ON RISK ASSESSMENT FRAMEWORKS

Presented at the
2nd U.S. - Japan Workshop on Risk Assessment/Risk Management
October 28, 1987

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The views expressed in this paper are those of the author and are not necessarily the views or policies of the United States Environmental Protection Agency.

INTRODUCTION

Earlier in this workshop I spoke about the U.S. Environmental Protection Agency's (EPA's) guidelines for risk assessment. In that talk, I presented some concepts of risk, some definitions for risk assessment and risk management, and some specific information about the guidelines themselves.

Now, I would like to turn to a discussion of the risk assessment process itself. Here, I will present some information on the development of risk assessment, on the history of its use in decision-making, on some impediments to its use, and on the ways it can be used.

HISTORY OF RISK ASSESSMENT

Risk assessment is not an invention of the 1970s, but has been with us since Adam assessed the risk and chose to bite into the apple in the Garden of Eden. As the modern science of toxicology developed, scientists developed techniques for setting safe levels of threshold toxicants. These were all variations of a theme: finding the No-Observed-Adverse-Effect-Level (NOAEL), and dividing that by a Safety Factor, Uncertainty Factor, Margin of Safety, or Margin of Exposure which yields what has traditionally been called an Acceptable Daily Intake or now, at the United States Environmental Protection Agency (EPA), a Reference Dose. This process is still widely used at the EPA for establishing criteria for air pollutants, water pollutants, pesticide tolerances, and the like.

During the past several decades, an emerging and very pressing concern has been the risk from cancer; the techniques developed for evaluating the risks from cancer are thought of by most people when, today, they refer to risk assessment.

During this time, the role of risk assessment evolved from an incidental role in any one regulatory decision toward a principal part of the decision-making process. It is important to understand that there were a number of forces, many associated with the legal and governmental process, that acted together (perhaps even synergistically) to accelerate the use of risk assessment in the decision-making process. We would like to point out briefly four of these forces: court decisions, congressional interest, regulatory agency actions, and advances in the biological understanding of disease mechanisms.

The first of these is court decisions. For instance, courts in the United States have suggested that quantitative risk assessment is required for an appropriate regulatory decision to be made in decisions on benzene [US Supreme Court, 1980] and urea-formaldehyde foam insulation [US Fifth Cir, 1983].

The United States Congress has also been encouraging quantitation and the use of comparative risk assessment. Their interest led to the key study on risk assessment in the federal government conducted by the National Academy of Sciences [NAS, 1983], and interest by individual congressmen has continued.

The regulatory agencies have also attempted to define risk assessment and describe how it is done. (See Preuss, et al, 1987, for details.) Two reports deserve special mention. The President's Office of Science and Technology Policy (OSTP) published a major report entitled Chemical Carcinogens: A Review of the Science and its Associated Principles [OSTP, 1985]. Perhaps the most important policy document, which has and will continue to ensure a focus on the topic of risk assessment, is the National Academy of Sciences (NAS) study entitled Risk Assessment in the Federal Government: Managing the Process [NAS, 1983] which I discussed earlier in this conference, and will also touch on in a moment.

Finally, there have been both apparent and real advances in the art of risk assessment and in basic biological understanding of disease mechanisms. As risk assessment techniques developed, scientific analyses often were not separated organizationally from the decision process. Generic procedures and assumptions, though supportable scientifically, were often unwritten or inconsistently applied. The apparent or real inconsistencies that developed led to a public perception that a scientific analysis was often fitted to the decision rather than the reverse. These problems led Congress to commission the study by the National Academy of Sciences referred to above. That report recommended that government agencies separate risk assessment from risk management, both procedurally and organizationally. They also recommended that agencies issue inference guidelines similar to those we discussed earlier. Once risk assessment became a clearly articulated component of the decision process, it was often possible to quantify risk, to evaluate the degree to which risk could be reduced in various regulatory to evaluate the degree to which risk could be reduced in various regulatory strategies, and to include these risk reduction analyses into the decision-making process.

This process of ensuring consistency and technical quality in risk assessments culminated at EPA with the publication of the risk assessment guidelines. As discussed previously, both the government-wide and EPA interest in this area began about ten years ago. It intensified in 1983 when former Administrator Ruckelshaus committed the Agency to following the NAS recommendations [US EPA, 1984a], and to the development of the risk assessment guidelines, five of which were published in September 1986 [Summary - Preuss and Ehrlich, 1987; detailed guidelines - US EPA, 1986a - e]. I discussed these guidelines earlier

in this workshop. This developing scientific, congressional, administrative, and scientific framework has been accompanied by a parallel expansion of the application and use of risk assessment in the regulatory decision process, for example, vinyl chloride at EPA [US EPA, 1976]; benzene at the Consumer Product Safety Commission [US CPSC, 1978; withdrawn, 1981], the Occupational Safety and Health Administration [OSHA, 1987], and EPA [US EPA, 1984b, c]; and many others.

IMPEDIMENTS TO USE OF RISK ASSESSMENT

That quick overview describes how risk assessment has developed as an analytical tool and how it has begun to be used as a decision-making tool by evaluating risk reduction; that is, in EPA's situation, the risks and the degree to which those risks can be reduced by selection of appropriate regulatory strategies. There are, however, several problems that have slowed its implementation. These include dealing with the inherent uncertainties in the risk assessment process, statutory requirements which ignore or downplay the use of risk assessment, and the lack of public understanding about--and confidence in--the use of risk assessment information. Let us first talk about some of the inherent uncertainties in the scientific process itself [Goldstein, 1984; Preuss, 1987]. Perhaps the most-discussed group of uncertainties are those having to do with the statistical quality of the dose-response assessment; that is, extrapolating the experimental results to inferences about human risk. Some of these concerns have to do with uncertainty about the biological basis for the mathematical models. Within the field of epidemiology, there are problems with the statistical power of the studies, and proper allowance for confounding factors. With animal studies, there are problems with choice of the appropriate mathematical model for extrapolating from high doses to low doses, problems with using the right scaling factor for extrapolating from

animal data to humans, and adjusting for the route of exposure if experimental and environmental exposure are by different routes of entry into the body.

An emerging area of concern has been in the field of pharmacokinetics. This rapidly growing area of research will, I hope, help us to reduce the uncertainties in relating external exposure to absorbed dose, in properly characterizing transport of the toxicant to the target organ, and in understanding the role of chemical transformations before the toxicant's metabolites reach the target organ.

Another area of uncertainty, in which EPA has been active for a number of years, is exposure modeling. Here there are uncertainties that develop because on-the-spot measurement data are often unavailable, because there is a need to estimate dispersion of the pollutants in the environment from available data through mathematical models which have their own uncertainties, and because of chemical and biological transformations as various toxicants disperse through the environment.

A fourth area of uncertainty is the lack of well-developed techniques for assessing risks for other kinds of end points besides carcinogenicity, mutagenicity, and--perhaps--developmental and reproductive toxicity. That is, there are significant deficiencies in our traditional techniques of evaluating threshold toxicants, since those assessment techniques are typically not specific for a particular target organ, such as the liver or kidney, or for a particular type of effect, such as neuro-behavioral responses. Beyond that, even when the techniques are available, appropriate toxicological information may not have been collected for specific chemicals of concern.

As EPA has become more and more concerned with hazardous wastes, we have also become more involved with risk assessment for mixtures [US EPA, 1984d, e; Stara and Erdreich, 1985]. This presents several more uncertainties in addition

to those discussed in the last few paragraphs. For example, we do not always know what toxicological significance there is to the physical form of a toxicant in a mixture relative to the physical form in the experiment from which the toxicity information was originally developed. There are uncertainties in selecting the appropriate methods for adding effects of several different toxicants in a mixture. There are uncertainties about the role of interactions in the mixtures (synergisms and antagonisms). Finally, we know that there are data gaps for known components of the mixtures, and there may be contributions from unidentified components of the mixtures.

The second impediment to the use of risk assessment as a regulatory tool occurs when Congress writes laws that ignore or downplay the use of risk assessment. In some cases, statutes provide only for banning upon a particular showing of adverse health effects. The classic case is the Delaney clause for food additives that are thought to be carcinogens. Another approach, directed in some EPA statutes, is the technology-based standard, where EPA is required to mandate the use of pollution control technology (commonly referred to as Best Available Technology) independent of any direct consideration of risk reduction or cost-benefit ratios. We will discuss the influence of such laws later in this paper. (For details, see Preuss et al, 1987.)

The third impediment to which we referred is the lack of public understanding about, or confidence in, risk assessment information. That issue is being discussed at this workshop by several people.

At EPA, we have been doing several things to try to resolve some of these problems. First, we have been trying to reduce some of the uncertainties in the scientific risk assessment process through targeted research [Preuss, 1987].

Some examples include developing new techniques in dose-response modeling for carcinogens and for developmental toxicity. We have also been interested in advancing the science of pharmacokinetics, and recently held a workshop on the use of pharmacokinetic models in risk assessment [Gillette and Jollow, 1987]. We recently convened two other workshops, on tumor promoters [US EPA, 1987] and on the relationship of maternal and developmental toxicity [Kimmel et al, 1987]. We expect these workshops to be the first of several on controversial risk assessment issues. Finally, we have been placing more emphasis on non-cancer health effects, specifically looking at techniques for evaluating additional health effects beyond developmental and reproductive toxicity to immunological effects, sensitization, and neurotoxicity; techniques for quantifying inhalation toxicity; and statistical techniques for assessing risks from these threshold toxicants. We are also doing more research on complex mixtures and total human exposure.

We have been attempting to develop ways to communicate both the concepts of risk assessment and information about risk assessment to the public. We have recently developed, and made available to the public, what we call the Integrated Risk Information System or IRIS [Preuss and Ehrlich, 1987]. This is a computer-based file of EPA risk assessment and risk management information for chemical substances. It is designed especially for federal, state, and local environmental health agencies as a source of the latest information about EPA health assessments and regulatory status for specific chemicals. It is intended for users without extensive training in toxicology, but with some knowledge of health sciences.

In the past several years, EPA has put greater emphasis on working directly with the public concerned about environmental hazards or potentially affected by proposed EPA regulations. For example, the Agency worked directly with

people living in the Takoma, Washington, area who were faced with the possibility of closure of a smelter because of EPA's arsenic regulation, to explain the trade-offs between estimated health risk and economic impact, and to give the community a voice in the ultimate decision [Ajax and Meyer, 1985]. We have also been developing pilot activities in specific geographic areas that integrate risk assessment, communication of these risk assessments in laymen's terms, and discussions with affected government and private groups to address environmental problems on a regional basis. Earlier in this conference Dan Beardsley has talked about some of those activities. EPA works closely with people living near hazardous waste sites and with their communities in regulating and cleaning up the sites. EPA is also in the process of implementing the Community Emergency Preparedness and Right-to-Know Act (Title III of the Superfund Amendments and Reauthorization Act of 1986, PL 99-499), whose basis intent is to inform the public about chemical risks in their communities and establish community planning for chemical emergencies. As a last example, EPA is attempting to gain a better understanding of how the general public perceives EPA's explanations of the degree and nature of risks it is regulating so that EPA can improve its communications with general public. You have heard from Vincent Covello about some of those activities.

HOW RISK ASSESSMENT IS USED

Risk assessment is used in three major ways - for priority setting, for regulatory decision-making and for evaluating the benefit side of a cost-benefit analysis. The first use is quite obvious. Many risk assessments lead to specific numbers - Reference Doses, LD_{50}'s, carcinogen risk estimates, and the like. It is quite commonplace for managers to use lists of numbers like these to decide which chemicals should be regulated first, or which problems

should receive the largest share of a program budget. The very existence of the numbers encourage this use.

The use of risk assessment in regulatory decision-making is best illustrated with examples from different kinds of regulations. We pointed out earlier that health and safety regulations can be based on three kinds of theories, depending on the specifics of each environmental law. The three theories are risk-based, technology-based or some kind of balancing between risk and other factors like costs or technological feasibility. Let us review regulatory development under each concept.

One example of the risk based approach is the development of regulations for hazardous air pollutants under Section 112 of the Clean Air Act. The first step is actually a priority ranking exercise similar to those I just referred to. In the air program, this step is referred to as a screening assessment. We rank chemicals we are considering by a combination of numerical ratings - volume of production (as an estimate for exposure), health effects indices, and the like. From this screening assessment, if a chemical remains of concern, a brief risk assessment, called a Tier I, is done consisting of a review of acute toxicity, estimate of oncogenic potential, and estimate of sources and magnitude of exposure. If this brief analysis continues to indicate a cause for concern, both a comprehensive Health Assessment Document and detailed exposure assessment are prepared. Part of this preparation is a peer-review process consisting of invited expert review, public comment on external review drafts, evaluation of the documents by our Science Advisory Board, and revision of the documents in light of those comments. Once these steps are completed, the process shifts from an emphasis on risk assessment to an emphasis on risk management. The air office makes a preliminary decision to regulate and publishes that intent to list the chemical as a hazardous air pollutant. In

the United States a regulatory decision like that is first proposed for public comment, the comments considered, and the regulation, in this case the listing decision, subsequently issued in final form. Once work on a listing decision has been completed, a specific regulation deciding limits for that chemical is first proposed for public comment and then issued after the public comments are considered.

Examples of a technology-based approach can be found in the effluent guidelines program under EPA's Clean Water Act (or Water Quality Act, as it is now called). Here, risk assessment has been used prior to consideration of effluent guidelines to establish independent water quality criteria, but those criteria are used only as guidelines for control of the potential sources of of pollution. Once a decision has been made to regulate a particular industry, the focus of the regulations is controlling the amount of each pollutant that can be emitted by mandating the use of the best technology available, taking into account the feasibility and cost of the treatment and the established water quality criteria for the receiving stream. The controls might be in terms of best practicable control technology or best available technology (for existing production facilities discharging wastes directly into receiving waters), pretreatment standards for production facilities discharging into municipal sewage systems, or new source performance standards for new production facilities. The effluent guidelines are, in turn, enforced by a permit system which includes the specific technology, permitted emission levels, and required monitoring for compliance.

The Safe Drinking Water Act, in comparison, contains a two-tiered approach, starting off with a risk-based approach and switching to a technology-based approach. When a potential problem is identified, a risk assessment is done, and - if regulation is considered necessary, a Maximum Contaminant Level Goal

(MCLG) - strictly health based - is established. For instance, the MCLG is set, as a matter of policy, at a risk of zero for known or probable human carcinogens, below the RfD for possible human carcinogens, and at the RfD for other threshold pollutants. In concept, once the MCLG is established, the Agency then shifts to a technology-based approach, selects the best available technology (BAT), and sets Maximum Contaminant Levels (MCLs) based on that BAT. In practice, under the revisions to the Safe Drinking Water Act, the proposal and subsequent promulgation of the MCLG, and MCL takes place together. Proposed MCLGs and MCLs for several chemicals should be published soon and selects the best available technology that comes as close to the MCLG as possible. For threshold toxicants, the BAT usually achieves protection well below the MCLG. For carcinogens, since obtaining zero is not possible, the technology is evaluated in terms of parameters like analytical detection limits, degree of risk reduction, and residual risk.

EPA uses a risk-balancing approach for regulation of pesticides under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). One can see why a risk-balancing approach is legislated for pesticides, since it is clear that these are toxic materials, and one must carefully balance the benefits to society from their use against the risks to society from their use. One must also carefully control how they are used and to what extent they will be permitted FIFRA may also be a good example to discuss at this conference because it is one of the few EPA examples in which government approval in advance is required before the chemical can be used. We understand this is similar to regulatory approaches used in many other countries of the world, including Japan.

In the case of a pesticide, once the Agency has completed the risk assessment, i.e. both determined the degree and nature of the hazard and determined whether the pesticide is released into the environment, it then

balances that information against the need for the pesticide and a consideration of appropriate restrictions on its use. The restrictions can include:

- labelling instructions
- restriction of use to licensed application who have the required skills and safety equipment
- restriction of approval to specific physical forms (e.g. solids, aerosols, aqueous liquids, organic liquids)
- denial of approval for its use

We have used examples from EPA, but other Agencies approach their regulations in similar ways, again, depending on whether their legislation requires a risk-based approach, technology-based approach, or balancing approach. Thus, for instance, the Food and Drug Administration uses a risk-based approach for direct food additives, but balances risks and benefits for unintended additives or for drugs; and the Occupational Safety and Health Administration balances risks and costs in setting its work-place standards.

The third use of risk assessment is for estimating the benefits of a particular regulation in order to conduct a cost-benefit analysis, also frequently called an economic impact analysis or a regulatory impact analysis. Once a risk assessment is completed, we can estimate the degree to which the risk is reduced, and can then estimate the value of the reduction in injury costs, increased longevity, reduced environmental damage, and the like. (Of course, once economic factors have been added, the risk assessment has been transformed into, or become part of the risk management decision.) These kinds of analyses are now required of Federal agencies, and they are routinely performed whether the authorizing statute provides for such assessments or not.

THE FUTURE OF RISK ASSESSMENT

In discussing where we go from here, I want to point out again that there is no general agreement or consensus regarding the use of risk assessment. Some agencies strongly question whether risk assessments should be done at all, or, if so, prefer that they be restricted only to qualitative analyses of the risk; other agencies use risk assessment to a greater or lesser extent. The extent to which risk assessment is used depends, in part, on how agencies have reacted to the combination of two managerial issues: (1) whether the risk assessment responsibility is centralized in headquarters or decentralized to regions and specific sites, and (2) the extent to which risk assessment and the evaluation of risk reduction are part of the agency's decision-making process.

We see EPA at one end of the spectrum. EPA has been firmly committed to the use of risk assessment, the evaluation of risk reduction, and the making of careful risk management decisions, regardless of whether those decisions are being made in headquarters or the field. There has been a major shift in EPA toward local analysis of environmental problems and local control strategy development at hazardous waste sites, municipal incinerators, and the like. These local analyses include such factors as matching available technology to existing facilities; adjusting exposure assessments to local variations in geography, terrain, and population; and accounting for local variations in the political, social, economic, and legal environment. Therefore, in addition to upgrading and improving risk assessment techniques themselves, as I have discussed throughout this presentation, we have also had to adjust our risk assessment processes to ensure effective use of risk assessment in those decentralized activities.

Therefore, as we have discussed and will discuss over the next few days, you may want to keep in mind that we expect to see more and better risk assessments as an integral part of the regulatory process, greater decentralization in the conduct of risk assessments, and a much greater expansion of knowledge and expertise in the science, or perhaps more properly art, of risk assessment.

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