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4 Uses and Limitations of Risk Assessment for Risk Management Decision-Making

Risk assessment is the systematic, scientific characterization of potential adverse effects of human exposures to hazardous agents or activities. Risk assessment as an organized activity of the federal agencies began in the 1970s. Earlier, the American Conference of Governmental Industrial Hygienists had set threshold limit values for exposures of workers, and the Food and Drug Administration (FDA) had set acceptable daily intakes of pesticide residues and food additives in the diet. In the mid-1970s, the Environmental Protection Agency (EPA) and FDA issued guidance for estimating risks associated with low-level exposures to potentially carcinogenic chemicals. Their guidance made upper-bound estimated risks of one extra cancer over the lifetime of 100,000 people (EPA) or 1 million people (FDA) action levels for regulatory attention. Estimated risks below those levels are considered negligible because they individually add so little to the background rate of about 240,000 cancer deaths per 1 million total deaths in the United States. The ultimate goal is, of course, to lower the background rate itself, a part of which can be attributed to an array of pollution-generating activities.

During 1977-1980, an interagency regulatory liaison group was actively engaged in bridging scientific, statutory, and policy responsibilities and activities of EPA, FDA, the Occupational Safety and Health Administration, the Consumer Product Safety Commission, and the Food Safety and Quality Service of the Department of Agriculture. The White House Office of Science and Technology Policy participated in the scientific discussions supporting risk assessment and risk management and published a scheme for identifying potential hazards, characterizing risks, and managing the risks, usually by reduction of use, emissions, or exposures (Calkins et al. 1980) (see Table 4.1).

That scheme makes clear that information about potential hazards can come from epidemiologic studies of workers and other people who are exposed to hazards, from direct experimental tests in animals and in cells in the laboratory, and from comparisons of chemical structures. The next stage involves the potency of the chemical (dose-response relationship), detailed understanding of exposure pathways, and the reasons for variation in responses among exposed people. Risk, then, is characterized both qualitatively (the nature of effects, the strength of evidence, and the reversibility or preventability of effects) and quantitatively (the probability of effects of various kinds and severities).

Performing full-scale risk assessments is a formidable task, requiring data, technical expertise, and peer review. Deciding to go forward with a risk assessment is a risk-management decision, and scaling the effort to the importance of the problem, with respect to scientific issues and regulatory impact, is crucial.

This section examines some of the risk assessment issues that are under debate, such as assessing toxicity and relevance to humans, accounting for variations in population exposures and susceptibility, describing uncertainties, evaluating risks of chemical mixtures, conducting ecologic risk assessments, and assessing risks associated with microorganisms and radiation.

Toxicity Assessment

Basing risk management decisions on observations and assumptions about the potential human toxicity of chemical exposures presents many challenges. The nature and magnitude of a population's exposures to chemical contaminants generally must be extrapolated from a few data on samples obtained from the contaminated sources (see Exposure Assessment on page 72). The nature of chemical hazards and the relation-

ships between exposures and effects often must be extrapolated to humans from toxicity tests in laboratory animals. In many cases, observations made using high doses in the laboratory or from high exposure levels in the workplace must be extrapolated to much lower environmental levels of human exposure. Extrapolating among species requires scientific information that can be used to make predictions about the relevance of a substance's toxicity in laboratory animals to human risk. Because the results of standard toxicity tests alone often do not provide enough information to make well-informed qualitative judgments about human relevance, testing strategies that rely on mechanism-based tests to evaluate substances' toxicity and carcinogenicity have been developed. Information about chemicals' modes of action can make important contributions to scientifically based human health risk assessment.

This section evaluates three issues: the use of detailed toxicity information to assess the relevance of rodent bioassay results to human cancer risk, the need for more toxicity testing of chemical mixtures and ways to evaluate their risks, and the need for risk assessments to consider information about variation in susceptibility to toxic effects.

Using Rodent Tests To Predict Human Cancer Risk

Finding

Chemicals that cause cancer in rodents are appropriately considered potentially carcinogenic in humans. Investigations of chemicals' mechanisms of action can greatly strengthen the link between findings in rodents and likely effects in humans. They can also provide biological plausibility for statistical associations in epidemiologic studies. However, some chemicals elicit tumors in rodents only through mechanisms or at doses that have been clearly demonstrated to be very different from mechanisms and exposures in humans. Regulatory agencies have been cautious in recognizing the distinctions and in issuing guidance on when such rodent responses should be discounted or disregarded.

Table 4.1. Framework for Regulatory Decision-Making.

Hazard Identification	Epidemiology Lifetime rodent bioassays Short-term, in vitro tests Structure/activity
Risk Characterization	Potency (dose/response) Exposure analysis Variations in susceptibility
Risk Reduction	Information Substitution Regulation/Prohibition

Recommendation

In general, tumors and other adverse effects observed in properly conducted animal bioassays should be considered predictive of similar effects or risks in humans. Chemicals found to elicit such effects should be regulated accordingly. If after adequate testing a chemical is found to produce only tumors that occur as a result of mechanisms or doses that have been clearly demonstrated to be not relevant to humans, that chemical should not be regulated as a carcinogen and should not require extensive risk assessment. Regulatory agencies should distinguish between tumor responses that are predictive and those that are not (see Table 4.2), and these judgments should be updated with advances in scientific knowledge about the underlying mechanisms.

The policy of presuming that a chemical that causes cancer when tested in laboratory rodents is potentially carcinogenic in humans is justified by considerable evidence and by the precautionary principle of being protective when uncertain. Rodent bioassays have played an important role in identifying human carcinogens numerous times. All 23 recognized human carcinogens are also carcinogenic in laboratory animals; for 18 of those, cancers occured in one or more organ sites in humans that are the same as those identified in the animal studies (see Table 4.3) (Rall 1988). There are other cases, however, where rodent tumor responses have been shown to be irrelevant to humans or may occur at doses far exceeding any recognized human exposures including workplace exposure. The Delaney clause prohibits chemicals that have been identified as carcinogens in rodents from being used as food additives, reguardless of whether the effects they produce are relevant to human carcinogenicity;other statutes permit scientific judgment.

From a risk management perspective, it is wasteful to expend limited risk assessment resources, risk management time, and public and legal involvement revisiting the issue of human relevance of the specific rodent response chemical by chemical. Of

Table 4.2. Rodent tumor mechanisms that may not be relevant to human cancer risk if they are the only responses observed and those responses are due to the mechanisms listed.

Tumor Mechanism	Tumor Site	Rodent Carcinogens
α-2u globulin-induced	Male rat kidney nephropathy	D-limonene, isophorones
Local hyperplasia	Forestomach	BHA, propionic acid, ethyl acrylate (administered by gavage)
Reactive hyperplasia from cytotoxic precipitated chemicals	Male rat bladder	Saccharin, melamine, nitrilotriacetic acid, fosetyl-Al
Overwhelming of clearance mechanism	Rat lung	Various particles, including titanium dioxide and carbon black (except ultrafine particles)
Sustained excessive hormonal stimulation	Thyroid	Amitrole, goitrogens, sulfamethazine

Table 4.3. Recognized human carcinogens (Rall 1988).

Chemical Carcinogens	Same Organ Sites Observed in Humans As in Laboratory Animals
4-Aminobiphenyl	✓
Analgesic mixtures with phenacetin	✓
Arsenic and arsenic compounds[1]	✓
Asbestos	✓
Azathioprine[2]	
Benzene[1]	✓
Benzidine	
Chlornaphazine	
Bis(chloromethyl)ether	✓
Myleran	✓
Certain combined chemotherapy for lymphoma	✓
Chlorambucil	✓
Chromium and certain chromium compounds	✓
Conjugated estrogens	✓
Cyclophosphamide	✓
Diethylstilbestrol	✓
Melphalan	✓
Methoxsalen with ultraviolet A	✓
Mustard gas	✓
2-Naphthylamine	✓
Soots, tars, and oils	✓
Treosulphan[2]	
Vinyl chloride	✓

[1]Not carcinogenic in standard rodent bioassays; shown to be carcinogenic in non-standard rodent bioassays only after clear evidence in humans was obtained.

[2]Not yet adequately studied in laboratory animals.

course, the evidence for hazard identifecation, exposure levels, and other effects must be evaluated for each chemical. Table 4.2 lists examples of rodent mechanisms and tumor responses that are candidates for classification as "not likely" to be predictive of carcinogenicity in humans according to EPA's *Proposed Guidelines for Carcinogen Risk Assessment* (EPA 1996b). That classification includes a subcategory of agents that elicit only rodent tumors that are irrelevant to human risk and another of agents that produce tumors at doses and via routes of exposure that need to be compared with known human occupational and general population exposures to determine relevance to human risk. Chemicals that produce tumors only in rodents because of striking pharmacokinetic differences can also be addressed. In general, the chemicals listed in Table 4.2 are not genotoxic; that is, they do not react directly with DNA. Instead, they cause local injury or otherwise stimulate local hyperplasia and cell division, which is associated with a low incidence of tumor formation.

For example, some chemicals are recognized to induce the accumulation of large amounts of α-2u globulin protein in the male rat kidney. Most scientists agree that this accumulation leads to damage to the kidney tubules, cell death, sustained cell proliferation, and tumor formation. Some scientists do not agree (Melnick et al. 1996). This response is not believed to occur in female rats or in other species, including humans. After 4 years of extensive study and review by EPA's Risk Assessment Forum and Science Advisory Board, the agency decided to disregard that particular rodent response for certain chemicals (EPA 1991). If that response is disregarded, risk assessment and regulation can be directed, as appropriate, at any other adverse effects, including kidney tumors not due to this protein-mediated mechanism.

Another tumor response that is believed to be irrelevant to humans is that which occurs only in the rodent forestomach after administration of a chemical by gavage (that is, via a tube placed in the stomach). Gavage is convenient for determining whether a chemical can cause tumors in organs distant from the stomach after absorption into the bloodstream, but can result in local cytotoxicity and hyperplasia. At least three commercially important chemicals (Table 4.2) have been found to produce tumors only in the forestomach and only following gavage. For example, butylated hydroxyanisole (BHA) was reviewed for FDA by a Federation of American Societies for Experimental Biology panel, which concluded in 1994 that there is a threshold for its tumor-producing cell proliferation. There is no evidence of a similar effect in humans (who lack forestomachs) and no scenario in which similar high dose local exposure would occur.

The saccharin debate of 1978-1979 highlighted rodent bladder tumors. An International Life Sciences Institute panel on rodent bladder carcinogenesis ultimately concluded that chemicals that precipitate in urine, or that elicit effects leading to precipitation of other chemicals, should be considered carcinogens only at high doses (Neumann and Olin 1995). If human exposures to such chemicals are much lower than the doses tested, the rodent response can be disregarded. Of course, bladder tumors can arise by other mechanisms that are relevant to human cancer.

Grossly overloading the rat lung's clearance mechanisms by administering particles directly to the lung has also been considered irrelevant to humans (Oberdörster 1995). EPA delisted titanium dioxide from the Toxic Release Inventory in 1988 for this reason (Fed Reg 53:23107-23202, 1988). The phenomenon may be applicable to particles in general, not only to titanium dioxide, but it has been declared irrelevant to humans only in the case of titanium dioxide. Declaring responses to other particles as not likely to predict human cancer risk would require criteria to determine what are "gross" particle overloads. Ultrafine particles (<0.1 microns) may well present a risk at much lower concentrations. Particles may also be carriers of hazardous chemicals that have adsorbed to them.

High doses of several pesticides and fungicides induce liver enzymes or thyroid enzymes that affect thyroid hormone levels, leading to hyperplasia and ultimately to thyroid tumor formation in ro-

dents. Because the feedback and transport systems for rodent thyroid hormones are very different from those in humans (McClain 1994), many believe that humans are far less sensitive to this response. EPA still assesses rat thyroid data on a case by case basis.

Finally, there have been many challenges to the interpretation of mouse liver tumor formation (not listed in Table 4.2). At least six potential mechanisms have been described, some of which occur in humans. Mouse liver tumors are among the most common seen in bioassays and pose particularly vexing problems for interpreting effects of chlorinated organic solvents.

Judgments about the likelihood of a chemical's or a tumor's human relevance should include careful evaluations of the weight of the scientific evidence. Some considerations include:

- Adequacy of experimental design and conduct.
- Occurrence of common versus rare tumors.
- Progression, or lack thereof, from a benign to a malignant tumor.
- Latency until tumor induction.
- Dose-response relationships.
- Genetic toxicity.

Toxicity testing protocols used to evaluate a chemical's carcinogenicity are a subject of intense debate. Leading toxicologists are eager to substitute newer tests for at least one of the two rodent species generally used in standard lifetime cancer bioassays. These newer tests employ newborn mice, which are quite sensitive and yield results in a few months, and specially developed transgenic mice with mutant p53 genes or other cancer-predisposing genes to make the mice more sensitive and provide mechanistic information. The goals are to apply scientific advances, get more information, and hopefully do so at lower cost and in less time.

Bringing a risk management perspective to the scientific review process might galvanize action. EPA reviews of the male rat kidney and rat thyroid tumor responses have required many years. The Commission recognizes that time is required to investigate chemicals' modes of action and endorses EPA's current plans to identify tumor responses in rodents that are not likely to be relevant to humans. We encourage EPA to apply those distinctions as early as possible in the risk assessment process, before time and resources are wasted. Other agencies should follow similar practices.

Evaluating Chemical Mixtures

Finding

Humans are exposed to many chemicals and other potentially toxic agents in the environment, but toxicity testing and regulations generally focus on one chemical at a time, often just in air, water, or food. Most risk assessments evaluate individual chemicals and then combine them by simple addition to estimate risk related to chemical mixtures. This method ignores potential synergistic or antagonistic interactions that could lead to under or overestimation of total risk, respectively. Knowledge of mechanisms of action can guide judgments of whether risks related to combinations of particular chemicals will be additive or independent.

Recommendation

Toxicity testing of complex environmental mixtures of regulatory importance should be performed for hazard identification and to generate comparative potency estimates of human risk. For risk assessments involving multiple chemical exposures at low concentrations, without information on mechanisms, risks should be added. If the chemicals act through separate mechanisms, their dose-response relationships should be considered separately.

As commonly practiced today, risk assessment and risk management consider exposures and risks in isolation from one another, typically chemical-by-chemical. For example, risks associated with air pollution are not put into the context of concurrent risks associated with contaminated drinking water or foodborne pesticide contamination. That fragmented approach to risk characterization is mostly a result of the fragmentation of responsibilities of different regulatory agencies and programs, but it can also be attributed to the limitations in our knowledge of the interdependence of different risks.

Failure to account for multiple and cumulative exposures is one of the primary flaws of current risk assessment and risk management, according to testimony received from Michael McCloskey, chairman of the Sierra Club, and others. Many people are surprised to learn that scientists usually do not test mixtures and that risk assessors and managers do not even try to account for the full array of exposures and health (or ecologic) risks. If the Framework is implemented and experience with testing and evaluating multiple chemical risks increases, it should be feasible to move beyond fragmentation. A promising new statute, the Food Quality Protection Act of 1996, requires estimates of aggregate, cumulative, and combined exposures to pesticides; some 9,000 tolerances for registered pesticides will need to be reassessed under this new mandate during the next 10 years.

Toxicity testing

Many complex mixtures—such as automobile exhaust, cigarette smoke, and other combustion products—have hundreds or thousands of chemical components. Attempting to identify and characterize each component and then adding their risks is clearly impractical. In those cases, the mixtures themselves can be tested for toxicity and their risks can be characterized on the same basis. For example, toxicity studies of diesel exhaust and other emissions have been conducted by the Health Effects Institute, jointly supported by EPA and motor vehicle manufacturers. The valuable results of those studies and others, such as tests of smoggy air from the Los Angeles basin, encourage us to recommend the testing of other important chemical mixtures.

Predicting a complex mixture's toxicity or risk can be assisted by testing it in bioassay systems and comparing the results with those from similar mixtures of known toxicity or risk. Bioassays that might be useful for testing mixtures could range from mutation tests in microorganisms to evaluation of effects on organs in culture or short-term tests of rodent respiratory function. A validated database of methods, bioassays, and biologic markers of effect and knowledge of the behavior of known mixtures in those bioassays will be needed to facilitate risk predictions for environmental mixtures. Such whole mixture testing could be considerably less expensive to perform than routine monitoring by chemical analysis for over 100 drinking water contaminants, for example, and might provide results that can be more easily extrapolated to human toxicity and discussed with stakeholders. The index of biotic integrity (see Ecological Risk Assessment on page 77) is another example of the use of a bioassay to integrate effects of numerous chemical exposures.

The experimental and epidemiologic database available for generating estimates of comparative potency of mixtures is not large. Most work has been applied to predicting lung cancer risks; for example, epidemiologic data are available on the carcinogenic potencies of coke oven emissions, coal roofing tar, coal smoke, aluminum smelters, and cigarette smoke. The human cancer risks of those emissions have been characterized and compared with their potencies in experimental systems to estimate the risks associated with mixtures that lack epidemiologic data, including automotive emissions (diesel and gasoline), woodstove emissions, residential oil furnace emissions, and ambient air particles; it is assumed that the relative carcinogenic potencies

observed in experiments would be similar for humans (Harris 1983, Lewtas 1993).

Enlarging the toxicity database for complex mixtures would be facilitated by coordinated research programs among epidemiologists, toxicologists, and clinical investigators (Mauderly 1993). For example, epidemiologists could provide information on the types of mixtures to which humans are exposed, patterns of exposure, populations of concern, health effects of concern, and the level of effects observed (or observable). Clinical studies could provide information on short-term responses and dose-response relationships, biological markers revealing short-term exposures and effects, and the likelihood of sensitive subpopulations. And toxicologists could provide judgments about the biological plausibility of the suspected exposure-response relationsip, the potential for chronic disease resulting from repeated exposures, causal and predictive relationships betweeen acute and chronic effects, identity of active constituents of mixtures, and effects of the exposure patterns.

Complex mixtures seemingly from the same source can vary considerably. For example, neither automobile engines nor gasolines are identical, so automobile exhaust is likely to vary substantially among sources and over time. The composition of air pollution varies with time of day and time of year, not to mention geographic location and source, so the toxicity of such mixtures is likely to vary considerably. Probabilistic approaches to describing the variability of composition within a class of mixtures and the relationship between that variability and toxicity should be explored. Coupling mathematical/statistical modeling (e.g., Monte Carlo techniques and physiologically based pharmacokinetic/pharmacodynamic dosimetry) with mechanistically based short-term toxicology studies may prove useful (Yang et al. 1995).

Assessing risks from multiple chemicals

Most of the information that is available on interactions among chemicals comes from human occupational studies and from rodent bioassays. Those studies generally evaluate doses that are much higher than the low, environmental doses commonly encountered. Interactive effects (either synergistic or antagonistic) depend heavily on dose; therefore, characterizing interactions that occur at one set of doses (such as those used in a rodent bioassay) is likely to provide very little information about interactions at very different doses (such as those generally encountered in the environment). "High" doses for combined effects are defined as those at which statistically significant increases in detrimental outcomes are observed in either laboratory or occupational studies. For the most part, exposure to chemical mixtures in the environment occurs at "low" doses—typically, one thousandth (or less) of the doses at which toxicity is observable in rodent bioassays or in epidemiologic studies of highly exposed workers. The ratio of exposures observed to cause adverse effects and actual human exposures is called the margin of exposure (EPA 1996b) (see Need for a Common Metric on page43).

The combined effects of exposure to chemicals in a mixture are determined by how individual components of the mixture affect the biological processes involved in toxicity. Components of a mixture can affect biological processes in many ways. For example, anything that affects the absorption, distribution, metabolism, or elimination of a chemical will affect the amount of that chemical that is available to react with DNA or other cellular targets. Because interactions leading to synergism or antagonism are the result of reactions of many molecules at many cellular sites, a mathematical dose-response model of a synergistic or antagonistic response that depends on such mechanisms is most likely nonlinear at low doses. Such logic strongly suggests that any disease process that depends on such interactions is only marginally important at low exposure levels. Only at high doses of one or more mixture components—such as cigarette smoke, alcohol, and some substances

in occupational exposures—is the combined effect likely to be detectably greater than the sum of the individual effects. For example, occupational exposure to asbestos is associated with a mortality ratio for lung cancer of up to 5 (that is, in comparison to persons not occupationally exposed to asbestos) and smoking with a mortality ratio for lung cancer of about 10; but asbestos workers who smoke have a mortality ratio for lung cancer of 50, not 15. Similarly, the risk of liver cancer associated with aflatoxin is increased markedly by hepatitis B virus infection.

The National Academy of Sciences report *Complex Mixtures* (NRC 1988) also concluded that effects of exposures to agents with low response rates usually appear to be additive. The experimental evidence that can be used to infer effects at low doses appears to support the assumption that low dose additivity does not underestimate, and in most cases probably overestimates, risk (see, for example, Ikeda 1988).

When the individual components of a chemical mixture exhibit different kinds of toxicity or have different biological mechanisms of toxicity, they do not interact—they act independently at low doses. In that case, the dose-response relationships for each chemical should be considered independently. For example, if the chemicals of concern at a Superfund site are copper, a gastrointestinal toxicant; lead, a developmental toxicant; and heptachlor, a neurologic toxicant, their toxicity should be evaluated independently and not combined into a single "noncancer" risk estimate. Experiments have shown that when groups of unrelated chemicals with unrelated targets of toxicity were administered to rodents simultaneously at doses equal to their separate NOAELs, no cumulative effects were observed; each chemical acted independently (Jonker et al. 1990, Groten et al. 1994). The same is true of groups of chemicals with the same target but different mechanisms of action (Jonker et al. 1993); studies in which similar chemicals with similar mechanisms and targets were administered simultaneously indicate that antagonism, is the usual outcome (Falk and Kotin 1964, Schmähl et al. 1977).

Accounting for Differences in Susceptibility

Finding

Genetic, nutritional, metabolic, and other differences make some segments of a population more susceptible than others to the effects of a given exposure to a given chemical; however, current regulatory approaches for reducing risks associated with chemical exposures generally do not include information on differences in individual susceptibility or encourage gathering evidence to identify them. In the absence of specific information about differences in susceptibility, risk assessments rely on assumptions and safety factors that are presumed to be protective of sensitive individuals.

Recommendation

Risk assessments should include consideration of genetic and other host differences in susceptibility, recognize the spectrum of interindividual variations within normal populations, and identify subpopulations especially susceptible to specific chemical exposures. Available information on the range of a population's susceptibility should be considered and used in place of assumptions. Where appropriate, knowledge of differences in susceptibility should be used to support additional bright lines for risk to protect especially susceptible subpopulations (see Bright Lines for Risk Management on page 54) and to tailor specific risk management actions to protect those subpopulations.

Susceptibility to the effects of chemical exposures depends on the sensitivity of a person's response to different doses. Susceptibility is influenced by many factors, including age, sex, genetic variation in metabolism of chemicals, genetic variation in response to agents or stressors at their sites of action, ethnic origin and ethnic practices, socioeconomic status, geographic location, and lifestyle factors, such as smoking, alcoholic beverage consumption, diet, physical activity, and recreational habits. Dose-response relationships are chemical-specific and

depend on a chemical's mode of action; people are not hypersusceptible to all kinds of exposures (Omenn 1982). The influence of concurrent exposures on risk is discussed in "Identifying Highly Exposed Populations" on page 75. The following are examples of subpopulations potentially at higher risk.

Population	Factor Affecting Response to Exposure
Asthmatics	Increased airway responsiveness to allergens, respiratory irritants, and infectious agents
Fetuses	Sensitivity of developing organs to toxicants that cause birth defects
Infants and young children	Sensitivity of developing brain to neurotoxic agents such as lead
α_1-Antitrypsin-deficient persons	Inherited deficiency of a protein that protects against chemical damage
Glutathione-*S*-transferase deficient	Diminished detoxification of some carcinogens and medicines
Socio-economic groups	Underlying nutritional deficits and poor access to health care
Elderly	Diminished detoxification and elimination mechanisms in kidney and liver

There are opportunities to identify, evaluate, and reduce risks to sensitive people. Asthmatics, for example, make up 5 to 10 percent of the general population in the United States. Some air pollutants, especially sulfur oxides, particles, and ozone, are respiratory irritants that pose a greater risk to this subpopulation than to the general public. Both the number of cases of asthma and the number of deaths from asthma are increasing in the United States. Blacks have a 15% higher prevalence of asthma than whites. Likewise, susceptibility to lung cancer appears to vary among ethnic groups; in the United States, the incidence of lung cancer in black men is 1.5 times that in white men, 2.5 times that in Hispanic men, 2 to 4 times that in Asian men, and 8 times that in American Indian men (NCI 1984). One source of individual and ethnic differences in susceptibility is differences in the activity of enzymes that affect chemical toxicity. Increased risks of cancers of the bladder, skin, colon, lung, and stomach have been associated with differences in the activity of specific enzymes that can activate or deactivate carcinogens. Susceptibility to organophosphate pesticide toxicity is also markedly influenced by the activity of a specific enzyme in the blood. Metabolism however is only one of many contributors to an individual's susceptibility .

Amendments to the Safe Drinking Water Act and to the Federal Insecticide, Fungicide and Rodenticide Act require such recognizable subpopulations as the elderly, children, and women of child-bearing age to be identified and considered more explicitly than they are currently in risk characterization and in standard-setting. The Food Quality Protection Act of 1996 requires an additional safety factor of 10 be used when pesticide risks are assessed, to allow for children's greater intake on the basis of body weight and potentially greater susceptibility, unless data are sufficient to justify a different safety factor. Recognition of subgroup susceptibility does not necessarily result in more stringent regulation, however. For example, people allergic to particular chemicals or pet animal proteins might modify their exposures or modify their responses (with medication). Identifying the size of the population at higher risk and describing the risk peculiar to that population during risk characterization, perhaps using biologic markers of susceptibility, will make it possible to characterize risks more realistically than is possible using only estimates for the general population. Risk communication messages can then be targeted more effectively.

Exposure Assessment

Exposure assessments can be simple or complex, depending on the needs of a particular risk management question. They are based on measurements, models, and assumptions, and generally focus on individual chemicals, media, and sources. Often, unvalidated mathematical models are used to make predictions about a population's exposure on the basis of limited information on chemical con-

tamination and assumptions about the population. The results oversimplify actual exposure magnitudes and conditions, in part to allow for population variability. And the methods generally do not consider other sources of exposure to the same or similar chemicals and their interdependence.

This section recommends ways to generate credible and understandable exposure information for informed decisions by risk managers and the public about the need for risk reduction. The Commission recommends that agencies show a preference for actual exposure data on communities and populations at risk.

Design of Exposure Assessments To Meet Risk Management Goals

Finding

Exposure assessments vary greatly in design and content. Complex risk management decisions often are based on simplistic, deterministic estimates of exposure derived from few data, many assumptions, and inadequately validated models. In contrast, some exposure assessments are more complex than is needed for straightforward risk management decisions.

Recommendation

Exposure assessments should be designed to be commensurate with the needs of the risk management decisions at issue. The design of an appropriate exposure assessment should take place at the problem/context stage of the risk management process.

Several measurement tools, statistical methods, and other procedures and considerations can be used to design and conduct an exposure assessment. No method or group of methods should be used in all cases. Selection of appropriate methods should be discussed and evaluated during the planning stages of a risk management process (the problem in context stage of the Commission's Risk Management Framework) to ensure that they meet the needs and expectations of risk managers and other stakeholders. The following general principles are suggested as the planning basis for an exposure assessment:

- Simple methods should be considered before more complex methods. Such a tiered assessment strategy is increasingly used in risk assessment and can be cost-effective.
- Chemicals are more biologically available in some media than in others; that is, the matrix within which chemicals occur (such as air, water, food, or soil) can greatly affect the extent of human exposure. The effect of the matrix should be considered in assessing exposure before assuming that contaminants are 100% bioavailable.
- Whenever possible, measurements should be obtained to support or validate any generic values used in exposure assessments, to check modeling results, or to provide more realistic estimates of exposure than can be obtained with models. Such measurements might include collecting data at locations where exposures are anticipated, monitoring the exposures experienced by individuals, collecting data on the physical and chemical conditions that affect the movement and bioavailability of chemicals, and providing information that relates exposure to effects, possibly using biologic markers. Measurements of exposure can be very different from estimated exposures based on source characteristics.

Using Realistic Exposure Scenarios

Finding

Because of statutory requirements and the desire not to underestimate chemical exposures, many risk assessments have estimated risks for a hypothetical, nonexistent "maximally exposed individual" (MEI) and have neglected information about the frequency, duration, and magnitude of actual population exposures. More recent assessments have used less extreme exposure scenarios. Con-

gress specified in the 1990 amendments to the Clean Air Act that, after maximum available control technology is implemented for stationary sources, further controls must be considered if the lifetime excess cancer risk to the "individual most exposed to emissions from a source" in a category exceeds 10^{-6}. The criteria for the "individual most exposed" were not stated; in fact, Congress mandated this Commission to advise what exposure scenarios should be used.

Recommendation

Exposure assessments should not be based on a hypothetical MEI. Screening risk assessments should rely on more representative estimates, such as EPA's high-end exposure estimate (HEEE) or a maximally exposed actual person and estimates of the total number of potentially exposed people in the geographical areas of interest. Risk management decisions should be based on refined exposure assessments that evaluate the distribution of a population's varied exposures and should address explicitly any segments of the population that have unusually high exposures. Exposure assessments should rely on population exposure data where possible instead of assumptions about exposure derived from source characteristics and models. The characteristics of actual or potential future populations in relation to specific sources of exposure should be emphasized and multiple sources of exposure should be reflected as appropriate in each case.

With the intention of protecting public health, past exposure assessment and health risk assessment practices have relied on exposure estimates derived from a hypothetical MEI who might spend a 70-year lifetime living at the point of greatest deposition from a plume of industrial contaminant emissions or who might spend a 70-year lifetime drinking only ground water with the highest concentrations of contaminants detected. The MEI was often so unrealistic that its use impaired the scientific credibility of health risk assessment.

Federal agencies have generally moved away from exposure assessments relying on such MEIs. For example, EPA's exposure assessment guidelines have adopted the use of distributions of individual exposures and HEEEs chosen from values in the upper tail of those distributions (EPA 1992a). EPA's risk characterization guidelines provide guidance on the use of exposure descriptors to characterize risk (EPA 1995a). At this time, implementation of those guidelines among EPA regional offices is uneven; some continue to use point estimates, while others use probability distributions of exposure estimates.

The Commission supports distributional approaches to exposure characterization that are based on knowledge of the characteristics of a population's variability. Where possible, the entire distribution of the variability associated with exposure should be used in a risk characterization (see Effective Risk Characterization To Support Decision-Making on page 85). That distribution should be based on the characteristics of the entire exposed population and not solely on a highly exposed subpopulation; any highly exposed subpopulations known to exist should be considered separately. If a single value representing a population's or subpopulation's exposure is required, such as for priority setting, a point in the upper end of the distribution should be used, such as the 95th percentile.

Agencies should develop standard distributions to use in exposure assessments as defaults when population-specific information is unavailable. If data limitations do not permit the development of a defensible exposure distribution, a value representing a hypothetical highly exposed individual should be used. Such point exposure estimates are appropriate for screening level risk assessments. Probabilistic exposure estimates should be considered when standard default methods are expected to yield unrealistically conservative exposure estimates, when population estimates of exposure are desired, or when the exposure assessment is complex. Mark Van Putten, of the National Wildlife Federation, testified before the Commission that the environmental justice movement has provided some

impetus for considering distributions instead of point estimates, on the grounds that populations with disproportionate exposures can be more explicitly identified and considered in risk assessments. We agree.

One advantage of using distributions to describe a population's exposure is that it focuses attention on population risk, not just individual risk. Considering the size of a population in addition to the distribution of its exposures is important; for example, although emissions in a rural area might pose the same individual risk as those in an urban area, the total population risk for the latter is much greater. Another advantage is that it focuses attention on the characteristics of the population ("receptor-based" analysis) instead of basing exposure estimates primarily on the emission or other characteristics of a particular source of contamination ("source-based" analysis). A population-based approach can be source-specific but should include information on the variables that influence the mode, frequency, and duration of exposures. A complementary community-based approach would begin by determining a population's exposures and moving from that information to identify sources of exposure. The total exposure assessment methodology (TEAM) study conducted by EPA and the Harvard Six Cities Survey, in which representative members of several urban populations wore small personal samplers to measure individual exposure to airborne chemicals (EPA 1987a, Dockery et al. 1993), are examples of a community-based approach to exposure assessment. The TEAM study also illustrates how dissimilar source-based predictions of exposures and actual exposures can be. Monitoring blood lead in a community's children and tracing the sources of lead is another example of receptor-based analysis.

Many exposure assessments are based on source characteristics, not population characteristics. For example, air pollution sources typically have been licensed on the basis of modeled projections of their stack emissions. Few data on actual population exposures exist. (The Six Cities and TEAM studies are notable exceptions.) Such data deficiencies create problems, as emphasized by Ellen Silbergeld, representing the Environmental Defense Fund, in testimony before the Commission: there is no direct way to estimate the actual health risks experienced by an exposed population; there is no way to assess the relative contribution of multiple sources to risk; and there are no baseline data with which to evaluate the effects of new sources or of pollution reduction activities on existing sources.

Resistance to collecting data on populations' actual exposures arises from the substantial time and expense associated with monitoring efforts, especially given the large variations in local climate and the problems associated with accurate detection of small pollutant exposures. Environmental monitoring is needed, however, to generate actual data that are consistent with a public health approach to risk assessment and with the Commission's Risk Management Framework. In some circumstances, the costs of monitoring, such as for blood lead, are small compared to the overall costs of remediating a Superfund site, for example, and can save funds amounting to several times the cost of the study. Although multipathway modeling is not scientifically well developed, at present, exposure assessment must begin to address aggregate exposures (see also Section 2 and Evaluating Chemical Mixtures on page 68). Stimulated in part by Toxic Release Inventory reports, communities are interested not just in what they are exposed to because of a particular industrial facility, but in how that facility adds to the burden of exposures that they are already experiencing. Focusing on real populations is essential to identifying multiple exposure situations. We expect biomarkers of exposure to become useful in validating exposure estimates and in relating exposures to specific subgroups and even to individuals.

Identifying Highly Exposed Populations

Finding

Some population groups are at increased risk for toxic effects of chemical exposures because their exposures are greater than those of other population groups. Cultural practices, occupa-

tional exposures, behavior patterns, eating habits, and effects of related chemicals can be responsible. The high-risk subpopulations might be of special concern when risk assessments are conducted and risk management decisions are made. Risk assessors often have not sought information from knowledgeable citizens and consequently have not explicitly considered specific exposure conditions that might be present in minority group communities, certain occupational settings, or areas of particular socioeconomic status.

Recommendation

Risk assessments should be conducted so as to identify groups of people who are likely to have higher exposures to the chemicals of interest. Affected parties should be consulted in the early stages of an assessment to obtain information about all known sources of exposure to a particular chemical and related chemicals and to characterize exposure factors peculiar to particular subpopulations and link them with host susceptibility factors (see Accounting for Differences in Susceptibility on page 71).

Increased risks of adverse health effects from contaminant exposures can result from increased doses, as well as from increased susceptibility, which was discussed in the section Accounting for Differences in Susceptibility on page 71. Dose is a function of the concentration of a substance in the environment and the extent of exposure that a person has to the substance. Advances in the use of biologic markers will help to define relationships between exposure and dose. Below is a list of some factors that can increase risk as a result of increased exposure.

The Clinton Administration, the 103rd and 104th Congresses, interest groups, and the scientific community have attempted to address the issue of high-risk populations in several ways. For example, Executive Order 12898 on Environmental Justice requires that federal programs protect minority-group and low-income populations from disproportionately high exposures and adverse human health and environmental effects. EPA addressed the potentially greater susceptibility of children to pesticides and pesticide residues by requiring that assessments of environmental risks explicitly take health risks to children and infants into account (EPA 1995b). Congress reinforced that practice when it passed the Food Quality and Protection Act of 1996, which responded to a National Research Council report that variations in dietary exposure to pesticides related to nutritional intake, age, geographic region, and ethnicity were not addressed adequately by current regulatory practice (NRC 1993). Infants and children might be more heavily exposed to pesticides than adults because of their relatively high intake of fruit juices, for example, and they are more susceptible to the toxic effects of pesticides because of the sensitivity of their still-developing nervous systems and probably because of their greater concomitant exposures to lead and other environmental hazards.

Population	Examples of factors that affect exposure
Industrial and agricultural workers	Greater exposure to job-related hazardous chemicals through breathing and skin contact; more lung exposure associated with physically demanding work
Subsistence and sport fishers	Higher fish consumption; consumption of unusual parts of fish
Infants and children	Higher consumption of fruit, vegetables, and fruit juices; higher inhalation rates
Low-income and minority-group communities	Greater exposure to lead from lead paint in houses and soils; greater exposure to second hand cigarette smoke; inequitable distribution of risk-generating activities

Community assistance in characterizing exposure factors peculiar to particular segments of the population can focus a risk assessment and broaden risk management options. The Commission heard testimony from Asians and Pacific Islanders about their fish consumption patterns and about the role that education can play in risk management. Not only do they consume more fish, but they consume fish parts that are usually discarded by others and in which pollutants are often concentrated, placing themselves at higher risk than the general population for the effects of contaminants in fish. They reported that educational brochures, signs around contaminated bodies of water, and community involvement led to voluntary reduction in exposure through modest changes in fish eating in the Seattle area. Of course, education is only one risk management alternative, and other stakeholders might not consider it to be appropriate or acceptable. In contrast to the Asians and Pacific Islanders, Mark Van Putten, of the National Wildlife Federation, testified that in the Great Lakes region it was difficult to convince risk managers that subsistence fishers, such as Native Americans, should be considered in risk assessments.

Specific information gathered from the community and stakeholders could reduce the need for default assumptions and improve the quality of risk assessments in communities with multiple polluting operations, such as a municipal incinerator, a chemical plant, a dry cleaning establishment, and an abandoned hazardous waste site. Involving the community and other stakeholders in the planning stages of a risk assessment can help to engage individuals, families, schools, businesses, and municipalities in targeted pollution prevention and pollution reduction actions that reduce exposures. The Commission's Risk Management Framework calls for stakeholders to be involved in every step of the process, including evaluation of the actions taken.

Ecological Risk Assessment

Ecological risk assessment was not included in the Commission's legislative mandate, but we would be remiss if, in a report on the use of risk assessment in regulatory programs, we considered only human health. Indeed, protection of human health and protection of the environment are often dual goals of the laws and regulations that use risk assessment to inform decision-making. The ability to sustain our ecosystems is crucial to our well-being, as they are used for producing food, building materials, and fiber, as well as recreation and spiritual sustenance. Of course, sustainability of ecosystems is a benefit regardless of human benefits. In addition, many environmental problems, such as global climate change and hormonally active contaminants, pose an inseparable combination of health and ecological risks. Nonetheless, this is not intended to be a comprehensive discussion of ecological risk assessments.

Framework for Evaluating Ecological Risk

Finding

Continuing efforts to develop a uniform ecological risk assessment approach persist. EPA's framework for evaluating ecological risk (Figure 4.1) has emerged as a useful way to organize many kinds of information about risks to the environment, although it does not yet include an explicit role for stakeholders. General guidelines for implementation of the EPA framework have been issued and meet immediate needs. As ChemRisk said in comments to the Commission, guidelines must be flexible to account for the many variables in any individual ecological risk assessment. As the effort to add complexity to the analyses continues, additional guidance on the developing technique will be needed while maintaining flexibility.

Recommendation

EPA and other agencies should continue together to implement the EPA ecological risk assessment framework. EPA's guidelines should be improved by an explicit discussion of how and when stakeholder involvement should be sought so that it is consistent with the Commission's Risk Management Framework and by a description of how measures and models should be selected. Other

agencies should develop clear guidance for putting various problems into context, choosing methods and tools for characterizing exposure and effects, characterizing uncertainty, and applying weight-of-evidence evaluations.

Ecological risk assessment has been used informally for many years to make decisions about resource management and pollution control. Within the last few years, a concerted effort has been made to define ecological risk assessment and to establish a common language for discussing approaches and results. At the same time, ecological risk assessments have been conducted by an increasing number of agencies, such as the Department of the Interior, the Department of Agriculture, and the National Marine Fisheries Service. As detailed in the Menzie-Cura report prepared for the Commission (see Appendix A7 for abstract), there is a growing consensus that the EPA ecological risk assessment framework (EPA 1992b), as it has evolved since 1992, can fulfill a wide range of needs, from providing information on environmental pollution to informing resource management and regulatory decision-making.

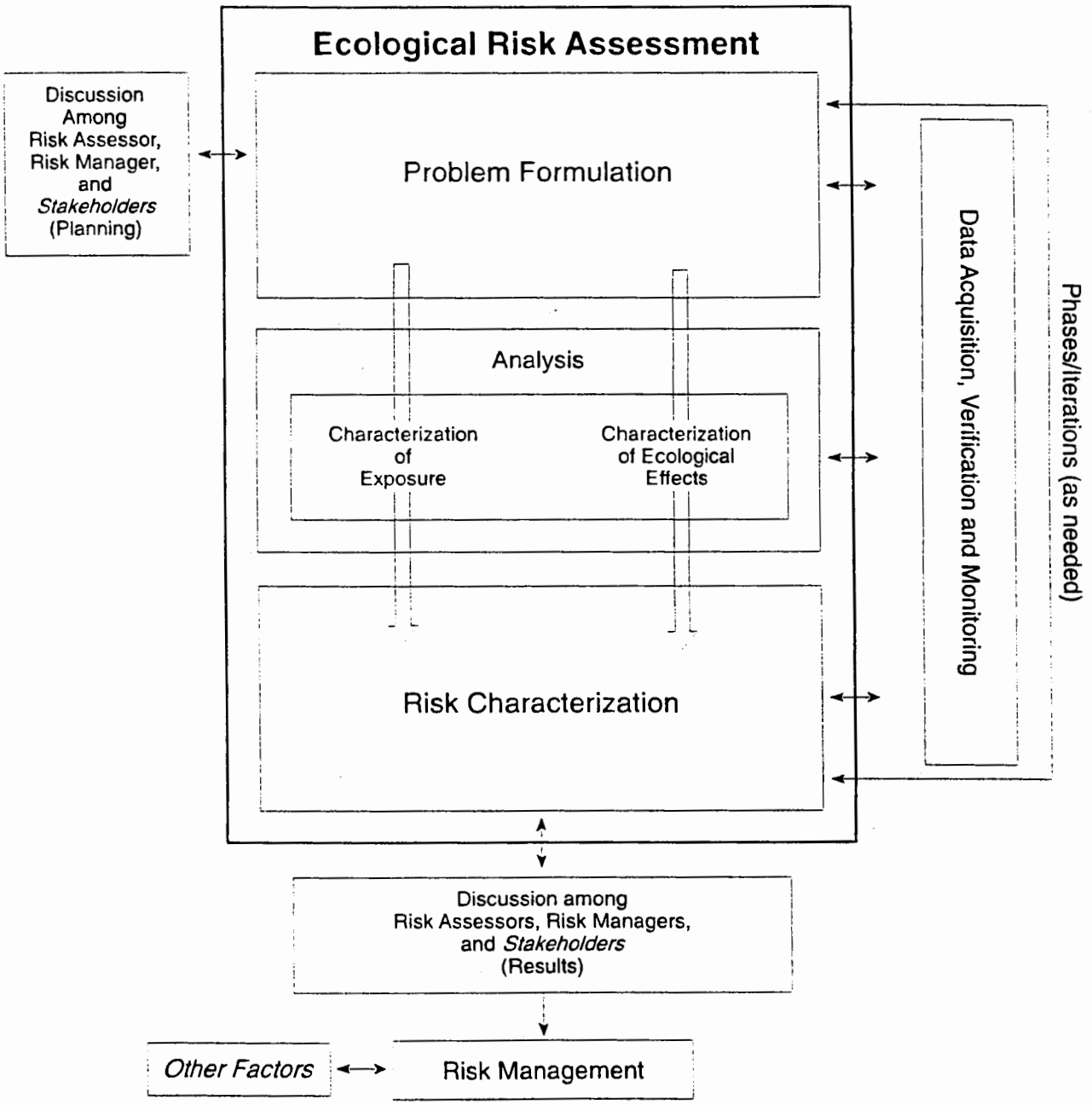
Each agency should develop guidance on the use of the framework appropriate to its needs. Considerable effort has been directed toward this end over the past few years. California, Massachusetts, Texas, and Washington have developed state-specific guidance. Within the EPA, guidance has or is being developed by Regions 1, 9, and 10. Other agencies and departments have produced guidelines tailored to their specific needs. The Tri-Service Procedural Guidelines for Ecological Risk Assessments prepared by the Department of Defense is a recent example. These efforts share conceptual elements reflected in the EPA Framework for Ecological Risk Assessment and the EPA Guidelines for Ecological Risk Assessment. Communication among these groups will foster sharing of developing concepts and tools.

Compared with the framework for human health risk assessment (NRC 1983), the EPA framework for ecological risk assessment changes the first step from hazard identification to problem identification in a holistic context. Thus, this approach is consistent with the Commission's Framework for Risk Management. In the problem formulation stage, the environmental values to be protected and the goals of the assessment should be defined. In addition, the appropriate level of ecological organization (such as individual species, population, or community), the end points, potential receptors, and ways to measure the end points must be identified.

Ecological risk assessment has no commonly accepted starting point. For example, some might focus on the need to maintain biological diversity, others might be drawn to protecting particular plants or animals, and still others might relate to aesthetic quality. Balancing those disparate goals is the challenge of the problem formulation stage. The likelihood of success will be increased by including stakeholders in the process at this early stage. Figure 4.1 reflects the Commission's proposal to add stakeholders, explicitly, to the participants in the problem formulation stage of EPA's framework. The brief discussion of stakeholders in the EPA guidelines puts too little emphasis on the important role stakeholders should play in ecological risk assessment. Many small or well defined assessments may be parts of established regulatory programs in which it would be impractical to involve stakeholders in every case; however, stakeholder involvement certainly should be considered for larger local or regional assessments in which affected parties hold a range of interests and values. In particular, stakeholder involvement seems especially important for place-based assessments, such as watershed and estuary assessments, for assessments of complex hazardous waste sites, and for the development of assessment methods that will be used in major regulatory programs.

In a review of ecological risk assessment case studies, EPA (1993b) concluded that the strengths and weaknesses of the studies frequently seemed to originate, from decisions made during the problem formulation stage. EPA's guidelines provide a good description of the problem formulation stage of the ecological risk assessment, but neglect to

Figure 4.1. EPA's framework for ecological risk assessment, modified to include stakeholders and factors in addition to risk. (Additions in italics.)



provide sufficient guidance on who should be involved and when and how to include stakeholders. It is especially important at this stage to identify federal, state, and local agency stakeholders with responsibilities for the resources being analyzed.

The collaboration that we recommend among risk assessors, risk managers, and stakeholders provides opportunities to bridge gaps in understanding, language systems, and values. If the affected parties do not participate in the early decisions about goals, end points, and measurements, the analysis is likely to fail to provide information useful for decision-making. Stakeholder involvement in the problem formulation stage of an ecological risk assessment has been endorsed by a range of organizations, including the Environmental Defense Fund, the American Industrial Health Council, the Risk Science Institute, the State of California, and Environment Canada.

The analysis stage of ecological risk assessment consists of two distinct, interrelated activities: characterization of exposure and characterization of ecological effects. During exposure characterization, the spatial and temporal distribution of a stressor or stressors and contact with ecological components are predicted or measured. During effects characterization, the adverse effects elicited by stressors and the cause-effect relationships are evaluated. Additional research is needed into the effects of multiple chemical, physical, and biological stressors and the appropriate metrics to assess effects.

One diagnostic tool for identifying effects is the index of biotic integrity developed by Karr (1991), who testified before the Commission in Seattle. Although not a perfect tool, this index is now used by more than 30 states in their water quality programs. The guidelines issued by EPA contain a good discussion of the strengths and limitations of various tools, but do not describe adequately how to select measures or methods, such as fate and transport models, toxicity tests, and field studies, that best evaluate different assessment endpoints or how to match tools to the scale of the problem or the level of the assessment. The most appropriate mix of tools must be decided on a case-by-case basis.

In its 1996 report *Ecological Risk Assessment: Sound Science Makes Good Business Sense*, the American Industrial Health Council suggested that addressing multiple species and multiple exposure pathways at different levels of ecosystem organization is best done with an iterative, tiered approach to data acquisition (AIHC 1993). The Commission agrees. Because ecological risk assessments can be data intensive, guidance on when and how to conduct a tiered, iterative approach is needed. Early tiers tend to be less expensive and more conservative; the more expensive, more sophisticated later tiers provide more accurate estimates of risk with less uncertainty. The intensity of data collection should be commensurate with the environmental benefits of greater certainty, the needs of stakeholders involved in the decision-making process, and the resources available.

Finally, in the risk characterization stage, characterizations of exposure and of ecological effects are integrated to evaluate the likelihood that exposures and adverse ecological effects will be associated with specific stressors. Risk characterization for ecological risk assessment has been subject to little standardization. If followed, EPA's proposed risk characterization guidelines should improve understanding and consistency. For example, there are many sources of uncertainty in ecological risk assessment; EPA's proposed guidelines indicate how to address them in the risk characterization.

The EPA guidelines use the term "lines of evidence" rather than "weight of evidence" to describe the evaluation of the underlying data and studies for accuracy, reliability, and relevance. It appears that there is no consensus on how to evaluate or apply the lines of evidence or weight-of-evidence in the context of ecological risk assessment. Because the approach reflects professional judgment, the conclusions might not be transparent to others. The professional judgments that underpin these weight-of-evidence evaluations should be examined and be made more explicit. The Massachusetts Department of Environmental Protection, for example, has been working with ecological risk assessors to develop quantitative and qualitative methods of evalu-

ating weight-of-evidence. The risk characterization must synthesize and provide information that can be applied to risk management decisions, again with extensive consultation with stakeholders (see Figure 4.1).

As in the Commission's Risk Management Framework, the risk assessor, risk manager, and stakeholders should consider other factors in making the risk management decision. Costs, legal constraints, feasibility of options, and enforcement mechanisms are among the issues that are not part of the risk assessment but are sometimes critical to the acceptability of the risk management actions. For that reason, we have added "other factors" as an explicit input to the risk management decision (see Figure 4.1).

The EPA ecological risk assessment framework has been most successful in analyzing risks associated with chemical stressors—the scenario most similar to typical human health risk assessments. However, the framework is being used with greater frequency for more complex problems. For example, EPA's Office of Water has experimented with changing the sequence of some of the components of the framework and has developed conceptual models at multiple organizational levels of the ecosystem; this version of ecological risk assessment is being used to assist in understanding stressors and their effects on watershed ecosystems (see Office of Water on page 128). In addition, the recently formed Office of Sustainable Ecosystems and Communities is leading an effort to focus on ecological risk assessment beyond toxic effects on individual organisms to a system approach that examines the food web or the broader landscape. Another appropriate use of EPA's ecological risk assessment framework would be in analyzing the impact on wildlife of chemicals that may disrupt endocrine functions.

The application of the ecological risk assessment framework must be refined as agencies gain experience so that complex biological, physical, and social stressors can be addressed in such important problems as protecting biological diversity, maintaining ecosystem health, and guiding sustainable development. It is timely to work with the international community to harmonize methods in the United States and abroad while the development of the paradigm is still evolving. As the Organization for Economic Cooperation and Development noted in its report *Environmental Performance Reviews: United States*, "knowledge about the conditions and trends of biodiversity in the U.S. is limited" (OECD 1996). Measurement tools, models, field studies, and surveillance of the consequences of risk management decisions are critically needed.

Environmental Hazards Other Than Chemicals

Public concern about risks associated with radioactive waste disposal, recent large-scale outbreaks of serious infectious disease from microorganisms such as *Cryptosporidium* in drinking water and *E. coli* in foods, and disasters from natural hazards such as floods, earthquakes, and hurricanes, remind us that chemicals do not constitute the only environmental threats to the public's health. In many situations, people (and ecosystems) are exposed to combinations of radiation, chemicals, and infectious agents—a broader version of the chemical mixtures problem (see Evaluating Chemical Mixtures on page 68). In many others, comparisons and tradeoffs among types of risk are necessary, such as potential risks associated with chemical byproducts of drinking water disinfection versus infectious risks associated with microbial contamination of drinking water). In such situations, chemical, radiation, and microbial exposures have to be evaluated concurrently.

To the public, environmental protection seems to be focused predominantly on chemicals, rather than radiation and microorganisms, although there is no doubt about the many serious health effects of exposure to ionizing radiation and microorganisms. Nell Ahl, director of the risk analysis program at the Department of Agriculture, expressed concern to the Commission about the disproportionate official emphasis placed on chemical hazards,

especially in view of the public outrage that was rightly engendered recently by the deaths and illnesses caused by toxin-producing *E. coli* contamination of under cooked hamburger or *Salmonella* contamination of eggs or ice cream. The public health consequences of exposing patients and workers to ionizing radiation and of exposing the general population to infectious agents are so well recognized that they are in the category of "familiar" risks, which psychologists have shown are far less frightening to the general public than "unfamiliar" or "dreaded" risks, even when the estimated magnitudes of the former are much higher. Nevertheless, small estimated risks from radiation, especially from potential radiation releases from nuclear power plant operations or wastes, continue to attract considerable public concern. For example, in testimony before the Commission in St. Louis, Kay Drey, of the Missouri Coalition for the Environment, expressed concern about our country's ability to manage its current radiation hazards and especially the anticipated decommissioning of commercial nuclear power plants at the end of their useful lives. The Department of Energy has recognized that a major challenge exists in decommissioning and disposing of nuclear reactors at federal facilities.

Risks From Radiation Hazards

Finding

Risk assessment methods for radiation hazards are well established, and regulatory strategies for occupational and environmental radiation exposures have been in place for many years. An elaborate standards process uses extragovernmental organizations, such as the National Council on Radiation Protection and Measurements and the International Commission for Radiological Protection; lead agencies are the Nuclear Regulatory Commission, Department of Energy, EPA Office of Air and Radiation, and FDA Division of Radiological Health. Unfortunately, scientists and regulators dealing with chemical hazards or with radiation hazards have been so independent of each other that there has been little combined analysis or combined risk management for medical, industrial, nuclear power, nuclear weapons production, and waste disposal settings where radiation and chemical contamination coexist.

Recommendation

A concerted effort should be made to evaluate and relate the methods, assumptions, mechanisms, and standards for radiation risks to those for chemicals to clarify and enhance the comparability of risk management decisions and investments, especially when both types of hazards are present.

The radiation protection literature began with devastating accounts of the health hazards of Roentgen rays (x rays), discovered in 1895 and introduced immediately into medical practice; pioneering scientists and workers developed radiation burns of the skin and internal cancers. We now know that radiation can affect genes, chromosomes, cell survival, and regeneration of rapid turnover tissues. The skin, bone marrow, intestine, oocytes, spermatogonia, lens of the eye, and respiratory tract are most vulnerable.

Natural sources of ionizing radiation include cosmic rays; radium and other radioactive elements in the earth's crust; potassium-40, carbon-14, and other radionuclides normally present in living cells; and inhaled radon and its progeny. The doses received from cosmic rays vary appreciably with altitude, so exposure is twice as high in Denver as at sea level and 100 times higher at jet aircraft altitudes. The largest exposures come from airborne radon-222, a colorless, odorless, alpha particle-emitting gas formed by the radioactive decay of radium-226 in the earth. Human exposure to radon varies—according to its concentration in indoor air—by more than a factor of 10. Smokers expose themselves to another decay product of radium—polonium-210 in tobacco—at up to 0.2 Sv/year, or 20 rems/year.

A discrepancy exists between the levels of risk that are considered negligible for radiation exposures and for chemical exposures. In the case of individual chemicals, exposure limits are generally set to keep incremental upper-bound cancer risks

for workers below one per thousand over a 45-year period of workplace exposure and, for the general population, below a range of one per 10,000 to one per million over a 70-year lifetime of exposure to the limits. In the case of radiation, the current occupational exposure limit is a whole body equivalent dose of 50 mSv/year or 5 rems/year (10CFR20, 1990 revisions), which would be equivalent to a lifetime excess total cancer risk of more than one in ten if experienced annually over a working lifetime, assuming a linear dose-response relationship (Upton 1996). (The rem is a composite of absorbed dose [rads] and energy transfer factors.) According to comments received from Tara O'Toole, Assistant Secretary for Environment, Safety and Health at the Department of Energy, occupational exposure limits recommended by the International Commission on Radiological Protection and the National Council on Radiation Protection and Measurements are equivalent to a lifetime cancer risk of one in one hundred (assuming about a 50-year exposure duration at the exposure limit in the absence of [as low as reasonably achievable] standards. Those risk estimates are well above those associated with similarly extreme scenarios of lifetime exposure to chemical carcinogens at the level of their occupational standards. However, risks from radiation and from chemicals are estimated differently; most importantly, radiation exposure limits integrate all ionizing radiation exposures, while chemical-specific exposure limits consider each chemical individually. O'Toole stated in her comments to the Commission that harmonizing radiation and chemical risk assessment methods will remain an elusive goal without these basic differences being articulated and discussed. We agree.

In other comments, O'Toole stated that she believes protective actions and the application of ALARA workplace practices lead to actual radiation exposures for workers that are much smaller than the limits. That view is echoed by comments received from several health physicists. Furthermore, radiation-exposed workers are continuously monitored so that high exposures can be detected promptly and corrected. For example, during the period from 1980 to 1994, the highest annual average dose equivalent per monitored Department of Energy worker receiving measurable exposure was 182 mrem/year, significantly less than the EPA's recommended annual exposure limit of 5 rem. Assuming an annual average occupational dose limit of 1,000 mrem, approximately five times greater than the Department of Energy's highest annual dose, the National Council on Radiation Protection and Measurements estimated a lifetime cancer risk from each year's exposure of between 10^{-5} and 10^{-4} (NCRP 1993). Multiplying these estimates by an assumed exposure of 35 years would make the risk level similar to the level used to limit workplace exposures to individual chemicals, roughly 10^{-3} lifetime excess cancer risk. Monitoring and job change lead to similarly lower actual exposures for workers exposed either to chemicals or to radiation. Chemical exposure limits are not annual averages or annual cumulative doses, however; rather, 24-hour average concentrations or even peak concentrations are the basis for limits. Staying below the limits thus requires mean exposures to be considerably lower than the regulatory limit.

The limit for unrestricted radiation exposure of a member of the public has been set at 1 mSv/year effective dose equivalent (100 mrems) by the Nuclear Regulatory Commission, one-fiftieth of the occupational exposure limit. This difference deserves some attention; pregnant women can be exposed to radiation both in the workplace and outside it, and the developing fetus presumably deserves the same level of protection in both places. As with workplace exposures, however, actual public (non-workplace) exposures are generally far lower than the limits, which represent only a small fraction of the amount of background radiation received annually from natural sources. Diagnostic and therapeutic uses of ionizing radiation in medicine constitute by far the greatest exposures.

The Conference of Radiation Control Program Directors issues a draft regulation in early 1997 that also adopted the 100 mrem exposure limit, aimed at protecting the general public from naturslly occuring radioactive materials that have accumulated from

industrial processes. Their appoach would leave to local analysis and negotiation how much less than 100 mrem per year should be the cleanup goal, allowing for consideration of specific site characteristica, identity of the radionuclides of concern, and other factors.

In contrast to radiation, the difference between occupational and general population exposure limits for chemicals is usually much greater than a factor of 50. For example, OSHA's limit on workplace exposure to nuisance dust is 15 milligrams per cubic meter of air, while EPA's national ambient air quality standard for particulates is 50 micrograms per cubic meter of air, 300 times less.

Low-level exposures to electric and magnetic fields, after extensive investigation and public debate, appear to have very low or negligible risk to the general population (NRC 1997).

Risks from Microorganisms

Finding

Methods for anticipating and assessing microbial hazards on a population basis, rather than on a clinical basis for individual patients, are less developed than those for chemicals or for radiation; they are hindered by limited data, especially epidemiologic and quantitative exposure data, and by the need for predictive models that can account for variation in infectivity, virulence, and uncertainties.

Recommendation

Efforts to improve risk assessment methods for microbiologic hazards and to collect data to validate and support those methods should be encouraged.

Interest in the public health aspects of infectious diseases and the need to improve their predictivity has been revived by several factors:

- The emergence and resurgence of infectious agents ranging from HIV and the Ebola virus to tuberculosis mycobacteria.
- The importance of antibiotic resistance mechanisms as a result of medical and veterinary overuse of antibiotics.
- The need for international sanitary and phytosanitary standards since the General Agreement on Tariffs and Trade was signed.

Inability to assess health risks associated with microorganisms and inattention to risk reduction can lead to disaster, as evidenced by the recent deaths and outbreaks of diarrhea caused by *Cryptosporidium* in Milwaukee's drinking water and by kidney failure in children who consumed *E. coli* toxin-contaminated hamburger meat in Seattle. Those deaths, unlike many cancer risks associated with low, environmental levels of exposure to chemicals, are observable and countable. FDA and USDA have primary responsibilities for foodborne, FDA for device-borne, and EPA for waterborne microbiological risks; the Centers for Disease Control and state and local health departments are active in public health monitoring. Internationally, Health Canada, Agriculture Canada, TNO in the Netherlands, and the Codex Alimentarius, jointly managed by the World Health Organization and the Food and Agriculture Organization, are engaged in microbiological risk management.

Empirical studies currently do not produce sufficient information to assess dose-response relationships in people, for several reasons:

- As with chemicals, most exposures to pathogens are below those associated with death or disease. However, microorganisms can multiply and greatly increase in numbers inside the human host.
- The body has effective defense mechanisms so long as white blood cell and immune systems are intact. Infectious agents can reduce the immune response or, in some cases, change their physical structure to avoid immune defenses.
- As with chemicals, susceptibility varies from person to person. Concurrent exposures to chemicals may affect susceptibility to infectious agents.

As a result, microbial risk assessment methods have increasingly relied on indirect measures of risk based on analytic models that estimate the extent of human exposure and the probability of human responses to exposure (Eisenberg et al. 1996a). Static models based on individual risks and population-based models that account for changes over time are being used conjunctively. (Haas 1983, Haas et al. 1993, Eisenberg et al. 1996a,b). It is difficult to quantify dose-response relationships for microorganisms using those models for several reasons:

- Epidemiologic factors, including secondary infection whereby someone who was infected by contaminated food or water infects other people.
- Host factors, such as the variable development of immunity to the organism.
- Complex contamination factors, such as meat being contaminated at the slaughterhouse, by infected food handlers, or during inappropriate storage by the retailer or the consumer.

Several ongoing efforts are intended to strengthen microbiological risk assessment. For example, the Committee on Food Hygiene of the Codex Alimentarius, a United Nations organization with responsibility for promoting international standards for food safety, has recently issued *Principles and Guidelines for the Application of Microbiological Risk Assessment* (FAO/WHO 1996). The report identifies the basic elements of a microbiological risk assessment, including the information needed and the decisions that must be made. It also identifies key information gaps, including the need for improved dietary intake information. An EPA-funded International Life Sciences Institute working group has recently produced a conceptual framework tailored to assessing risks from waterborne pathogens (ILSI 1996). Continuing efforts to systematically assess the applicability of existing and emerging models should be encouraged, along with monitoring and efforts to collect data comparable with data on chemical hazards, on characteristics of microorganism behavior, toxicity, dose-response relationships, and risks. In addition, potential effects of chemical and radiation exposures on susceptibility to microorganisms should be investigated.

These models and scientific studies would enhance the preventive strategy embodied in the Hazard Analysis Critical Control Point concept that has gradually been developed over the last 25 years to control foodborne pathogens (Van Schothorst 1990).

Risk Characterization

Effective risk communication requires sound risk characterization. Risks have generally been communicated to the public as single numerical estimates, which are easily misinterpreted and misused in the absence of qualitative information about the nature of the risk and about the weight of evidence that supports it. Effective risk characterizations should include clear messages about the nature, severity, and likelihood of risk rather than just numerical estimates. In some cases, mathematical descriptions of uncertainty can be useful for communicating about risks with decision-makers; in most cases, however, mathematical descriptions of uncertainty provide little useful information to support decision-making because most risk-related decisions are routine, made at the local level, and do not involve large stakes. Practical processes such as value-of-information techniques are needed for determining when risks have been sufficiently well characterized to reach a decision, when decisions should be made on the basis of the precautionary principle even if risks are not well characterized, or when data-gathering efforts are worth pursuing.

Effective Risk Characterization to Support Decision-Making

Finding

Risk characterization is the primary vehicle for communicating health risk assessment findings. Many risk characterizations have relied primarily on mathematical estimates of risk to communicate risk assessment findings, often conveying an unwarranted sense of precision while failing to con-

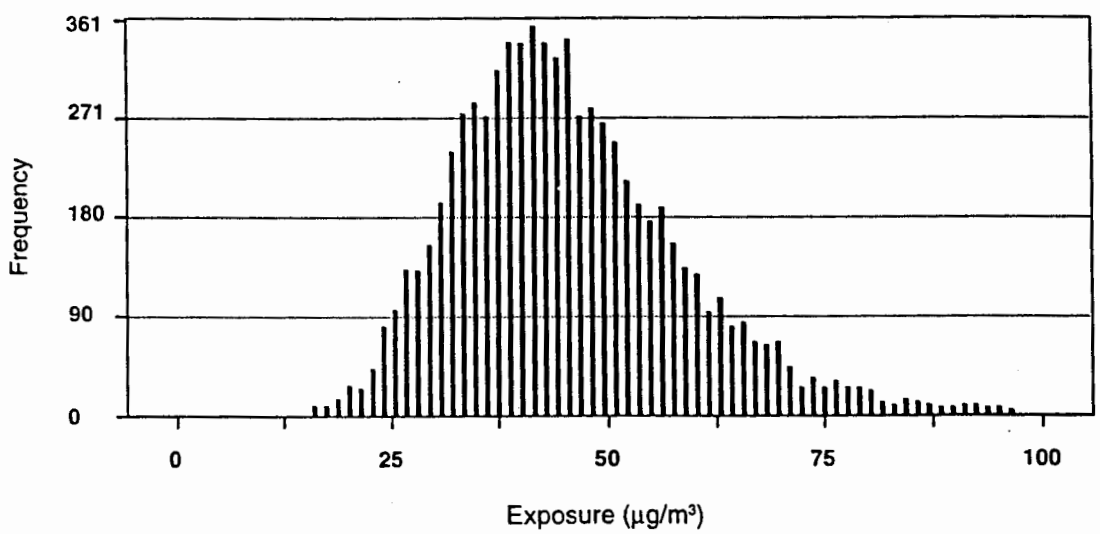
vey the range of scientific opinion. They are particularly difficult for audiences unfamiliar with risk assessment to comprehend. Effective risk management is impeded without effectively communicating information about who is at risk, how they might be affected, what the severity and reversibility of an adverse effect might be, how confident the risk assessors are about their predictions, and other qualitative information that is critical to decision-making.

Recommendation

Risk characterizations must include information that is useful for all parties participating in a risk management decision-making process. Mathematical estimates of risk are important and should be included, but qualitative information on the nature of adverse effects, the weight of the scientific evidence, and the risk assessment itself is likely to be most useful. Information on the range of informed views and the evidence that supports them also should be shared.

Risk assessment is an uncertain process that re-quires both scientific data and science-based judgment. Risk assessments are conducted to estimate risks below the range of observable events in people or in studies of laboratory animals. For example, 10-100 percent of laboratory animals exposed to a relatively high dose of a carcinogen throughout their lives might develop cancers, but regulatory agencies are expected to protect populations from exposure to doses of chemicals that might pose a risk of up to one in a million, not one in 10. The impact of a one-in-a-million cancer risk on a population cannot be detected or

Figure 4.2. Frequency distribution of a population's exposures to a contaminant released to air from a hazardous waste site, estimated using measurements of the contaminant concentration in the air at the site and Monte Carlo techniques.



The distribution reflects the number of people expected to experience each exposure concentration out of 10,000 people exposed. For example, about 270 people out of the 10,000 (y axis) are predicted to be exposed to 50 µg/m³ (x axis).

Source: David Burmaster

measured, because one-fourth of that population is already expected to die of cancer, even in the absence of a particular chemical exposure (see page 33). As a result, estimates of small risks are speculative; they cannot be verified. Expressing a small risk solely in numerical terms, especially in single numbers, is misleading and falsely conveys accuracy.

Communicating quantitative information about noncancer risks poses a different challenge because these risks are not expressed as numerical risk estimates, but as hazard indices. Noncancer risk is typically determined by comparing an estimated human dose to a dose that is considered to be "safe" or allowable (e.g., a reference dose or reference concentration); doses below the standard are considered unlikely to present any risk, while those just above that standard might be less safe, posing some uncharacterized risk of adverse health effects. Although is is possible to consider dose-response relationships for noncancer health effects above the standard, this has not been the general practice. Using a margin-of-exposure approach to cancer risk assessment instead of current methods would result in similar nonprobabilistic expressions of risk (see Need for a Common Metric on page 43).

Often, qualitative information is more useful and understandable than quantitative estimates of risk. Qualitative assessments include a careful description of the nature of the potential health effects of concern, who might experience the effects under different exposure conditions, the strength and consistency of the evidence that supports an agency's classification of a chemical or other exposure as a health hazard, and any means to prevent or reverse the effects of exposure. Qualitative information should also include the range of informed views about a risk and its nature, likelihood, and strength of the supporting evidence. For example, if an agency considers a substance likely to be a human carcinogen on the basis of studies of laboratory animals, but there is some evidence that the classification is flawed, both views should be presented. A discussion of that uncertainty would note the several types of evidence that support the substance's classification as a likely human carcinogen and also the contradictory evidence. Based on this type of discussion, the risk manager might conclude that because the weight of the scientific evidence supports the substance's classification, the best option is to regulate it as a carcinogen in the interest of protecting public health (i.e., invoking the precautionary principle). Alternatively, the risk manager might conclude that the evidence is so uncertain that it is best to focus on conducting additional research or to maintain the status quo. Useful guidance for including qualitative information in risk characterizations is found in EPA's Guidance for Risk Characterization (EPA 1995a). Effective ways to communicate quantitative and qualitative information about risks are discussed in more detail below and in Communicating and Comparing Risks on page 39.

While quantitative uncertainty characterizations are not always effective risk communication tools (see next section), we believe that using distributions to reflect the variability in a population's exposure characteristics can be useful. Considering exposure variabilities will also help clarify whose risks are being considered and the relationship between individual and population risk estimates. All stakeholders can easily comprehend that not all members of a population are exposed to identical doses of contaminants, and that different activities are associated with different exposures. For example, information on reference standards could be compared to a distribution of a population's exposures like that in Figure 4.2, derived using Monte Carlo techniques and exposure data from a hazardous waste site.

In this example, if the concentration of a chemical associated with a 10^{-5} cancer risk were 80 milligrams percubic meter of air, the risk manager and other decision-makers would recognize that most of the population is exposed to less than that concentration. The participants might decide that there is little cause for concern or might attempt to identify the characteristics of the segment of the population in the upper end of the distribution and consider risk reduction options directed at that seg-

ment. If the concentration of concern were 20 milligrams per cubic meter of air, participants would see that most of the population is exposed to higher concentrations, and would want to implement more extensive risk management measures directed at the entire population. The participants might also be interested in comparisons of exposures to contaminant concentrations associated with 10^{-4} or 10^{-6} cancer risks.

Comparing the distribution of a population's exposures to reference standards conveys information that can be more useful for decision-making than a single point estimate of risk or a hazard index, although care should be taken not to treat standards as inflexible bright lines. Priority-setting might not require exposure distributions, but more refined risk assessments that support decisions with greater regulatory impact would. Comparing the distribution of a population's exposures to a standard or family of standards (see Bright Lines for Risk Management on page 54) also conveys information to a risk manager that is less complex than a distribution of risks. In contrast with estimated risk levels, bright lines expressed as exposure concentrations can be measured; measurements facilitate implementation, evaluation, and compliance. The risk manager and the public can see clearly what the relationship between a reference standard and a particular population's or subpopulation's exposure is likely to be. That information can be used to evaluate the need for exposure reduction, and risk reduction can be directed at those who are likely to need it most.

Characterizing the Uncertainty Associated with Risk Estimates

Finding

Confusion persists regarding the differences between variability and uncertainty and their ramifications for decision-making. Variability comprises a population's natural heterogeneity or diversity. Using mathematical distributions to reflect the variability in a population's exposures can be a useful way to show that different members of a population receive different exposures, to help clarify whose risks are being considered, and to highlight the relationship between individual and population risk estimates. Uncertainty, in contrast, results from information that is only partly known or unknowable. Methods to mathematically describe uncertainty are still developing. The best way to present the results of a risk assessment so as to acknowledge uncertainty depends on the importance of the decision under consideration and the magnitude of the uncertainties. Sensitivity analyses of critical parameters for deciding among options are often desirable.

Recommendation

Risk characterizations intended for risk managers and the public should include narrative descriptions of the primary reasons for uncertainty and variability. They should summarize explicitly the weight of the evidence for conclusions about exposures, toxicity, and susceptibility. Probability distributions of the variability in a population's exposures should be used as appropriate to enhance characterization of exposures and communication of risks. The Commission recommends against routine use of formal quantitative analysis of uncertainties in risk estimation, particularly that related to evaluating toxicity. Continued development of quantitative methods should be encouraged by research and regulatory agencies.

Variability arises from differences in the nature and magnitude of a population's exposure to hazards and from variation in people's susceptibility to hazardous exposures. For example, people consume different amounts of fruits and vegetables, inhale different volumes of air according to their level of exercise, come into contact with different amounts of soil depending on occupational and recreational activities, and drink different amounts of water depending on physiological need, weather conditions, and activity level. Estimating a population's exposures to hazards depends on knowing how much contact people have with a contaminated medium. People vary in susceptibil-

ity due to nutritional, metabolic, genetic, and behavioral factors, as well as coexisting or previous exposures (see Identifying Highly Exposed Populations on page 75).

Uncertainty arises from information that is only partly known or unknowable, especially information about toxicity at low levels of exposure to a hazard. We often do not know all the reasons for variation in susceptibility, whether a chemical that produces tumors in rats will do so in humans, whether a site used for industrial purposes today will be needed for residential use in the future, and whether people who eat contaminated fish are likely to eat just the filet or also the internal organs where the contaminants are concentrated. A report prepared for the Commission by Cambridge Environmental, Inc., on health risk estimation (see Appendix A7 for abstract) suggests that most of the uncertainty in risk estimates can result from uncertainty about a substance's toxicity.

Risk assessors and regulators typically rely on assumptions and single numerical values to describe important quantities. For example, instead of describing variability in exposures, they may assume that everyone is exposed to the same amount by drinking 2 liters of contaminated water daily or breathing 20 cubic meters of contaminated air every day for 70 years. Instead of describing uncertainty about toxicity, they assume that, if a chemical causes cancer in laboratory rats, it will do so at equivalent doses in humans. They account for uncertainty in standard-setting for chemicals that cause reproductive effects, for example, by dividing NOAELs by uncertainty and safety factors (see page 110) based on judgments and assumptions. For example, they assume that interindividual variation in humans makes some people at least ten times more likely than laboratory animals to suffer noncancer health effects on lungs, the nervous system, or reproduction. Variability and uncertainty associated with risk estimates can and must be described qualitatively. There is a great deal of debate about the added value of describing them mathematically.

The Commission strongly supports using mathematical descriptions of variability, particularly distributions of a population's possible contaminant exposure concentrations (see previous section and Using Realistic Exposure Scenarios on page 73). In contrast, we are doubtful that much value is added, at least at present, by formal mathematical analyses of uncertainty. The National Research Council report *Science and Judgment in Risk Assessment* (NRC 1994a) addressed the extensive variability and uncertainty associated with estimating risks and concluded that, to the extent feasible, risk characterizations should not be reduced to a single number or even to a range of numbers intended to portray uncertainty. Instead, the report recommended, risk managers should be given risk characterizations that are both qualitative and quantitative and both verbal and mathematical, including mathematical descriptions of uncertainty to the greatest extent feasible.

The Commission concurs with *Science and Judgment in Risk Assessment* that *qualitative* descriptions of risk-related uncertainty are needed for most risk assessments. These narrratives should help to:

- Avoid the false sense that we know precisely the extent of the risk.
- Identify uncertainties with the largest impacts.
- Explain differences in risk estimates generated by different stakeholders.
- Suggest opportunities for valuable research.

EPA's proposed revisions to their guidelines for cancer risk assessment also endorse using narratives to identify reasons for uncertainty (EPA 1996b). As Granger Morgan of Carnegie Mellon University noted in his comments to the Commission, however, descriptors such as probable, likely, possible, improbable, and impossible mean very different things to different people and in different contexts, and may be more useful when they are calibrated with at least some quantification.

The Commission has concluded that *quantitative* uncertainty analyses of risk estimates are sel-

dom necessary and are not useful on a routine basis to support decision-making. Federal and state contractors have told the Commission that, when they perform comprehensive quantitative analyses of risk-related uncertainty and variability, they are ignored or misunderstood. For both uncertainty and variability, there is little consistency between practices at agency headquarters and what is considered acceptable by regional offices or states. Many risk estimates are crude yardsticks for decision-making; as Thomas Gentile, of New York State's Division of Air Resources, noted in his testimony before the Commission, many state-level risk managers want to know, "Is it safe or not?" They want their policy and technical staff to help them reach decisions based on the nature and severity of the problem, generally with single numbers that represent estimates of risk, generated in a consistent manner. Many risk managers told the Commission that they base their decisions on qualitative information and on the weight of the scientific evidence. In this context, the routine provision of a mathematical distribution representing the uncertainty of risk estimates was not encouraged. As noted by Commissioner Goldstein, many crucial economic policy decisions are made on the basis of point estimates of the gross domestic product, the unemployment rate, or the costs of major welfare or health care reform legislation, for example, without mathematical or even narrative descriptions of the considerable uncertainties.

Risk assessments are decision-making tools, not precise analyses of actual or measurable risk, so their focus should remain on how best to inform the ultimate goal—risk reduction—rather than on generating complex distributions of possible risk estimates. Probabilistic methods for quantitatively describing the uncertainties associated with toxicity and risk estimates are still under development and may be needed for using decision analysis and value of information techniques. Nevertheless, in many cases, resources are best spent on conducting research to reduce important sources of uncertainty. As Michael Jayjock of Rohm and Haas Company testified before the Commission, "Describing uncertainty is good. Reducing it is better." Uncertainties about risks and the absence of adequate data to adequately assess risk too often prolong the regulatory process.

Mathematical analyses may be useful among technical staff in generating their input to risk managers. However, it is inappropriate to delay the risk management decision-making process because of a requirement that each risk assessment at national, state, or local levels be accompanied by a formal uncertainty analysis. Many decisions are relatively straightforward, especially issuance of permits at the local or state level and judgments about compliance with specific measurable emission and ambient exposure concentration standards.

Support for routine, formal quantitative analysis of uncertainty is based on the desire to move away from poorly supported default assumptions and point estimates of risk that convey an unwarranted sense of accuracy. Providing a numerical range of possible risks is thought to allow more informed and more transparent decisions than are possible when only a single point estimate of risk is generated. However, in the absence of adequate explanation of the weight of scientific evidence, communication of a range or distribution of population risks has been misconstrued by those unfamiliar with quantitative methods as implying that all the numbers in the range may be equally plausible and therefore equally valid for regulation (Goldstein 1995, Goldstein 1996).

Providing distributions of risk is also thought to counteract the perceived bias toward overestimating risk that is due to a compounding of conservative default assumptions. However, when data are scarce and uncertainty is great, a range of probabilities based on assumptions would replace point estimates based on assumptions. Often disagreements arise about the underlying shapes of the distributions; folding assumptions about those shapes into a risk assessment incorporates the assessor's bias into the risk estimate. Furthermore, when confronted by an array of estimates, regulators and community groups are likely to choose from the more stringent portion of the range. Using formal

uncertainty analysis could lead to either stricter or less stringent regulation.

Value of Obtaining Additional Information

Finding

Risk management is complicated by uncertainty and by the issue of how much information is enough to justify regulatory action. Risk managers face a dilemma: is it better to make a regulatory decision now based on an inherently uncertain risk assessment, or is it preferable to collect additional information first and then decide? Value-of-information techniques provide an analytic framework for resolving this dilemma and for preventing the regulatory paralysis associated with unbounded data gathering and analysis.

Recommendation

Risk characterizations should provide insight into the potential costs and value of acquiring additional information as an alternative to acting immediately on the basis of available data and the precautionary principle. In those cases where the quality of the information is poor and the stakes in decision-making are large, agencies should experiment with formal value-of-information methods to determine whether it is most appropriate to act or wait for improved information). Continued research in the methodologic development and application of value-of-information techniques to environmental policy issues should be encouraged.

A potential barrier to the successful implementation of the Commission's Risk Management Framework or to the effective use of tiered approaches to risk assessment and priority setting is conflict over the need for more information. If a simple screening risk assessment performed for the purpose of priority-setting yields results indicating that a particular industrial facility might pose an unacceptable risk, a more refined risk assessment might be desired. A more refined risk assessment would require more data than the screening risk assessment, so there would be an incentive for the owner of the facility to generate those data in the hopes that the more refined assessment would show that it does not pose an unacceptable risk. However, if the more refined risk assessment still indicated that the estimated risk is too high, the owner of the facility might decide that collecting even more data would be worth the investment if regulatory action would be deferred. Meanwhile, the community might be outraged by apparent collusion to delay action. Ellen Silbergeld, representing the Environmental Defense Fund, emphasized in her testimony before the Commission that the greatest barriers to credible risk assessments are the absence of data and the need for guidelines to determine how much information is enough to conclude an iterative process and support a decision. Comments from David Roe of the Environmental Defense Fund and from John Adams of the Natural Resources Defense Council reinforced the need for more and better data on exposure and toxicity to improve the usefulness and credibility of risk assessments. Likewise, Warner North, of Decision Focus, Inc., recommended incentives for both data collection and for speedy risk management decisions.

The challenge for risk managers is to bring analysis to bear on the question of whether collecting additional data is likely to lead to a better, more confident, or more widely accepted regulatory decision. For example, if a statutory mandate compels a particular pollution control technology regardless of the level of risk, then collecting additional data about risk will not influence the regulator's decision (unless the statute itself is changed). When low-cost control options are readily available that will reduce or prevent a plausible yet unproven risk, it might be preferable to proceed on the basis of the precautionary principle, rather than await more knowledge about the precise level of risk. Alternatively, high-cost control options may be good candidates for deferral if there is reason to believe that better information about the level of risk might change the ultimate regulatory choice (e.g., under a discretionary "unreasonable risk" statute).

When the effects of pollution may be persistent, irreversible, or catastrophic, risk managers should be reluctant about committing to strategies that require long-term data collection prior to undertaking protective actions. On the other hand, the costs of action could be reduced considerably if the risk manager can phase in new regulatory requirements gradually rather than imposing them immediately. Even if information about risk is fairly precise, there may be considerable uncertainty about the cost and effectiveness of various control strategies. Under these conditions, additional data collection about cost or effectiveness would make more sense than development of more precise risk estimates. As soon as a risk-related problem is identified, however, social impacts can begin, especially at the community level. For example, decreased property values and fear of disease may occur regardless of the availability of information or uncertainty about the magnitude of the risk. Efforts to obtain additional information must be balanced against a community's desire to address the risk promptly.

Whenever additional research is proposed prior to taking regulatory action, risk managers should insist on a careful understanding of the purpose of the research, its probable cost, and the time horizon for completion. The results of risk-related research may not be predictable, but the risk manager can insist on a planned and orderly approach to acquiring the new information. Even if a risk manager decides to act rather than to acquire better information about risk or cost, it may nonetheless be wise to launch research activities that can inform future regulatory choices and evaluations of the original decision.

The peer-reviewed literature contains a number of examples of applications of value-of-information methods to environmental policy questions (e.g., Morgan et al. 1978, Campbell et al. 1982, Evans et al. 1988, Lave et al. 1988, Reichard and Evans 1989, Morgan and Henrion 1990, Siegel et al. 1990, Hammitt and Cave 1991, North et al. 1992, Taylor et al. 1993, Dakins et al. 1994, Dakins et al. 1996, Thompson and Evans 1996). Value-of-information methods provide estimates of the value (typically in monetary terms) that the decision-maker would place on having improved information and consequently provide a sense of the amount of resources that could reasonably be spent to obtain better information.

In many cases, considerations of the value of information can be thought through qualitatively, without any formal quantitative analysis. However, when the stakes in a decision are large and the uncertainties complex, risk managers or their technical staffs may find it useful to experiment with formal value-of-information tools. Value-of-information analysis, formal and informal, can be a useful component of the Commission's dynamic Framework for improving the process of risk management.