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ENVIRONMENTAL PROTECTION AGENCY

Use of Precautionary Assumptions in Health Risk Assessments and Benefits Estimates

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Contents

Abbreviations

EPA Environmental Protection Agency

GAO
Accountability * Integrity * Reliability

United States General Accounting Office
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October 16, 2000

The Honorable Bud Shuster
Chairman
Committee on Transportation
and Infrastructure
House of Representatives

The Honorable Frank R. Lautenberg
United States Senate

Some of the Environmental Protection Agency's (EPA) regulations set standards that limit environmental contaminants[1] to levels that are determined, in large part, on the basis of the health risks they pose. For example, EPA sets health-based air quality standards under the Clean Air Act. For such actions, EPA also estimates the benefits of the health-based standards.[2] These benefits primarily represent the estimated dollar value of reductions in assessed risks to human health—illnesses and deaths avoided as a result of decreased pollution.[3] However, when EPA assesses the health risks of contaminants, the agency is faced with uncertainties and gaps in scientific knowledge and data. As a result, EPA's risk assessments include assumptions about the relationship between specific contaminants and health effects, some of which are precautionary—that is, they are intended to ensure that the agency does not underestimate health risks. But using such precautionary assumptions to estimate benefits could produce overly optimistic estimates of the benefits of regulatory actions.

Because of concerns about the potential impact of precautionary assumptions on benefits estimates, you asked us to examine whether EPA's benefits estimates for major environmental regulations that establish health-based standards reflect precautionary assumptions about health risks. As agreed with your offices, this report identifies (1) key factors that

[1]In this report, we use the term contaminants to refer to substances that harm human health. EPA uses this and other terms, including toxins, toxic substances, and pollutants, to describe these substances.

[2]Analyses of benefits and costs are required for all regulations that are "economically significant" and includes those expected to have an annual impact on the economy of $100 million or more. These are also referred to as major rules or major regulations.

[3]Using the concept of the "value of a statistical life," economists have developed several methods to estimate a value of reductions in mortality risk.

explain why EPA uses precautionary assumptions in assessing health risks and (2) whether EPA used and identified precautionary assumptions in estimating the health risks and benefits of recent major regulations setting health-based standards.

In recent years, EPA has proposed or finalized a small number of major regulations establishing health-based standards, and these have been issued under two statutes—the Clean Air Act and the Safe Drinking Water Act.[4] To illustrate EPA's use of precautionary assumptions in setting health-based standards and estimating their benefits, we reviewed two of these regulations: (1) air quality standards for particulate matter (commonly called soot) and (2) drinking water standards for arsenic. As a result, our findings on these two rules may not be generalized to all of EPA's major regulations that set health-based standards. Consistent with our objectives, we did not review the economic aspects of EPA's benefits estimates, such as the methods used to estimate dollar values for lives saved and illnesses avoided, or the extent of EPA's compliance with guidance from the Office of Management and Budget and EPA on the preparation of benefits estimates. (See app. I for a detailed discussion of our scope and methodology.) We are also reviewing the health risk assessment procedures and assumptions of four agencies, including EPA, and plan to provide the results of this review in a forthcoming report to the Chairman, House Committee on Commerce.

Results in Brief

Three key factors influence EPA's use of precautionary assumptions in assessing health risks. First, EPA is influenced by its mission to protect human health and safeguard the natural environment. For example, in some instances, environmental statutes require EPA to protect the public health with an "adequate margin of safety." Second, EPA is influenced by the nature and extent of relevant data—in particular, whether studies of a contaminant's effects on people are available or whether the agency must extrapolate from studies using other animal species. Finally, EPA is influenced by the nature of the health risk being evaluated, such as whether the contaminant is suspected of causing cancer.

The two regulations that we examined differed in the extent to which they used precautionary assumptions in estimating health risks and benefits.

[4]According to EPA, the majority of its major regulations in recent years have established technology-based or performance-based standards that reduce pollution using available pollution control technology.

EPA generally did not rely on precautionary assumptions in estimating either the health risks or the benefits of the particulate matter regulation because the agency had better data than is often the case. In contrast, because of scientific uncertainties and data gaps, EPA relied on several precautionary assumptions in estimating the health risks and the benefits of the arsenic regulation. As a result, EPA's estimates of the risk of bladder cancer associated with arsenic in drinking water and the related benefits of the proposed rule may be overstated for this health risk. However, EPA used new analytical techniques in estimating the health risks and benefits that removed certain precautionary assumptions used in the past, thereby reducing the extent to which the benefits of reductions in bladder cancer may be overstated. In its proposed arsenic regulation, EPA identified the key health uncertainties and precautionary assumptions it used in assessing the risks of arsenic in drinking water but was less complete in identifying them in its formal cost-benefit analysis. Furthermore, although its guidance on cost-benefit analyses calls for assessing uncertainty using sensitivity analysis, EPA did not perform sensitivity analysis that could have shown how the estimated benefits would change depending upon the health assumptions used. We are recommending that, in developing its final rule on arsenic, EPA fully disclose and analyze the impact of the key precautionary health assumptions used in its benefits estimate.

Background

EPA assesses human health risks in the context of great uncertainty—both in terms of scientific theory and data—about the adverse effects on human health posed by a wide variety of environmental contaminants, the relationship between toxicity and dose, and the extent of people's exposure to contaminants. As a result, EPA must use assumptions, based on general scientific knowledge and policy judgments, when it lacks more specific scientific knowledge and data needed to assess the health risks posed by contaminants. The National Research Council of the National Academy of Sciences[5] has noted that risk assessment inevitably includes policy judgments as well as science.[6]

EPA has issued, over the past 25 years, a series of guidance documents that describe the principles, policies, and practices the agency employs in evaluating the health risks (toxicity) of environmental contaminants. EPA's guidelines cover many topics, including cancer, reproductive and developmental toxicity, neurotoxicity, exposure assessment, and mutagenicity, that is, the capacity to cause sudden change in the genetic material of a cell. EPA personnel who conduct risk assessments are to use EPA's guidelines to ensure consistency in the interpretation of scientific information across all of the agency's programs and regions.

EPA's risk assessment guidelines set forth "default" assumptions—generic approaches based on general scientific knowledge and policy judgment that are applied to various elements of the risk assessment process when specific scientific information is not available. In this report, we refer to the default assumptions that are intended to avoid underestimating risk as precautionary assumptions. There is an ongoing scientific and policy debate concerning whether and under what circumstances some of the assumptions used in estimating human health risks are precautionary. According to some analysts, using a series of protective default assumptions within the same risk assessment might produce results that seriously overstate actual risks. Other analysts believe that the degree of precaution may not be as great as some argue—or that the risk assessment

[5]The National Academy of Sciences, a private, nonprofit organization composed of scholars, is engaged in scientific and engineering research to further knowledge and advise the federal government. The National Research Council, the principal operating agency for the National Academy, provides services to the government, the public, and the scientific and engineering communities.

[6]See *Risk Assessment in the Federal Government: Managing the Process* (1983) and *Science and Judgment in Risk Assessment* (1994).

methodologies may in some cases actually underestimate risks—and that it is appropriate to be precautionary about health risks.

EPA's practice of including precautionary assumptions in its risk assessment policies and practices has been recognized and affirmed by the National Research Council. According to the Council, EPA's risk assessment practices rely heavily on default options or generic approaches. The Council stated that these default options, or assumptions, are for the most part chosen to "lead to risk estimates that, although plausible, are believed to be more likely to overestimate than to underestimate the risk to human health and the environment."[7] The Council said, however, that the choice of default assumptions should have a decreasing impact on regulatory decision-making over time because, as scientific knowledge increases, uncertainty diminishes and risk assessments should be less dependent on such assumptions.

Risk assessments of chemicals examine the types of adverse health effects that might occur in humans and wildlife following chemical exposure (hazard identification), how the effects vary with the degree of exposure (dose-response assessment), and the degree to which exposure actually occurs (exposure assessment). Combining this information enables the overall risk to be described for decisionmakers (risk characterization). Once the risk is characterized, risk management involves deciding what actions, if any, are needed to prevent or reduce the risk, such as limiting pollutant emissions.

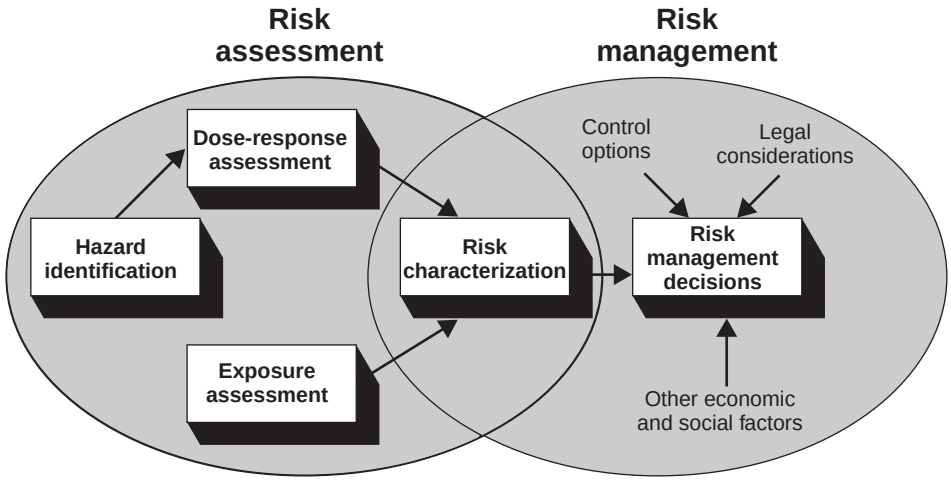
As shown in figure 1, the risk management decision considers other information in addition to the risk characterization. For example, the risk management decision may be affected by control options—that is, the technologies that are available to implement a standard—legal considerations, and economic factors. Economic information that may be considered includes cost-benefit analyses, which are required for economically significant regulations.[8] EPA's regulations that establish national health-based standards, such as drinking water standards under the Safe Drinking Water Act, typically have a significant effect on the

[7]See *Science and Judgment in Risk Assessment* (1994).

[8]Executive Order 12866 requires detailed cost-benefit analyses for all economically significant regulations that include those expected to have an annual impact on the economy of $100 million or more. EPA is also directed by the Unfunded Mandates Reform Act of 1995 to conduct regulatory cost-benefit analyses under certain circumstances.

economy. Therefore, EPA conducts both a risk assessment and a national benefits estimate in these cases, while in many other cases the agency conducts a risk assessment but conducts only a limited benefits estimate or none.

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



Source: *Research and Development: Fiscal Years 1997-1998 Research Accomplishments*, EPA (Dec. 1999).

EPA's various program offices, including those responsible for pesticides, toxic substances, and air and water pollution, conduct many health risk assessments that vary in purpose and the availability of data. They range from single-purpose screening assessments that receive limited review to fully developed, peer-reviewed assessments that serve as the basis for major regulations. The program offices may use the hazard identification and dose-response assessments conducted by EPA's Office of Research and Development.[9] However, the program offices usually conduct the exposure assessment and risk management phases and are also usually responsible for preparing the cost-benefit analyses for major rules.

[9]Some of the program offices, such as the Office of Pesticide Programs and the Office of Water, do all or some of their own hazard identification and dose-response assessments.

EPA's methodologies for conducting risk assessments and benefits estimates have changed in recent years in response to a number of factors, including recommendations from the National Research Council, changes in the agency's environmental statutes, the availability of more sophisticated mathematical and computer models, and new scientific data on and increased understanding of how cancer develops. For example, in its 1994 report on EPA's risk assessment activities, the National Research Council recommended that EPA's risk assessment guidelines identify the specific assumptions that are default options and clearly state the scientific and policy basis for each default assumption used. EPA has proposed revisions to its risk assessment guidelines for carcinogens (cancer-causing substances) that call for identifying the default assumptions used and for highlighting significant issues; they also provide some clarification on departing from default assumptions. The revised guidelines have been peer-reviewed by EPA's Science Advisory Board but are not yet final. EPA has started to incorporate some aspects of these new guidelines into some risk assessments.

Other changes include guidance on EPA's exposure policies and/or practices aimed at reducing the use of some precautionary assumptions. For instance, EPA's estimates of individuals' exposures to contaminants can be precautionary if the estimates assume that individuals are exposed at the highest levels. Past exposure assessment and health risk assessment practices at EPA have sometimes relied on exposure estimates derived from a hypothetical "maximally exposed individual" who might spend, for example, a 70-year lifetime drinking only groundwater with the highest concentrations of contaminants detected. According to the 1997 report of the Presidential/Congressional Commission on Risk Assessment and Risk Management, this approach was often based on such unrealistic assumptions that using it impaired the scientific credibility of risk assessments. EPA, like other federal agencies, has moved away from exposure assessments relying on such maximally exposed individuals. For example, EPA's exposure assessment guidelines have adopted the use of distributions of individual exposures. EPA's current guidance indicates that risk assessments should include both central estimates of exposure (based on either the mean or the median exposure) and estimates of the exposures that are expected to occur in small, but definable, "high-end" segments of the population.

Three Key Factors Affect EPA's Use of Precautionary Assumptions

Three key factors principally influence EPA's use of precautionary assumptions in assessing health risks: (1) the agency's mission to protect human health and safeguard the environment; (2) the nature and extent of relevant data—in particular, whether studies of a contaminant's effects on humans are available or whether the agency must extrapolate from studies using other animal species; and (3) the nature of the health risk being evaluated, such as whether the contaminant is thought to cause cancer. For example, in assessing the risks of contaminants that may cause cancer, the agency has typically made the precautionary assumption that there is no safe level of exposure—that is, that any exposure poses some risk of developing cancer.

EPA's Mission to Protect Human Health and the Environment

EPA's mission, articulated in its strategic plan and reflected in statutes, agency policies, and practices, is to protect human health and safeguard the natural environment. This mission is a key factor encouraging the agency to use precautionary health risk assumptions in the absence of convincing scientific knowledge. For example, to avoid underestimating risks to human health, EPA has incorporated a number of precautionary assumptions in its risk assessment guidelines to address scientific uncertainties.

In some instances, environmental statutes require EPA to protect the public health with a margin of safety either in assessing risks or in setting health-based standards. Under the 1996 Food Quality Protection Act, for example, EPA is required to give special consideration to children's susceptibility to pesticide residues when the agency sets allowable levels for such residues in food. Among other things, the statute requires EPA to make precautionary assumptions in its risk assessments about safe levels of pesticide residues for children when data are incomplete or unreliable.[10] Under the Clean Air Act, EPA is to establish national standards for ambient (outdoor) air quality to protect the public health from the effects of certain widespread air pollutants, such as carbon monoxide and particulate matter. The act requires that these standards be set at levels that allow for an "adequate margin of safety."

[10] *Children and Pesticides: New Approach to Considering Risk Is Partly in Place* (GAO/HEHS-00-175, Sept. 11, 2000).

The Type of Data, Particularly Whether Human or Animal Studies Are Available

The assumptions that EPA uses in assessing the health risks of contaminants depend largely on whether the agency has adequate studies of their effects on people, known as epidemiological studies, or only studies of other animals conducted under controlled laboratory conditions, called toxicological studies. Epidemiologists compare two or more groups of people to determine which characteristics, such as exposure to contaminants, distinguish people who get disease from people who do not. Data from epidemiological studies are preferred for characterizing human health risks because they can provide the most direct evidence that a substance poses health risks to people. If these studies are extensive and of good quality, EPA generally gives greater weight to epidemiological data than to animal data. Nonetheless, epidemiological studies require the use of assumptions to address uncertainties. Among the key assumptions in risk assessments based on epidemiological studies that may be precautionary are the following:

- *Causality.* A key challenge inherent in the use of epidemiological studies is establishing a causal relationship between the contaminant being assessed and the identified health effect. That is, epidemiological studies may show that a particular substance is associated with a higher incidence of disease in an exposed population, but generally the studies do not provide clear evidence that the substance causes the disease. Furthermore, other scientific information that would help establish a causal relationship—such as how a contaminant causes the health effect, referred to as the "mode of action"—often does not exist. In addition, simultaneous exposures to other contaminants can reduce the certainty that exposure to a specific contaminant is producing the health effect that has been identified. Such exposures, referred to as confounding factors, can only be recognized, controlled, and measured to a certain extent. Because it is difficult to establish causation on the basis of epidemiological evidence, EPA must determine whether it can infer a causal relationship between exposure to a contaminant and observed health effects through its review of the available epidemiological and other data.
- *Extrapolation from high doses.* The populations analyzed in epidemiological studies may be exposed to doses of contaminants that are higher than the doses normally occurring in the environment. For example, epidemiologists often study more highly exposed populations, such as factory workers. As a result, EPA must make assumptions when it extrapolates the effects of high doses to the lower dose levels to which the general population may be exposed. These assumptions may or may not be precautionary.

- *Extrapolation from a study population to other populations*. Using epidemiological data from one population to estimate the health risks for another population is sometimes precautionary. For example, epidemiological data on the health risks of arsenic have been developed principally from a Taiwanese population whose diets may make them more susceptible than the U.S. population to cancer from exposure to arsenic. EPA used the Taiwanese data to estimate health risks in the United States but acknowledges that extrapolating from the Taiwanese data to the United States may tend to overstate the risk to the U.S. population. On the other hand, extrapolating from other epidemiological studies, such as those of U.S. workers, may tend to understate some health risks for the U.S. population because the workers in the studies would not include individuals with higher health risks, such as children, the frail elderly, and those with weakened immune systems that make them more susceptible to disease.

For most contaminants, epidemiological studies are less commonly available than animal studies. As a result, EPA relies primarily on studies of laboratory animals to support its health risk assessments.[11] Laboratory studies of animals can be controlled, and thus establishing causation is generally not an issue. Another advantage of animal studies is that they can provide information on the toxicity of contaminants before they are used, whereas epidemiological data can be collected only after human exposure. When using these toxicological studies to assess human health risks, however, risk assessors must rely on a number of assumptions that may be precautionary. EPA's assumptions relating to the use of toxicological data in risk assessment include the following:

- *Species-to-species inference*. The use of toxicological studies in assessing health risks relies on the assumption that laboratory animals, such as rats, mice, and monkeys, are surrogates for humans. According to the National Research Council, extrapolation between different species is supported by biological principles and empirical observations for many forms of biological responses, but the scientific basis of such extrapolation is not established with sufficient rigor to allow broad and definitive generalizations. The Council has also stated that toxicity is very often a function of chemical metabolism and that differences among animal species in metabolic handling of a chemical are not

[11]According to EPA officials, a growing literature suggests that cancer health risks derived from both human data and animal data are similar.

uncommon. The Council has further noted that, in most cases, information on a chemical's metabolic profile in humans is lacking and identifying the animal species and toxic response most likely to predict the human response accurately is generally not possible. While risk assessors assume that health effects seen in laboratory animals are likely to be seen in humans as well, some tests on laboratory animals have not identified human health problems. Perhaps the best known case is that of the drug thalidomide. No adverse health effects were found in animal testing; however, in humans it caused severe birth defects in the children of women who took the substance. Similarly, while epidemiological studies have shown that arsenic is a human carcinogen, test animals have not developed cancer from exposure to arsenic.

- *Extrapolation from high doses to low doses.* Animal studies must use much higher doses than the doses that people are typically exposed to because millions of animals would have to be exposed to low doses in order to detect adverse health effects. Although some critics question the validity of extrapolating the effects of high doses of contaminants given to research animals to low doses that people encounter in the environment, the National Research Council recommended that EPA continue to assume adverse effects from lower doses in the absence of other information.
- *Use of highly sensitive animal species.* Toxicology studies often use animals that are highly sensitive to the contaminant being studied in order to ensure a detectable response. Similarly, when there are multiple studies assessing the toxicity of a substance but information is lacking on which species responds most like humans, EPA uses the most sensitive species in assessing human risk.[12]

In addition to assumptions inherent in the use of toxicological data that may be precautionary, there are other assumptions, such as the following, that are generally seen as not being precautionary:

- *Studies account for exposure to only one chemical.* Animal studies usually address an individual chemical, even though people are often exposed to multiple contaminants in the environment. There is evidence that for some contaminants, combinations of exposures may increase health risks to higher levels than would be estimated by simply adding the individual risks together. Therefore, a toxicity assessment that relies

[12] *Reference Dose (RfD): Description and Use in Health Risk Assessments*, EPA (Mar. 1993).

on animal studies that address a single contaminant may tend to underestimate toxicity to people who are exposed to multiple contaminants.

- *Studies account for exposure through only one route*. Similarly, people may be exposed to a contaminant by more than one route, which could mean that risks assessed on the basis of an animal study using only one such route could underestimate the risks to people.
- *Studies generally use mature animals*. According to EPA officials, most toxicology studies use mature animals, thereby ignoring effects of exposure on the developing animal—which may be more frequent, more severe, or very different in nature from the effects on mature animals.

The Type of Health Risk Being Assessed

Over time, EPA has developed different policies and methodologies for assessing different types of health risks. Most notably, EPA's approach for cancer risk assessment has differed from its approaches for noncancer risk assessment. Both types of risk assessments rely on assumptions, including precautionary assumptions; however, the specific assumptions used differ with the type of risk being assessed. Central to the development of EPA's approach to risk assessment for carcinogens has been the theory that even a small number of changes in a single cell can lead to the uncontrolled growth of cells known as cancer. This theory implies that there is no safe level of exposure, or threshold, below which the contaminant does not pose a risk. In contrast, for health problems other than cancer, EPA has generally posited that there is some safe level of exposure to a contaminant before health effects occur.

EPA's Assessment of Cancer Risks

In assessing cancer risks, EPA develops a quantitative estimate of the expected increase in the incidence of cancer resulting from varying exposures to a contaminant. This estimate is called the dose-response relationship. In dose-response assessment, EPA has not traditionally speculated as to how the potential carcinogen induces cancer, and such data have generally not been available, according to the director of the quantitative risk methods group within EPA's Office of Research and Development. In developing the dose-response relationship, EPA generally uses two key precautionary assumptions:

- *A linear, no-threshold relationship between the dose and the health effects at low doses*. This assumption posits no safe level of exposure to a carcinogen—that is, any exposure presents some risk of developing cancer. However, for some contaminants, a nonlinear dose-response relationship is believed to exist, while other contaminants are believed

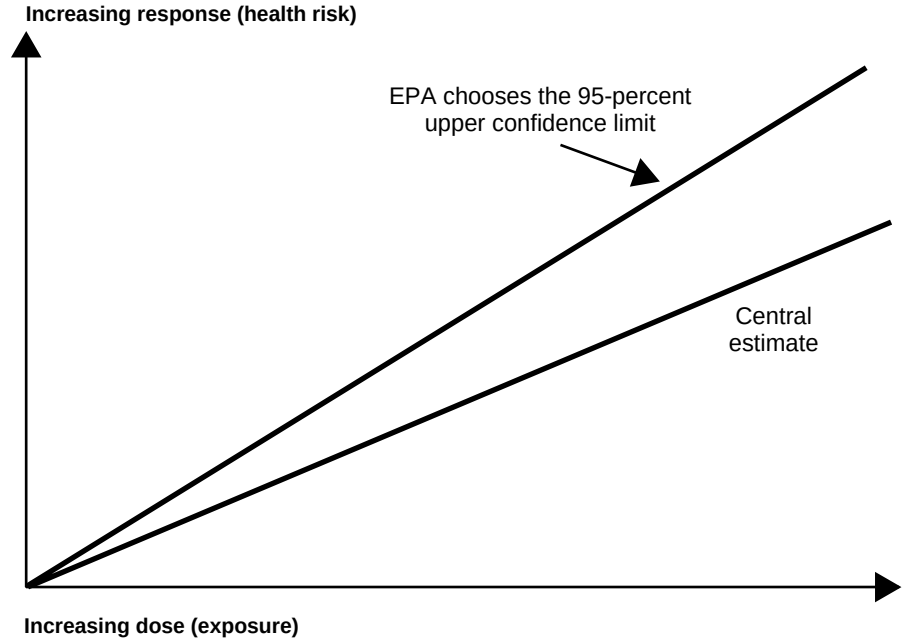
to have a threshold (see app. II). In addition, this assumption relies on the observed relationship between high doses and the incidence of cancer—based on either epidemiological or toxicological data—to predict or extrapolate the cancer risk at the much lower levels for which no data on health responses are available. When EPA does not have sufficient data or a model for extrapolating the cancer risk at lower doses, EPA's guidelines for cancer risk assessment call for estimating a linear relationship between dose and health effects. That is, each additional increment of exposure is assumed to produce the same proportional change in the health effect.

- "*Upper bound" estimates of risk.* EPA uses statistical procedures to develop an estimate of the dose-response relationship that is very unlikely to be exceeded by the true risk. This estimate, typically set at the 95-percent upper confidence limit, represents an upper bound on risk (see fig. 2).[13] According to a report prepared for the National Commission on Risk Assessment and Risk Management,[14] if the unknown dose-response relationship is linear at low doses, this procedure overestimates the true risk by a relatively small factor, usually two- to threefold. If, however, the true relationship at low doses is nonlinear, this approach will overestimate risks by larger factors that increase as the dose levels decrease.

[13]The 95-percent upper confidence limit is a statistically derived upper-limit estimate of risk that is designed to overstate rather than understate human risk.

[14]*A Survey of Methods for Chemical Health Risk Assessment Among Federal Regulatory Agencies*, prepared for the National Commission on Risk Assessment and Risk Management by Lorenz R. Rhomberg, Ph.D., Harvard Center for Risk Analysis, Harvard School of Public Health (1996).

Figure 2: EPA's Standard (Default) Dose-Response Relationship for Carcinogens



Note: The figure above is for a hypothetical contaminant. The relative difference between the 95-percent upper confidence limit and the central estimate varies across contaminants.

The National Research Council stated in 1994 that EPA should continue to use upper-bound estimates of lifetime cancer risks. It noted, however, that whenever possible, this estimate should be supplemented with other descriptions of cancer risk that more fully reflect the uncertainty associated with these estimates.

EPA's cancer risk assessment guidelines, issued in 1986, emphasize that its default assumptions lead to a plausible upper limit on the risk that is consistent with some proposed mechanisms for how cancer develops. The guidance also states, however, that the estimate is not necessarily a realistic predictor of risk, since the true value of the risk is unknown and may be as low as zero.

In addition to the precautionary assumptions that relate to the dose-response relationship, EPA's risk assessments for cancer reflect other precautionary assumptions such as the following:

- A substance that is carcinogenic in animals is likely to be a human carcinogen.
- When benign and malignant tumors are observed in animals, the incidence of both is combined to represent the substance's carcinogenic potential in humans.
- In the absence of information indicating which species responds most like humans, the animal species exhibiting the greatest carcinogenic sensitivity is given the greatest emphasis in developing estimates of human cancer risk.

As for other types of risk assessment, EPA's policies and practices for assessing cancer risks have been changing as new analytical techniques are developed and scientific knowledge increases. For example, the agency's guidelines for assessing carcinogenic risk are being revised. Among the issues addressed in the draft guidelines is the no-threshold assumption for carcinogens. As more research into the mechanisms of how cancer develops has become available, there have been challenges to the theory that there is no safe level of exposure to a carcinogen. For example, in 1994 the National Research Council reported that risk models that use a threshold are plausible for many carcinogens.

In March 2000, a federal appeals court ruled that in setting a health-based maximum contaminant level goal for chloroform (a chemical byproduct of chlorination, the most widely used technique for ensuring the safety of drinking water) under the Safe Drinking Water Act, EPA "openly overrode the 'best available' scientific evidence," which suggested that there is a threshold for the carcinogenic effects of chloroform.[15] In 1998, EPA concluded that the assumption of a nonlinear relationship, which is permitted under its existing carcinogenic risk guidelines issued in 1986, would be more appropriate than a linear assumption. However, in the final rule, EPA used a no-threshold, linear assumption. According to EPA officials, staff responsible for conducting risk assessments have been reluctant to depart from the standard cancer defaults in EPA's existing policy because of uncertainties about when such a departure would be appropriate.[16] The criteria for departing from the defaults have not been clearly articulated in the past, and there is ongoing debate over whether departing would be protective of sensitive populations, including children. The revised guidelines, which are not finalized as of October 2000, will offer more direction to risk assessors in terms of when and how to depart from the traditional no-threshold assumption, according to EPA officials.

[15] *Chlorine Chemistry Council v. Environmental Protection Agency*, 206 F.3d 1286, 1290 (D.C. Cir. 2000).

[16] In the case of chloroform, the risk assessors departed from the standard cancer default, but EPA made the policy decision to use the standard default, in part, because not using the default would represent a "significant and precedential" application of new science that had important implications for other contaminants regulated under the Safe Drinking Water Act.

EPA's Assessment of Noncancer Health Risks

In addition to assessing carcinogenic risks, EPA assesses other threats to human health, such as respiratory problems associated with air pollution. Because of the wide variety of noncancer health effects and the diversity of ways in which contaminants are suspected of working, EPA does not have a single approach for assessing noncancer risks comparable to its agencywide guidelines for assessing cancer risks.[17] However, one approach—using what is called a reference dose, or RfD—is used most frequently to determine a threshold or safe level of exposure to a contaminant. The reference dose is an estimate of a daily exposure level that is not likely to cause "appreciable risk of deleterious effects during a lifetime."[18]

In estimating a safe level of exposure to the noncarcinogenic effects of a contaminant, EPA first determines the dose level at which no adverse effects have been observed. This level is then reduced because of uncertainties in the data—generally toxicological data from animal studies. That is, the dose at which no adverse effects have been observed is reduced (divided) by one or more uncertainty factors (sometimes called safety factors). The uncertainty factors account for the possibility that people might need a lower level of exposure to better ensure safety.[19] Each uncertainty factor typically reduces the level at which no adverse effects have been observed to one-tenth the original dose. The following two uncertainty factors are used most frequently:

- A factor of 10 is generally used to account for variation in sensitivity among people, such as the elderly and other populations that are more susceptible to diseases.
- A factor of up to 10 is generally used to account for the uncertainty associated with using the results of laboratory animal studies to estimate the health effects expected in people. This factor, usually set at 10, stems from the concern that people could be more sensitive to the toxic effects of a contaminant than are laboratory animals. For example,

[17]The agency has, however, issued risk assessment guidelines for several types of noncancer health threats, including developmental toxicity and reproductive toxicity.

[18]EPA also develops reference concentrations (RfC), estimates of a daily exposure level (in terms of air concentrations rather than dose) that is likely to be without an appreciable risk of adverse noncancer effects during a lifetime.

[19]EPA uses the term "uncertainty factor" rather than "safety factor" because of concerns that the latter term implies an absolutely safe level, an assurance the agency does not believe it can provide.

small animals have faster metabolic processes, allowing them to eliminate contaminants from their bodies more quickly than people can.

Other factors may be added to account for such uncertainties as a safe level for lifetime human exposure when only short-term animal studies are available. According to a report prepared for the National Commission on Risk Assessment and Risk Management, two or three factors are typically used in assessing noncancer risks. This could result in as much as a 100- or 1,000-fold decrease in the estimated safe level of exposure.

As for cancer risk assessment, EPA's approaches for noncancer risk assessment are changing over time with increases in scientific understanding of how contaminants cause adverse health effects and the relationship between the dose of a contaminant and the increased health risk expected. In some instances, EPA has enough information on the general human population to estimate a quantitative relationship between exposures to varying concentrations of the contaminant and the expected increased health risks. In these cases, EPA does not have to use the reference dose approach that relies on various factors to reflect uncertainties and data gaps. Such is the case with six widespread air pollutants for which EPA has established national health-based standards under the Clean Air Act, including particulate matter.

EPA's Use and Disclosure of Precautionary Risk Assumptions in Estimating Benefits for Two Major Regulations

The two major health-based regulations we examined differed in the extent to which they used precautionary assumptions in estimating health risks and benefits. EPA used such assumptions only to a limited extent in the case of the 1997 air quality standards for particulate matter but relied on them more in its recently proposed drinking water standard for arsenic. However, in assessing the health risks of arsenic and estimating the related benefits of the proposed standard, EPA used new analytical techniques that removed other precautionary assumptions used in the past. In its proposed arsenic regulation, EPA identified the key health uncertainties and precautionary assumptions it used in assessing the risks of arsenic in drinking water but was less complete in identifying them in its formal cost-benefit analysis. Furthermore, although its guidance on cost-benefit analyses calls for assessing uncertainty using sensitivity analysis, EPA did not perform sensitivity analysis that could have provided information on the potential impact of the precautionary health assumptions that underlie its benefits estimate.

EPA's 1997 National Ambient Air Quality Standards for Particulate Matter

Under the Clean Air Act, EPA sets health-based National Ambient Air Quality Standards for certain widespread air pollutants including particulate matter—the generic name for a mixture of air pollutants commonly found across the United States.[20] EPA is required to review the existing standards every 5 years to ensure that the standards are based on the most recent scientific information. EPA last revised the particulate matter standards in July 1997, at which time it added standards for fine particulate matter (particles less than 2.5 micrometers in diameter).[21] (See app. III for information on the several standards EPA set for particulate matter.) EPA estimated that the new standards for fine particles could save between 3,300 and 15,600 lives annually. EPA's monetary estimate of the health benefits of the new standards, which included not only lives saved but also other benefits, such as cases of chronic bronchitis avoided, ranged from $14.5 billion to $96.1 billion per year.[22]

When EPA evaluated the health risks from particulate matter in developing its 1997 standards, it generally did not rely on precautionary assumptions. This was largely because EPA had better data at relevant exposure levels than is often the case when the agency assesses risks. The strengths of the data included the following:

- EPA had a large body of epidemiological research upon which to base its risk assessment. This contrasts with most of EPA's risk assessments, which must rely on animal studies. Thus, EPA did not have to make the assumptions needed when animal studies are used to predict human health risks. Moreover, the epidemiological research showed largely consistent associations between particulate matter in the outdoor air and a variety of health problems, including premature death from respiratory and cardiovascular causes, particularly among the elderly; exacerbation of cardiopulmonary and respiratory illnesses; an increased

[20]Particulate matter can include many chemically and physically diverse substances and can vary significantly by location. A number of activities typically add to the concentration of particulate matter in the air, including combustion from power plants, industrial facilities, cars, trucks, and wood stoves; construction and demolition activities; and road dust. Among the major chemical components of particulate matter are sulfates, nitrates, acids, metal compounds, and water.

[21]A micrometer, also known as a micron, is one-millionth of a meter.

[22]The particulate matter rule accounts for as much as 54 percent of the total benefits of the 48 major rules issued governmentwide from Apr. 1, 1995, to Mar. 31, 1999, for which federal agencies estimated benefits.

incidence of bronchitis in children; and an increased number of childhood asthma attacks.

- EPA had sufficient data to estimate a range of risks showing how risk would vary with different concentrations of particulate matter in the air. Typically called a dose-response relationship, this is referred to as a concentration-response relationship in the case of air pollutants, where the observed relationship is between the concentration of the pollutant in outdoor air and the given health effects. In contrast, for most other noncarcinogenic pollutants, EPA would typically make only one estimate—that of a dose likely to be safe (a reference dose discussed above). In estimating a dose likely to be safe, EPA would typically reduce the allowable exposure by applying uncertainty factors to account for such things as people's differing susceptibilities to the pollutant's health effects.
- Furthermore, EPA had information about directly relevant concentration levels of particulate matter in the air, that is, at levels to which the population was actually exposed. Thus, the agency did not have to extrapolate exposure information from studies using higher doses. Because the studies EPA relied on were based on U.S. data for a number of urban areas, EPA did not have to extrapolate the effects observed in one population to estimate the health effects in another population. Moreover, in assessing the health effects of particulate matter on the basis of findings from numerous epidemiological studies, EPA used risk levels that represented central tendency estimates rather than upper-bound estimates of the health effects.

Despite the strengths of the available epidemiological data, there were significant scientific uncertainties in EPA's evaluation of particulate matter's health effects, which led EPA to use at least one precautionary assumption. EPA's sensitivity analyses showed that the most significant uncertainty was whether a threshold concentration existed, that is, whether the health effects would be associated with particulate matter at any level of exposure. In the quantitative health risk assessment used in the standard-setting process, EPA made the precautionary assumption that there was no threshold for the health problems associated with particulate matter. EPA officials said they made this precautionary assumption because they did not have information that indicated the existence of a threshold for the various health effects included in the risk assessment.

However, EPA's methodology did not estimate the health risks down to a concentration of zero. EPA estimated the health effects associated with particulate matter starting at the larger of

- the level of naturally occurring particulate matter (also called the background level)[23] or
- the lowest average annual level of particulate matter observed in the epidemiological studies EPA relied upon.[24]

EPA's estimate of adverse health effects was lower than it would have been had the agency included health risks at the lowest levels. However, EPA officials believe it was appropriate to measure health effects only above the naturally occurring levels of particulate matter because it is unlikely that concentrations of particulate matter could be reduced below such levels. Also, EPA did not estimate health effects below the levels reported in the epidemiological studies because of the uncertainties about health effects at such levels.

[23]EPA made the following "base case" assumptions about background concentrations of particulate matter (expressed in terms of micrograms per cubic meter of air) in the two locations included in its risk analysis: fine particulate matter (also called PM2.5)—3.5 in Philadelphia County, Pennsylvania, and 2.5 in Southeast Los Angeles County, California; course and fine particulate matter (also called PM10)—8 in Philadelphia County and 6 in Southeast Los Angeles County. EPA also conducted sensitivity analyses looking at the effects of alternative assumptions about background levels.

[24]For example, the lowest median annual concentration of particulate matter in a key study assessing the mortality risks associated with this pollutant was 9 micrograms per cubic meter of air.

When EPA estimated the health benefits of the particulate matter standards as part of its cost-benefit analysis, it used essentially the same dose-response relationships used in the risk assessment. EPA's cost-benefit analysis also identified the scientific uncertainties associated with this dose-response relationship. However, in estimating the benefits of this rule, EPA did not include the risk assessment's precautionary assumption that there was no threshold (above certain levels) for the health effects. Rather, EPA estimated benefits using two different assumptions about thresholds above background levels—at concentrations of 12 and 15 micrograms of fine particulate matter per cubic meter of air. According to EPA officials, the additional benefits from risk reductions at concentrations of particulate matter below 12 micrograms per cubic meter would not be as significant as at the higher levels because few geographic locations would achieve concentrations at the lowest pollution levels.[25]

Another assumption that EPA made in evaluating particulate matter's health risks and in estimating benefits, an assumption that is typically used when epidemiological data are involved, was causality—that is, EPA assumed that there is a causal relationship between particulate matter and the health effects with which it has been associated. Some scientists and other commenters on EPA's proposed particulate matter regulation believed that the causality assumption was precautionary. EPA, however, did not characterize this assumption as precautionary because it believed the consistency of the results from a large number of locations and the coherent nature of the results suggest a likely causal role of particulate matter in contributing to these health effects.

Nonetheless, many questions remain about how particulate matter may be causing premature death and other adverse health effects, including questions of whether there may be confounding agents, such as other air pollutants (e.g., sulfur dioxide and ozone), that may be causing at least some of the problems. The National Research Council has cited the "relatively consistent but poorly understood associations between ambient particulate matter concentrations and various adverse health effects."[26] Because of the many unknowns, EPA's Clean Air Scientific Advisory

[25]As a result of guidance from its economic advisory committee, EPA's more recent benefits estimates done for other regulations, such as its estimate of the prospective benefits of the Clean Air Act, have assumed, among other scenarios, that there is no threshold above the background level of particulate matter.

[26]See *Research Priorities for Airborne Particulate Matter*, Vol. 1 (1998), p. 19.

Committee strongly recommended that EPA implement a targeted research program to address these unanswered questions and uncertainties. In its fiscal year 1998 appropriations, the Congress provided funding of $49.6 million specifically for research on particulate matter. The Congress also directed the EPA Administrator to arrange for an independent study to, among other things, monitor and report on progress toward improved understanding of the relationship between particulate matter and its health effects. The National Research Council is carrying out this mandated work.

Some research findings have recently been released that buttress the findings in the studies EPA relied on in making its decisions to regulate fine particles in 1997. For example, in July 2000, the Health Effects Institute reported that its reanalysis and additional analysis of the underlying data essentially validated two key studies, as well as these studies' findings of an association between particulate matter and mortality, that EPA had relied on in issuing its 1997 rule.[27]

Although EPA develops what it considers best estimates rather than precautionary estimates of the risks from particulate matter, the Clean Air Act requires that the health-based standards be set with an "adequate margin of safety." According to officials from EPA's Office of Air and Radiation, building in the required margin of safety for the particulate matter standards was a risk management decision, not part of the assessment of risk. That is, the margin of safety was incorporated into the allowable concentration levels, or standards, chosen by the Administrator. These standards have been challenged in court. A summary of the issues associated with the decision over the levels at which the standards were set, as well as the court case, is included in appendix IV. While the judicial review of the 1997 particulate matter standards proceeds, the next 5-year mandated review of the standards, expected to be completed in 2002, is also under way.

[27]The Health Effects Institute is a nonpartisan, independent research organization whose major funding is from EPA and the auto industry. See its *Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality. A Special Report of the Institute's Particle Epidemiology Reanalysis Project* (July 2000).

EPA's June 2000 Proposed National Primary Drinking Water Regulation for Arsenic

Under the Safe Drinking Water Act, EPA sets health-based, legally enforceable drinking water standards limiting the level of contaminants in the nation's drinking water systems that can adversely affect public health. First, EPA establishes a health-based goal at a level at which no known or anticipated adverse health effects occur and that allows an "adequate margin of safety." If a contaminant, such as arsenic, is likely to cause cancer, EPA generally sets the goal at zero. After setting the goal, EPA typically establishes an enforceable standard, called a maximum contaminant level, that is as close to the health-based goal as is feasible, considering the available technology and costs.[28] EPA is also to complete an economic analysis to determine whether the benefits of the standard justify the costs. If the benefits do not appear to be justified, EPA may adjust the standard to a level that "maximizes health risk reduction benefits at a cost that is justified by the benefits."[29] This latter provision is a new authority the Congress gave to EPA under amendments to the Safe Drinking Water Act in 1996.

The 1996 amendments to the Safe Drinking Water Act also require EPA to propose a new arsenic standard by January 1, 2000, and to issue the final rule by January 1, 2001. Recognized as a toxic element for centuries, arsenic has also been associated with skin, bladder, and other cancers.[30] EPA issued its proposed arsenic standard in June 2000. Specifically, EPA proposed setting the maximum contaminant level goal at zero and lowering the enforceable contaminant standard from 50 micrograms per liter to 5 micrograms per liter.[31] EPA is using its new authority to set the standard at a higher level than the technologically feasible level of 3 micrograms per liter both because (1) it did not believe that the costs were justified by the benefits at that level and (2) there were a number of uncertainties, including scientific uncertainty about the health effects of arsenic at low levels of exposure in drinking water. EPA also requested public comment on alternative standards of 3, 10, and 20 micrograms per liter.

[28]Drinking water standards also often apply to contaminated groundwater at hazardous waste sites regulated under EPA's Resource Conservation and Recovery Act and Superfund programs, and arsenic is a key contaminant at many of these sites.

[29]P.L. 104-182, 110 Stat. 1613, 1624 (1996).

[30]These cancers have been associated with arsenic present in drinking water at concentrations higher than those observed in U.S. drinking water supplies.

[31]A microgram is one-millionth of a gram. The Public Health Service first established the standard of 50 micrograms per liter in 1942.

Arsenic occurs naturally in the environment, for example, in rocks, soil, and groundwater, and has been used in a variety of commercial activities, most notably today as a component of wood preservatives. Because arsenic does not degrade in the environment, contamination from historical releases is cumulative. EPA estimates that about 10 percent of groundwater and surface water systems have average arsenic levels above 5 micrograms per liter, and about 4.5 percent have average arsenic levels above 10 micrograms. Arsenic concentrations in groundwater generally are highest in the Western United States, where EPA estimates that 12 percent of groundwater systems exceed 10 micrograms per liter. In setting this standard, EPA sought to protect public health at a level such that at least 90 percent of the exposed population would face a lifetime risk of less than 1 in 10,000 for developing bladder cancer. EPA estimates that the new standard will avoid 16 to 36 bladder cancer cases each year, 4 to 9 of which would be fatal. As discussed below, EPA reported that several other health benefits are expected to result from the proposed standard, including reductions in lung cancer, that it cannot reliably quantify at this time.

For the proposed arsenic standard, EPA estimated the health risks of bladder cancer on the basis of epidemiological studies,[32] relying primarily on a review of arsenic health effects research conducted by the National Research Council at EPA's request. The Safe Drinking Water Act requires EPA to consider peer-reviewed scientific information on health effects in setting drinking water standards, and EPA considered the Council's study as presenting the best available peer-reviewed science. EPA used four alternative dose-response relationships reported by the National Research Council. These relationships were based on epidemiological data on bladder cancer mortality in a high-arsenic region in Taiwan. The median arsenic concentrations in the 42 Taiwanese villages studied ranged from 10 micrograms per liter to 934 micrograms per liter; 29 of the villages had median arsenic concentrations at or above 100 micrograms per liter. The National Research Council noted that studies in Chile and Argentina observed risks of lung and bladder cancer of the same magnitude as those reported in Taiwan at comparable levels of exposure.

EPA's estimate of the reductions in health risks and the benefits of its proposed arsenic standard relied on the following key precautionary assumptions:

[32]As noted earlier, arsenic is one of the few contaminants that causes cancer in humans but not in laboratory animals.

- EPA assumed that the dose-response relationship for arsenic is linear without a threshold, even at low concentrations, rather than sublinear and/or with a threshold. (For either of these alternative assumptions, the response at low doses would have been less than that predicted by a linear dose-response relationship.) EPA made this assumption because it concluded that the scientific evidence suggesting a sublinear dose-response relationship is not strong enough to depart from its default assumption of a linear, no-threshold dose-response relationship. While the National Research Council noted that the most plausible scientific evidence on how arsenic causes cancer supports a sublinear dose-response relationship, the Council concluded that the available evidence was inconclusive and did not meet EPA's stated criteria in its 1996 proposed cancer risk assessment guidelines for departure from the default assumption of linearity. In its proposed rule, EPA solicited comments on this issue.
- EPA assumed that the National Research Council's risk estimates based on epidemiological data for a rural population in Taiwan could apply to the U.S. population, even though the Taiwanese diet, compared to the U.S. diet, includes (1) higher levels of arsenic and (2) lower levels of selenium, which has been shown to moderate the adverse health effects of arsenic in animal studies. The Council noted that available data suggest that arsenic intake from food is higher in Taiwan than in the United States, and EPA stated in its proposed rule that "arsenic intake (by persons in the Taiwanese study region) from sources other than drinking water would overestimate the unit risk calculated from the Taiwan study." The Council also noted that these differences "could affect the relevance of the results" of its Taiwanese-based risk estimates for a risk assessment for the U.S. population. In light of this concern, the Council recommended that EPA investigate the relationship between nutritional factors in study populations and susceptibility to arsenic-induced cancer. Without this information, the Council indicated that it might be appropriate to be precautionary in risk assessments of arsenic.
- Because of data limitations, EPA relied on the National Research Council's assumption that the individuals in the Taiwanese study who got bladder cancer were exposed to the median (50th percentile) level of arsenic found in the water of their villages' wells. In its notice of the proposed standard, EPA acknowledged that this assumption is precautionary, citing its Expert Panel on Arsenic Carcinogenicity, which said that biases from using average doses for groups lead to overestimation of risk.

Each of these assumptions tends to overestimate the risk of arsenic exposure and the benefits associated with reducing those risks. EPA's proposed rule clearly identifies the precautionary assumptions discussed above and also indicates that the agency will reexamine the use of these assumptions before issuing the final rule.[33] The proposed rule also indicates that EPA's use of these assumptions may have resulted in a significant overestimation of the risk of bladder cancer. Consequently, EPA's estimate of the related benefits may also be significantly overstated. EPA officials told us that they did not attempt to determine the effects of varying these precautionary assumptions by conducting sensitivity analyses because they did not have sufficient information to do so. We note, however, that even in the absence of sufficient data, sensitivity analyses can use "what if" assumptions to assess the potential impact of precautionary assumptions. Furthermore, EPA's guidelines for preparing economic analyses state that sensitivity analyses should be performed on key assumptions, if feasible, in assessing and presenting uncertainty.[34] Finally, EPA's cost-benefit analysis report identified the precautionary assumption of a linear dose-response relationship but did not identify the other precautionary assumptions discussed above.[35] Thus, some key scientific uncertainties associated with the arsenic benefits estimates are not reflected in this report.

[33]EPA's proposed rule represents the agency's documentation of its risk assessment on arsenic at this time. EPA also cites the report of the National Research Council from which it derived its risk estimates, *Arsenic in Drinking Water*, National Academy Press (1999).

[34]This guidance is consistent with GAO's 1997 recommendation to EPA to ensure that the agency's cost-benefit analyses identify the sensitivity of benefit and cost estimates when there are major sources of uncertainty. See *Air Pollution: Information Contained in EPA's Regulatory Impact Analyses Can Be Made Clearer* (GAO/RCED-97-38, Apr. 14, 1997). We have also recommended that the Office of Management and Budget amend its guidance to strengthen the clarity and credibility of cost-benefit analyses. See *Regulatory Reform: Agencies Could Improve Development, Documentation, and Clarity of Regulatory Economic Analyses* (GAO/RCED-98-142, May 26, 1998).

[35]*Proposed Arsenic in Drinking Water Rule: Regulatory Impact Analysis*, EPA 815-R-00-013 (June 2000).

The National Research Council concluded that risk assessments of bladder, lung, and other cancers associated with arsenic can be performed and also recommended further study to characterize a number of adverse noncancer effects, including heart disease and diabetes. Because EPA based its risk estimate only on bladder cancer, the agency believes that it underestimated the combined risk of all arsenic-induced health effects. In its proposed rule, EPA said that its decision to use only bladder cancer was a judgment call that was guided by the best available science. In addition, EPA did develop a rough estimate of the benefits of reductions in lung cancer, using what it termed a "what if" scenario, and it identified them as potential benefits in its cost-benefit comparisons.[36] EPA expects to have a peer-reviewed quantitative analysis of lung cancer risk available for its risk assessment and benefits estimate for the final rule. EPA's cost-benefit analysis report also indicates that the monetary benefits associated with reductions in skin cancer would be minimal. Finally, EPA does not believe it has sufficient information to quantify the numerous noncancer health effects associated with arsenic.

Although EPA's risk assessment and benefits estimate included several precautionary assumptions, EPA also used new analytical techniques that removed other precautionary assumptions used by the agency in the past:[37]

- According to officials in EPA's Office of Water, past risk assessments and benefits estimates for drinking water standards typically relied on the precautionary assumption that all individuals consume 2 liters of drinking water per day over his or her lifetime, which is more than the average individual is believed to consume. This assumption tended to overestimate risk because health risks from contaminants in drinking water increase with water consumption. For the proposed arsenic rule, however, EPA assumed that different individuals consume different amounts of water. EPA's estimates of these varying amounts were based on recent survey data indicating that, on average, an individual consumes only about 1 liter of drinking water a day. By using more

[36]For its rough estimate of lung cancer benefits, EPA relied on the National Research Council's statement that "some studies have shown that excess lung cancer deaths attributed to arsenic are 2- to 5-fold greater than the excess bladder cancer deaths." EPA acknowledged that this estimate is probably too high because a reanalysis of the studies indicates that the excess lung cancer deaths attributed to arsenic are approximately equal to the excess bladder cancer deaths.

[37]EPA calculated risks using Monte Carlo analysis, which employs computer simulations to calculate a range of risk values rather than a single "point estimate" of risk.

realistic water consumption assumptions, EPA produced both risk and benefits estimates that were significantly less than they would have been if it had continued to use the precautionary assumption about water consumption.

- EPA's risk assessment and benefits estimate for arsenic also did not include another significant precautionary assumption that EPA typically uses for carcinogens. Although EPA did make the precautionary assumption that the dose-response relationship is linear with no threshold, it did not use the upper-bound estimate of this linear relationship. Instead, it used ranges of linear dose-response relationships derived from a range of risk estimates reported by the National Research Council. Because EPA used ranges of dose-response relationships, its risk estimates and benefits estimates were significantly less than they would have been if it had used its typical precautionary assumption of an upper-bound dose-response relationship.

Conclusions

The particulate matter and arsenic rules demonstrate some of the key uncertainties that EPA must address in evaluating the health effects of contaminants and determining the appropriate actions to take. In terms of the types of precautionary assumptions that EPA may use to address scientific data gaps and uncertainties, these cases are perhaps atypical in that sufficient epidemiological data are available in both cases to evaluate human health risks, whereas EPA generally must extrapolate from animal data. However, they are quite typical in that their fundamental uncertainty is about adverse health effects at the lowest levels of exposure—specifically, whether there is a threshold below which adverse health effects do not occur. Neither epidemiological nor animal data can provide complete information on health effects at the low levels to which people are typically exposed, and therefore assumptions about these health effects must be made. Greater uncertainty about the effects at low levels may exist for arsenic than for particulate matter because the epidemiological information on particulate matter is based on actual exposure levels in the United States, whereas the data on arsenic are primarily from Taiwanese populations exposed to much higher levels of arsenic than U.S. populations. However, the case of particulate matter illustrates how difficult it is to scientifically resolve uncertainties about causality associated with the use of epidemiological data—how challenging it is to conclusively demonstrate that the health effects associated with particulate matter are, in fact, primarily caused by exposure to the particulate matter rather than other factors, including other pollutants.

While EPA identified in its proposed regulation the key health uncertainties and precautionary assumptions it used in assessing the risks of arsenic in drinking water, it did not identify all of them in its formal cost-benefit analysis. Because this regulation is still being developed, EPA has the opportunity both to fully disclose the precautionary assumptions used and to incorporate some additional analyses into its final regulation. For example, sensitivity analyses showing the impact of precautionary assumptions on the risk assessment and benefits estimate could help the Administrator in setting the standard and could also provide other interested parties with a more complete understanding of the potential range of benefits of the standard.

Recommendation for Executive Action

To better inform decisionmakers about the effects of precautionary health assumptions on EPA's estimates of the benefits associated with the arsenic rule, we recommend that the EPA Administrator ensure that EPA's cost-benefit report for the final rule fully disclose the precautionary assumptions used and provide sensitivity analysis on the key precautionary assumptions included in the agency's benefits estimate.

Agency Comments

We provided a draft of this report to EPA for review and comment. In commenting on the draft, officials from the National Center for Environmental Assessment, Office of Research and Development, stated that the report presents a fair and informative discussion of the characteristics of data typically available for risk assessment. In addition, the officials supported the recommendation that the cost-benefit report for the arsenic rule disclose precautionary assumptions and provide sensitivity analysis, subject to the availability of data pertinent to such an analysis. Officials from the Offices of Air and Radiation; Water; and Policy, Economics, and Innovation provided technical comments and clarifications that we incorporated as appropriate.

The scope and methodology for our work are discussed in appendix I. We conducted our work from October 1999 through October 2000 in accordance with generally accepted government auditing standards.

We will send copies of this report to the Honorable Carol M. Browner, Administrator, EPA, and to other interested parties. We will also make copies available to others on request. Please call me or Christine Fishkin at

(202) 512-6111 if you or your staff have any questions. Other key contributors to this report are David Goldstein, Bruce Skud, and Susan Swearingen.

David G. Wood

Director, Natural Resources and
Environment

Objectives, Scope, and Methodology

Objectives

The Honorable Bud Shuster, Chairman of the House Committee on Transportation and Infrastructure, and Senator Frank R. Lautenberg asked us to examine whether the Environmental Protection Agency's (EPA) benefits estimates for major environmental regulations that establish health-based standards reflect precautionary assumptions about health risks. As agreed with our requesters, we focused our work on (1) key factors that affect EPA's use of precautionary assumptions in assessing health risks and (2) whether EPA used and identified precautionary assumptions in estimating the health risks and benefits of recent major regulations setting health-based standards.

Scope

The issue of whether EPA's estimates of the benefits of health-based environmental standards reflect precautionary health risk assumptions is relevant to major regulations that set health-based standards and estimate health benefits. The benefits of major regulations—that include those with an impact on the economy of $100 million or more—are provided in economic analyses (also referred to as regulatory impact analyses) required by Executive Order 12866. In fiscal years 1997 through 1999, four of EPA's major regulations set new health-based standards—two each under the Clean Air Act and the Safe Drinking Water Act. In fiscal year 2000 through June 2000, EPA proposed two health-based standards under the Safe Drinking Water Act. We selected one rule each from EPA's air and water programs in order to report on the agency's current methodologies and practices for estimating health risks and benefits: EPA's regulations (1) establishing air quality standards for particulate matter in July 1997 and (2) proposing a drinking water standard for arsenic in June 2000.

These regulations generally reflect EPA's current practices and procedures for risk assessments and benefits estimates for major categories of contaminants regulated by EPA under the Clean Air Act and the Safe Drinking Water Act. For example, the particulate matter rule covers one of the six widespread air pollutants that EPA is required to set standards for and to review every 5 years. EPA uses similar approaches in estimating health risks and health benefits for the other criteria pollutants, including the ozone rule that was also promulgated in 1997. As of June 2000, EPA had not proposed or finalized other health-based standards for criteria pollutants since 1997. Similarly, we reviewed EPA's proposed rule to revise standards for arsenic in drinking water under the Safe Drinking Water Act, issued for comment in June 2000, because it incorporates new approaches to setting health-based standards and estimating benefits reflecting the

requirements of the 1996 amendments to the Safe Drinking Water Act. This rule incorporates the general approach the agency plans to use in setting health-based standards under the act.

Although these regulations provide examples of the differing extent to which EPA may use precautionary assumptions in risk assessments and benefits estimates, the results may not be generalizable to all of EPA's major regulations setting health-based standards. In addition, our review of the benefits estimates is limited to examining the extent to which EPA used precautionary assumptions in assessing health risks and in estimating the benefits of the proposed or final health-based standards. As a result, we did not review the economic aspects of EPA's benefits estimates, such as the methods used to estimate dollar values for lives saved and illnesses avoided. Finally, we did not assess the extent to which EPA's benefits estimates comply with the agency's and the Office of Management and Budget's guidance for preparing economic analyses of significant regulatory actions, which include guidance on the treatment of risk and uncertainty and reporting the "best" or most likely estimate.

Methodology

To determine the key factors that affect EPA's use of precautionary assumptions in assessing health risks, we reviewed EPA statutes that address health-based standards, EPA policy guidance on risk assessment and risk characterization, and relevant reports by the National Academy of Science's National Research Council and the Presidential/Congressional Commission on Risk Assessment and Risk Management. We also interviewed officials in EPA's Offices of Policy, Economics, and Innovation; Water; Air and Radiation; and Research and Development. To obtain perspectives on the use of precautionary assumptions in health risk assessment, we interviewed experts from the Health Effects Institute, the Harvard School of Public Health, Resources for the Future, and an official of the American Industrial Health Council. We also reviewed a variety of scientific articles on health-based risk assessment. Finally, we attended risk assessment and environmental regulation seminars at the Harvard School of Public Health's Center for Risk Analysis, from which we obtained information incorporated into this report.

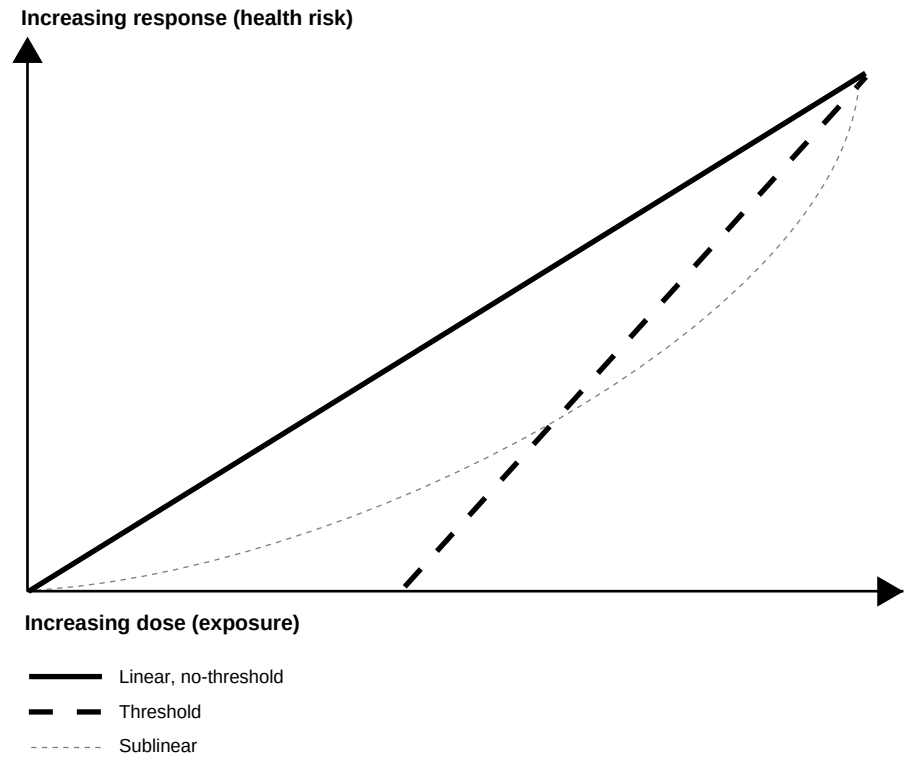
To determine how precautionary assumptions affected the health-based standards and the estimated benefits of recent major regulations and whether EPA clearly identified these assumptions, we reviewed (1) the proposed and final rules for particulate matter, the quantitative health risk assessment, the regulatory impact analysis, and other key documents,

including EPA's criteria document on particulate matter and recent judicial findings on the particulate matter rule and (2) the proposed rule for arsenic, regulatory impact analysis, and other supporting documents, including the 1999 report, *Arsenic in Drinking Water,* by the National Research Council that EPA relied on for its risk assessment. We attended the June 2000 meeting of EPA's Science Advisory Board on the proposed arsenic regulation. We met with officials in the air and water program offices to obtain, among other information, their views on the use of precautionary assumptions in these rules.

Dose-Response Relationships Based on Varying Assumptions

In assessing cancer risks, EPA generally assumes a linear, no-threshold relationship between the dose of a contaminant and its health effect at low doses. This assumption posits that (1) dose and health effect vary linearly, that is, if a dose is doubled, the health effect doubles; and (2) there is no safe level, or threshold, of exposure to a carcinogen—that is, any exposure presents some risk of developing cancer. However, for many contaminants, a threshold and/or a sublinear dose-response relationship is believed to be plausible. Both sublinear and threshold dose-response relationships typically lead to lower risk estimates at the lowest dose levels than does a linear, no-threshold dose-response relationship.[1] These varying dose-response relationships are shown in figure 3.

Figure 3: Dose-Response Relationships Based on Varying Assumptions



[1]According to EPA officials, some contaminants, such as vinyl chloride, pose a higher risk at low doses than that predicted by a linear dose-response relationship. The dose-response relationship for such contaminants is referred to as supralinear.

Summary of EPA's 1997 Particulate Matter Standards

In July 1997, EPA established its most recent National Ambient Air Quality Standards for particulate matter (commonly called soot), which included new standards for the fine fraction of particulate matter, also known as fine particulate matter.[1] The standards are for annual and daily concentrations of particulate matter measured at various locations across the United States. The annual standards are intended to provide protection against typical day-to-day exposures as well as longer-term exposures. The daily standards are intended to provide protection against days with high peak concentrations of particulate matter, localized "hot spots," and risks from seasonal emissions that would not be well controlled by national annual standards.

Table 1: 1997 Particulate Matter Standards

Standards in micrograms per cubic meter

Type of particulate matter	Annual standard	24-hour (daily) standard
Particulate matter (PM10)[a]	50[b]	150[c]
Fine particulate matter (PM2.5)	15[d]	65[e]

[a]Includes both coarse and fine particles.

[b]Based on the 3-year average of annual arithmetic mean concentrations of PM10 at specified monitors.

[c]Based on the 3-year average of the 99th percentile of 24-hour concentrations of PM10 at specified monitors.

[d]Based on the 3-year average of annual arithmetic mean concentrations of PM2.5 at specified monitors.

[e]Based on the 3-year average of the 98th percentile of 24-hour concentrations of PM2.5 at specified monitors.

[1]These are the primary standards, intended to protect the public health. The Clean Air Act also calls for secondary standards, set at a level to protect the public welfare, e.g., to address effects on visibility, vegetation, and wildlife.

Issues Associated With EPA's Setting of the 1997 Particulate Matter Standards

Although EPA develops what it considers best estimates rather than precautionary estimates of the risks from particulate matter, the Clean Air Act requires that the health-based standards be set with an "adequate margin of safety." According to EPA, the margin of safety was incorporated into the allowable concentration levels, or standards, chosen by the Administrator. Under EPA's interpretation of the Clean Air Act, the agency is not required to set air quality standards at a zero-risk level to achieve an adequate margin of safety, but simply at a level that avoids unacceptable risks. For example, to build in this margin of safety for the standard for the allowable annual concentration of particulate matter (also called the "annual standard"), the Administrator chose 15 micrograms of particulate matter per cubic meter of air.

This concentration was somewhat lower—that is, it was more protective of health—than the concentration at which the epidemiological evidence of adverse health effects, particularly mortality, was most consistent and coherent. For example, several key epidemiological studies reported statistically significant associations between mortality and illness and annual particulate matter concentrations of about 16 to about 21 micrograms per cubic meter of air. According to EPA, even differences of 1 microgram per cubic meter of air in the annual concentration in this range, such as the difference between 16 and 15, can significantly affect health risks. The Administrator believed that an annual standard of 15 micrograms per cubic meter of air would provide an adequate margin of safety against the health problems reported in the scientific literature. Although some studies did show health effects at lower levels, EPA believed that the scientific uncertainties about the health effects at such levels were too great to support standards at those concentrations.

As soon as the particulate matter standards were promulgated in July 1997, they were challenged in court by industry representatives, small businesses, and some states, which were concerned about the potential economic impact of the stricter standards, among other things. Many of these parties had fought the issuance of the standards. Critics had argued, for example, that the costs of implementing the standards could run as high as $46 billion per year and would cause serious financial harm to key segments of the U.S. economy without providing significant health benefits. The parties challenged the rule on a variety of grounds, including questions about the scientific uncertainties associated with the health effects of particulate matter. In May 1999, a U.S. Court of Appeals remanded the particulate matter standards, as well as the ozone standards issued at the same time, to EPA for further consideration.[1] EPA appealed this ruling to the Supreme Court, and in May 2000, the Court agreed to review the case. Oral arguments in the case are scheduled for November 2000.

A key concern expressed by the appeals court in its ruling remanding the standards dealt with EPA's rationale for setting the allowable annual concentration of particulate matter at 15 micrograms per cubic meter of air. The court found that the factors EPA used in determining the degree of public health concerns associated with different concentrations of particulate matter were reasonable, but that neither the Clean Air Act nor EPA had articulated an "intelligible principle," or definitive criterion, to direct how the agency would apply these factors. Specifically, for particulate matter, the court indicated that EPA had not adequately articulated how a standard of 15 micrograms per cubic meter could meet the Clean Air Act's requirement to set National Ambient Air Quality Standards with a margin of safety when it is also EPA's judgment that particulate matter poses health risks at any level above zero. Because no intelligible principle was articulated, the court held that EPA's construction of the Clean Air Act in setting the particulate matter and ozone standards resulted in an unconstitutional delegation of legislative authority. Shortly after the Supreme Court agreed to review the case, it also agreed to consider an industry petition arguing that EPA could provide the intelligible principle needed for setting the air quality standards, at least in part, by taking the costs of implementing the regulations into consideration when setting the standards. While the judicial review of the 1997 particulate

[1] *American Trucking Associations v. EPA*, 175 F.3d 1027 (D.C. Cir. 1999).

matter standards proceeds, the next 5-year mandated review of the standards, expected to be completed in 2002, is also under way.

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