

EPA could more thoroughly evaluate its analytic choices and incorporate or develop a wider variety of analytic tools. Some experts said that, with regard to EPA's use of default options, risk assessors should more thoroughly document why available data are insufficient to allow EPA to use another analytic approach and commented that the revised cancer guidelines may provide a useful framework for making this decision.

Furthermore, several experts said EPA could use a tool like sensitivity analysis to assess and clearly communicate the extent to which the choice of a method or default assumption affects the risk assessment outcome. For example, if sensitivity analysis demonstrated that the impacts were significant, EPA could use the analysis to identify the critical areas where additional studies might reduce the need to rely on a default assumption for that assessment. One expert pointed out that the Office of Pesticide Programs uses sensitivity analysis in its exposure assessments to estimate which uses of a pesticide present the greatest risk to workers and how to mitigate those risks. In addition, several experts recommended that EPA make better use of existing analytic tools and develop new ones, where needed. For example, some experts said EPA should more frequently employ probabilistic analyses in risk assessments and incorporate the latest scientific tools, such as genomics and computational toxicology, to better assess uncertainty and variability. In addition, several experts noted that EPA needs to develop tools and methodologies to better analyze certain aspects of risk assessment, such as the combined effects of exposure to multiple chemicals through multiple pathways.

Experts also said EPA risk assessments should clearly describe the sufficiency of the data and the scientific basis for its choice of a default assumption, method, or model. Some experts pointed out that risk assessments should identify and clearly discuss any data that are not available for the analysis, including the form the data need to be in and the most appropriate study design or methodology to obtain the needed data. In addition, several experts said EPA needs to more explicitly communicate which default assumptions were used in a risk assessment and why the defaults were chosen. For example, one expert said that even though a risk assessment may be perfect, if the public does not understand the rationale behind the agency's choices, the risk assessment might be seen as flawed. Furthermore, in individual risk assessments, the agency could more transparently identify which critical studies would help the agency avoid relying on default assumptions. Some experts also suggested that EPA use as case studies completed assessments for which the agency had sufficient data to use models and other analytic tools rather than default assumptions to more accurately assess risks. Finally, some experts said that EPA should more transparently consider alternate methods and models in each risk assessment. For example, EPA should be more transparent about the judgments it makes when it employs certain methods, such as the benchmark dose method, which identifies the dose that produces a small increase in the risk of an adverse effect.

Finally, experts suggested that EPA increase internal reviews of risk assessments by staff members with extensive risk assessment experience. Internal reviews could improve the risk assessment process in two ways: first, to assure the quality of risk assessments and second, to ensure that the design of its risk assessments match the needs of risk managers. For example, one expert suggested EPA reinstate a senior peer review group, composed of experienced risk assessors from throughout the agency. Others suggested that EPA could also internally peer review risk assessments prepared by less experienced staff to ensure that default assumptions are applied appropriately and transparently explained. In addition to increased review of individual risk assessments, some experts also felt the risk assessment process could benefit from additional examination of agencywide cross-cutting issues applicable to all program offices. For example, one expert said that some analytic tools, such as Monte Carlo analysis, were not developed specifically for use in risk assessments and suggested that EPA work with ORD's National Center for Computational Toxicology to define how these tools could be used in risk assessments across EPA. Moreover, according to several experts, agencywide discussions and activities promote consistency in risk assessment practices. For example, some experts thought EPA could benefit from a systematic agencywide discussion of the sources of uncertainty in risk assessment.

More Training Could Improve Risk Assessor, Risk Manager, and Stakeholder Understanding of the Process

Experts emphasized the importance of training for risk assessors, risk managers, and the stakeholder community on all elements of the risk assessment process. Several experts said risk assessors are not adequately trained in basic risk assessment principles, such as available default assumptions and when they should be used or replaced. Some experts also suggested risk assessors receive training in using and applying models and in how to interpret data from emerging scientific fields to improve their ability to use these data, as appropriate, in risk assessments. Several experts also believe that training for risk managers would help improve risk assessments because risk managers need to better understand the role risk assessment plays in risk management. According to some experts, risk managers who are more familiar with the process are better equipped to support risk assessors and ensure that the risk assessment considers all appropriate factors. Finally, a few experts also suggested that EPA hold training for stakeholders in the risk assessment process. For example, one expert suggested that EPA develop Web-based training for both the regulated community and regulators themselves to help ensure consistency in how they understand the process. As part of this training,

EPA could explain how risk assessment fits into the overall risk management process.

EPA Faces Barriers to Improving Its Risk Assessment Process, Such as the Complexity of Risk Assessment, Difficulty of Acquiring and Applying Data, and a Culture Resistant to Change

While experts identified a number of actions EPA could take to improve the risk assessment process, they said EPA may face barriers such as the highly complex, technical, and time-intensive nature of preparing risk assessments, challenges in acquiring and applying data from all available sources, and a general reluctance to deviate from its established methods and assumptions. Several experts pointed out that EPA's risk assessments have grown more technically challenging and require risk assessors and managers to possess different skills than in the past. For example, some experts told us risk managers have different levels of expertise and background in risk assessment, and may not fully understand how risk assessment helps inform regulatory decisions. Moreover, some experts said that because risk assessment is just one piece of information used to make a regulatory decision, it is difficult to explain to stakeholders and the public the impact of risk assessments on risk management decisions. Experts also pointed out that scientific knowledge on subjects, such as uncertainty and variability, is limited and analytic tools are still being developed. For example, several experts said that while it would be useful for EPA to more fully consider the risks of exposure to a single chemical from all exposure pathways, at present it is an emerging science with few well developed analytic tools to use in risk assessments. In addition, using tools, such as probabilistic analysis, to assess variability requires large amounts of data that are seldom available. Finally, several experts said that improving the process by such steps as incorporating new analytic techniques and conducting thorough internal review requires more time and coordination. For example, one expert pointed out that EPA does not always have the staff and time to analyze all sets of data or to examine alternative methods or models that might provide a more robust risk estimate.

In addition to barriers attributable to the complexity of preparing risk assessments, experts also said EPA may face barriers in acquiring and applying data from all available sources. Many experts commented that data are expensive to obtain, and EPA has limited financial resources to devote to such activities. For example, some experts pointed out that some of the more direct studies of human exposure, such as epidemiological or biomonitoring studies, are quite expensive to conduct. Furthermore, EPA may be reluctant to use available data from all sources. As several experts pointed out, data from industry-sponsored researchers might be perceived as biased, potentially subjecting EPA to criticism.

Despite potential perceptions of bias, some experts thought EPA should have the ability to use all available data, regardless of its source, as long as the data in question have been appropriately peer reviewed. In addition, some experts said statutory requirements may limit EPA's ability to use certain data. For example, the Toxic Substances Control Act limits EPA's authority to require extensive data from industry before deciding whether to approve a new chemical. Some experts also pointed out that research does not always produce clear-cut results. For example, one expert commented that epidemiological studies of the general population may not account for confounding factors, such as exposure to other chemicals, which complicate efforts to draw conclusions about the effects of a single chemical. In addition, some experts said that variability, an important but scientifically complicated issue, often creates inconsistencies across studies because many factors such as geography, lifestyle, and food intake affect an individual's response.

Finally, experts said that EPA has a general reluctance to deviate from using methods and assumptions it has used in the past. As a result, experts said EPA prefers to use techniques that have been generally accepted in the scientific community than to use methods that rely on recent scientific advances. For example, some experts told us EPA is often reluctant to deviate from its established default assumptions. Furthermore, some experts also commented that risk assessors may not have an incentive to deviate from methods and assumptions they have used in the past because it may make the risk assessment more easily challenged by those who disagree with it. In addition, some experts said the level of comfort in using new methods varies throughout the agency. For example, one expert believes that probabilistic models have been applied inconsistently because some risk assessors have been unwilling to deviate from the standard models.

Conclusions

While technical and difficult to understand by nature, risk assessment is a key element in EPA's efforts to protect human health from the potentially harmful effects of chemicals, pollutants, and toxic substances that people encounter in their everyday lives. Since 1994, EPA has taken a number of steps, including greater involvement by the public and other stakeholders, to strengthen and improve its process for preparing assessments of the risks posed by contaminants in the environment. Independent reviewers as well as the experts and EPA risk assessors we contacted said overall EPA's efforts have improved the agency's risk assessments. However, the agency itself and the individuals we contacted acknowledge that EPA needs to do more. While some barriers to further improvement depend on

scientific advances that are largely beyond EPA's control, other actions to improve its risk assessment process are within its control. Specifically, when EPA engages the stakeholder and research communities after the risk assessment has largely been completed, it misses opportunities to benefit from their expertise. By working with stakeholders early and periodically throughout the process to identify key issues, studies, methods, and default assumptions that need to be considered in the analysis, EPA would help ensure consistent, transparent, and high-quality risk assessments. On the other hand, failure to take full advantage of stakeholders' knowledge and points of view is likely to contribute to the perception among stakeholders that their concerns are not adequately represented in the risk assessments and that EPA's decisions lack transparency. While EPA has issued a number of guidance and policy documents advocating the benefits of early planning, it acknowledges it could do more to ensure that such planning and consultation take place and involve relevant stakeholders. Furthermore, EPA does not always systematically communicate its data needs to the research community. While EPA has begun to better identify and prioritize its specific data needs, it has not been able to consistently develop data it needs in a timely manner. A more proactive approach to communicating its research needs to outside public and private researchers would help EPA more efficiently use the limited resources it has to obtain the data it needs. Furthermore, this approach would increase the likelihood that EPA would have data it needs to complete risk assessments now and into the future and that appropriately designed research projects would be conducted. Transparently communicating its research needs would also enhance EPA's ability to produce high-quality, scientifically defensible risk assessments and reduce the uncertainty associated with the effects of many contaminants on human health. Although experts we interviewed said EPA may hesitate to seek and use data from a wide range of sources because it could be seen as biased, EPA could take steps to ensure the quality of data generated by others. By doing so, EPA would expand its cache of available data and, potentially, reduce its reliance on default assumptions. Finally, current workforce models of high-performing organizations stress the need to formally and comprehensively assess the skill and competency requirements for staff and to identify related training and developmental needs to ensure that the workforce retains a high level of needed skills. In recent years, EPA's emphasis on training for its risk assessors and managers has declined in the areas risk assessors and experts say are needed to improve the quality of risk assessments and take advantage of recent scientific and analytic advances. Without an agencywide training program for its risk assessment and risk management workforce, the quality, consistency, and transparency of risk assessments

and risk management decisions will likely continue to be challenged by stakeholders and the public.

Recommendations for Executive Action

To improve the overall quality, consistency, and transparency of its risk assessments, we recommend that the Administrator of EPA direct the appropriate agency entities to take the following three actions:

- Develop a strategy to ensure that offices engage in early planning to identify and seek the expertise needed, both within the EPA workforce and from external subject matter experts. The strategy should delineate such things as how EPA could use the available expertise to determine the needed data, the relevant default assumptions, the extent of internal and external review that needs to be included in the assessment, and the approach used to consistently involve a broad range of stakeholders—including the public, regulated industry, federal agencies, and advocacy groups—as appropriate to the risk assessment.

- More proactively identify the data most relevant to the current risk assessment needs, including the specific studies required and how those studies should be designed, and communicate those needs to the research community. Increased collaboration among program offices in identifying needed data would help ensure that the resulting data will meet the needs of multiple offices. In addition, EPA should better communicate these data needs and better coordinate research planning with the external public and private research community to help focus EPA's limited resources.

- Ensure that risk assessors and risk managers have the skills needed to produce quality risk assessments by developing and implementing in-depth training. This training should address the needs of risk assessors and managers with varying levels of expertise by including basic courses, such as an overview of risk assessment, as well as more advanced courses on topics such as modeling, toxicology, and other advanced scientific techniques.

Agency Comments

We provided EPA with a draft of this report for review and comment. EPA neither agreed nor disagreed with our findings and recommendations. However, the agency provided specific comments to improve the report's technical accuracy, which we incorporated as appropriate.

As agreed with your office, unless you publicly announce the contents of this report earlier, we plan no further distribution until 30 days from the report date. At that time, we will send copies to the Administrator, EPA, as well as to appropriate congressional committees, and other interested Members of Congress. We also will make copies available to others upon request. In addition, the report will be available at no charge on the GAO Web site at http://www.gao/gov.

If you or your staff have questions about this report, please contact me at (202) 512-6225 or stephensonj@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. GAO staff who made key contributions to this report are listed in appendix II.

Sincerely yours,

John B. Stephenson
Director, Natural Resources
and Environment

Appendix I: Objectives, Scope, and Methods

Our objectives for this review were to (1) identify the significant recommendations to improve human health risk assessment that have been made since 1994; (2) describe what the Environmental Protection Agency (EPA) has done to modify its human health risk assessment process over the same period; (3) determine the effects these past modifications have had on the preparation of risk assessments; and (4) identify any additional actions experts believe EPA could take to improve its risk assessment process in the future, and the barriers EPA would face in doing so.

To identify significant recommendations to improve human health risk assessment since 1994, we reviewed EPA documents, including those produced by EPA's Risk Assessment Forum (RAF), Science Policy Council (SPC), Council for Regulatory Environmental Modeling (CREM), and Science Advisory Board (SAB) as well as each of EPA's program offices. We also reviewed our own reports and documents produced by the National Academy of Sciences and the Presidential/Congressional Commission on Risk Assessment and Risk Management. To gain an external perspective, we spoke with experts in the risk assessment field, who identified many of these documents in the course of our discussions and provided insight into some of the documents' recommendations.

To describe what EPA has done to modify its human health risk assessment process, we interviewed program office managers from the Office of Air and Radiation (OAR), Office of Pesticide Programs (OPP), Office of Pollution Prevention and Toxics (OPPT), Office of Water (OW), and Office of Research and Development (ORD). We did not include the site-specific risk assessment activities of the Office of Solid Waste and Emergency Response in our review. Within ORD, we interviewed managers in two of EPA's laboratories (the National Health and Environmental Effects Laboratory and the National Exposure Research Laboratory) and three of EPA's research centers (the National Center for Environmental Assessment, National Center for Environmental Research, and National Center for Computational Toxicology). We also interviewed officials from RAF, SPC, CREM, SAB, and the Office of the Science Advisor. Furthermore, we attended various EPA and stakeholder group training sessions and meetings. Since we limited our review to the human health aspects of risk assessment since 1994, our analysis does not highlight EPA's modifications prior to 1994, including publication of guidance documents that are highly relevant to risk assessment practices, and does not address issues specifically related to ecological risk assessment.

To assess the effects these modifications have had on the preparation of risk assessments, we conducted a Web-based nonprobability survey of all human health risk assessors from ORD and four EPA program offices that conduct human health risk assessment (OAR, OPP, OPPT, and OW). We used the survey to obtain an internal perspective on the usefulness of many of the modifications EPA made since 1994, as well as on aspects of EPA's risk assessment process, including guidance documents, training, organizational structure, and collaboration. In developing the Web-based questionnaire, we met with EPA officials from the five offices surveyed to gain a thorough understanding of the risk assessment issues specific to each office and identify the sampling frame. In order to identify human health risk assessors—a label that is not an EPA job series—we obtained from EPA officials in each program office being reviewed the names of agency staff who worked on any part of the human health risk assessment process since January 2001. Our sampling frame consisted of 270 staff that met this criterion. This report does not contain all the results from the survey. The survey and results can be viewed at http://www.gao.gov/cgi-bin/getrpt?GAO-06-637SP.

The practical difficulties of conducting any survey may introduce nonsampling error. For example, differences in how a particular question is interpreted, the sources of information available to respondents, or the types of people who do not respond can introduce unwanted variability into the survey results. In order to reduce nonsampling error, we pretested the questionnaire with five risk assessors, one from each of the offices surveyed. During these pretests, we asked agency officials to complete the survey as we observed the process. We then interviewed the respondents to ensure that (1) the questions were clear and unambiguous, (2) the terms used were precise, (3) the questionnaire did not place an undue burden on the agency officials completing it, and (4) the questionnaire was independent and unbiased. On the basis of the feedback from the pretests, we modified the questions, as appropriate. Information about accessing the questionnaire was provided via e-mail for all survey participants. The survey was activated, and staff informed of its availability on October 17, 2005; it was available until January 13, 2006. To ensure security and data integrity, we provided all participants with a personal password that allowed them to access and complete a questionnaire. No one else could access that questionnaire or edit its data. We included steps in both the data collection and data analysis stages for the purpose of minimizing such nonsampling errors. To reduce survey nonresponse, we sent e-mail reminders and conducted follow-up telephone calls with nonrespondents. Overall, 82 percent of the 270 risk assessors in our sampling frame

responded to our survey, and all offices had a response rate of at least 80 percent.

We used general modifiers (i.e., many, several, some, a few, and a couple) to characterize written responses to some open ended survey questions. We used the following method to assign these modifiers to our statements about risk assessor's survey responses: "many" represents 22 to 44 respondents (roughly 10 to 20 percent), "several" represents 12 to 21 respondents (5 to 10 percent), "some" represents 4 to 11 respondents, "a few" represents 3 respondents, and "a couple" represents 2 respondents. These divisions do not represent technically established categories; rather, we chose these divisions because they aligned with natural breaks in response "themes" highlighted in the report.

To assess further actions EPA could take to improve its risk assessment process and to identify barriers it may face in doing so, we interviewed experts representing a range of stakeholders in the process. Specifically, we contacted risk assessment scientists; toxicologists; scientific advisers to EPA; state officials; and representatives from regulated industries, government agencies, and environmental advocacy groups who have an expertise in risk assessment. We used an iterative process (often referred to as the "snowball sampling" technique) to identify these knowledgeable experts and selected for interviews those who would provide us with a broad and balanced range of perspectives on EPA risk assessment practices.

We first contacted the National Academy of Sciences' Board of Environmental Studies and Toxicology, which is the academy's principal study unit for environmental pollution problems affecting human health and the assessment and management of related risks to human health and the environment. We presented our engagement to the board and sought its input on the areas in which EPA has made the most progress improving its risk assessment practices and areas EPA will need to focus on in the future. We also asked members if they would be willing to participate in a future interview and solicited the names of other experts who would be appropriate for us to contact about this engagement. We selected for interviews experts who would provide us with a broad and balanced range of perspectives on EPA risk assessment practices. We continued interviewing and soliciting names until we determined we had appropriate coverage from all the relevant stakeholder groups. Our sampling identified 22 experts, listed alphabetically, as follows: Elizabeth L. Anderson, Ph.D.; Gail Charnley, Ph.D.; Harvey J. Clewell, M.A.; Shannon Cunniff; Kerry Dearfield, Ph.D.; Michael L. Dourson, Ph.D.; Elaine M. Faustman, Ph.D.;

Paul Gilman, Ph.D.; Gary Ginsberg, Ph.D.; Sherri Goodman, Esq.; Judith A. Graham, Ph.D.; Dan Greenbaum; Leslie J. Hushka, Ph.D.; Annie M. Jarabek, B.S.; James H. Johnson, Ph.D.; Elizabeth Julien, Ph.D.; Dorothy Patton, Ph.D.; Jonathan M. Samet, Ph.D.; Jennifer Sass, Ph.D.; Chris Whipple, Ph.D.; Richard Wiles, M.A.; and Lauren Zeise, Ph.D.

We used a standard set of questions to interview each of these experts to ensure we consistently discussed each aspect of EPA risk assessment policies and practices. To develop the questions, we reviewed documentation on EPA's risk assessment process and reports prepared by the National Academy of Sciences. We pretested our questions with two of the experts and refined the questions accordingly. We used content analysis to identify the main themes among their responses. In addition, we asked the experts for their opinions about the many risk assessment modifications EPA has made since 1994, and used content analysis to synthesize their comments.

We conducted our work from February 2005 through March 2006 in accordance with generally accepted government auditing standards.

Appendix II: GAO Contact and Staff Acknowledgments

GAO Contact

John B. Stephenson, (202) 512-6225 or stephensonj@gao.gov

Staff Acknowledgments

In addition to the contact named above, Cheryl Williams (Assistant Director), Jennifer Cook, Michelle Cooper, Elizabeth Erdmann, and Rebecca Shea made key contributions to this report. Also contributing to this report were Nancy Crothers, Richard Frankel, and Roderick Moore.

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