

Framework for the Integration of Health and Ecological Risk Assessment

Glenn W. Suter II,^{1*} Theo Vermeire,² Wayne R. Munns, Jr.,³ and Jun Sekizawa⁴

¹National Center for Environmental Assessment, Office of Research and Development, U.S. Environmental Protection Agency, 26 W. Martin L. King Drive, MS-117, Cincinnati, OH 45268, USA . ²Toxicology Advisory Centre, National Institute of Public Health and the Environment, The Netherlands. ³National Health and Environmental Effects Research Laboratory, Office of Research and Development, U.S. Environmental Protection Agency, Narragansett, RI, USA. ⁴Division of Information on Chemical Safety, National Institute of Health Science, Tokyo, Japan

ABSTRACT

The World Health Organization's International Programme on Chemical Safety (IPCS), the Organization for Economic Cooperation and Development (OECD), and the U.S. Environmental Protection Agency have developed a collaborative partnership to foster integration of assessment approaches for human health and ecological risks. This paper presents the framework developed by that group. Integration provides coherent expressions of assessment results, incorporates the interdependence of humans and the environment, uses sentinel organisms, and improves the efficiency and quality of assessments relative to independent human health and ecological risk assessments. The paper describes how integration can occur within each component of risk assessment, and communicates the benefits of integration at each point. The goal of this effort is to promote the use of this internationally accepted guidance as a basis for harmonization of risk assessment.

Key Words: risk assessment, integration, guidance, ecological risk, health risk.

I. INTRODUCTION

This paper presents a framework for integrated health and ecological risk assessment that was developed by an international working group for the World Health Organization (WHO 2001). For reasons discussed below, the authors and other members of the working group believe that, by treating humans and the environment as an integrated system exposed to a common set of chemical contaminants

* Corresponding author: Tel(voice): 513-569-7808, Tel(fax): 513-569-7475; suter.glenn@epa.gov

and other stressors, we can better protect both human and nonhuman populations. Accompanying papers present case studies that were performed by the working group to test the framework and a discussion of other forms of integration that may be important in particular risk assessments.

What Is Included in the Integrated Framework?

In this document we define the term integrated risk assessment as a science-based approach that combines the processes of risk estimation for humans, biota, and natural resources in one assessment. Such an integrated approach can be applied to a wide variety of types of assessments, including (1) assessments that predict the effects of proposed actions, (2) those that estimate the ongoing effects of past actions, (3) assessments of actions at particular places, and (4) assessments of risks from hazardous agents independent of location. Integration extends across all phases of the assessment process from the planning of the assessment to decision making. This framework addresses environmental risks, that is, risks from chemicals and other stressors in the environment.

Why Integrate?

The objective of risk assessment is to support decision making by assessing risks of adverse effects on human health and the environment from chemicals, physical factors, and other environmental stresses. For practical reasons, the methodologies for human health and ecological risk assessment developed independently. However, with increased recognition of the need to more effectively protect both humans and the environment, it is time to consider a move to a more integrated, "holistic" approach to risk assessment.

The ability of environmental managers to make appropriate decisions may be limited by the incomplete or incoherent information provided by risk assessments that are too limited in scope. We believe that it is particularly important to integrate assessments of risks to human health and well being with risks to nonhuman organisms, populations, and ecosystems. Decisions are not fully informed if they consider only one or the other. Protection of humans will not inevitably result in protection of nonhuman organisms and ecosystems. In most cases of environmental contamination or disturbance, some nonhuman receptors may be more exposed or more sensitive than humans (Suter 1993). Integration of health and ecological assessments is the focus of this paper, but additional types of integration may also be relevant to the risk manager's needs (Suter *et al.* 2003).

Integration of health and ecological assessments provides five major advantages. Three of these address general concerns, while the last two relate to methodological issues:

Coherent Expression of Assessment Results — Coherent results of integrated health and ecological risk assessments provide a strong basis for action to support decision making. However, when the results of independent health and ecological risk assessments are inconsistent and the bases for the inconsistency are unclear, decision making is complicated. This may occur because the results of the health and ecological risk assessments are based on different spatial and temporal scales, different degrees of conservatism, or different assumptions,

Framework for the Integration of Health and Ecological Risk

ranging from assumed parameter values to assumed land use scenarios. As a result, decision-makers may find it difficult to decide whether, for example, the reported risks correspond to expected effects on humans that are sufficient to justify taking a remedial action that will destroy an ecosystem. As another example, consider a decision whether to license a new pesticide that poses an increased risk to humans and a decreased risk to aquatic communities relative to a current pesticide. If the ecological risk estimates are based on expected effects on a spatially distributed community while the health risks are based on provision of a margin of safety on an effect level for a hypothetical maximally exposed individual, the two estimates of risk cannot be compared. Finally, if variance and uncertainty are not estimated and expressed equivalently for health and ecological risks, a decision-maker cannot determine the relative need for additional research to support future assessments. For example, variance in dilution should be either included or excluded in both assessments, and, if it is included, the same estimates should be used. Integration of health and ecological assessments can avoid these impediments to defensible decisions.

Interdependence — Ecological and human health risks are interdependent (Lubchenco 1998; Wilson 1998). Humans depend on nature for food, water purification, hydrologic regulation and other products and services, which are diminished by the effects of toxic chemicals. In addition, ecological injuries may result in increased human exposures to contaminants or other stressors. For example, addition of nutrients to aquatic ecosystems and the resulting changes in algal community structure may influence the occurrence of water-borne diseases such as cholera as well as toxic algae such as *Pfiesteria piscicida* which kill fish and potentially affect humans. The need to assess ecological risks in order to estimate indirect effects on human health is particularly apparent in the assessment of climate change (Bernard and Ebi 2001). More subtly, the occurrence of fish kills or the disappearance of formerly familiar birds may diminish people's sense of well being leading to both psychological and physical effects (Kellert and Wilson 1993; Conway 1999). As a result of this interdependence, assessments that do not integrate health and ecological risks are likely to miss important modes of action that involve interactions between effects on the environment and effects on humans.

Sentinel Organisms — Because nonhuman organisms often are more heavily exposed to environmental contaminants and may be more sensitive, they can serve as sentinels, suggesting potential sources of human hazards (NRC 1991; Burkhardt and Gardner 1997; Sheffield *et al.* 1998; van der Schalie *et al.* 1999; Colborn and Thayer 2000). There are significant technical difficulties in extrapolating from nonhuman species to humans (Stahl 1997). However, if human health assessors reject the analogy, the public often makes it themselves. If the fish have tumors or the birds have deformities, the public that shares the environment with these organisms will be concerned, and assessors who have not integrated the health assessments with ecological assessments may have difficulty explaining why the public should not be concerned. Nonhuman organisms may also serve as sentinels for modes of action that have not been identified in humans. For example, opportunistic infections in marine mammals appear to be related to accumulation of polychlorinated biphenyls (PCBs) and organotin compounds which cause immunosuppression in laboratory animals (Ross 2000; Ross *et al.* 2000). This has raised concern for human populations that also

accumulate these compounds through fish consumption (Takahashi *et al.* 1998). Effects on sentinel organisms may even serve as estimators of human risks. For example, the New York State Department of Health has used “dead crow density” to estimate human risks from West Nile virus (Enserink 2001).

Quality — The scientific quality of assessments is improved through sharing of information and techniques between assessment scientists in different fields. For example, in assessments of contaminated sites, human health assessors may use default uptake factors to estimate plant uptake, unaware that ecological assessors are measuring contaminant concentrations in plants from the site. Conversely, knowledge of mammalian toxicokinetics has been used in risk assessments for humans but is seldom used in assessments for wildlife. The data sets available for the safety evaluation of chemicals in human food and drinking water are relatively large and they are used to support intensive assessments. In contrast, ecological risk assessments for chemicals have relatively small data sets and few resources to perform assessments even though the receptors include thousands of species including plants, invertebrates, and vertebrates. Integration of efforts may help to alleviate this imbalance in quality.

Efficiency — Integration of human health and ecological risk assessments offers significant increases in efficiency. For example, the processes of contaminant release, transport, and transformation are common to all receptors. Although only humans shower in water and only aquatic organisms respire water, the processes that introduce the contaminants to water, degrade or transform them, and partition them among phases are common to both. Therefore, there are clear efficiencies in integrated exposure models. This will provide benefits even to sector related risk assessments that do not have an integrated assessment as their goal (*e.g.*, work-place risk assessments).

What Is the Nature and Purpose of this Paper?

The purpose of this paper is to provide a common framework for integrated human and ecological risk assessments. For other discussions of integrated assessment, the reader is referred to references in Munns *et al.* (2003).

II. FEATURES OF THE PROPOSED FRAMEWORK

The discussion of integration of ecological and human health risk assessment is facilitated by using a framework that identifies the elements of risk assessment. Although several frameworks are being employed throughout the world, most reflect four basic elements or steps: some form of problem definition, a characterization of exposure, a characterization of the relationship between effects and exposure, and a synthesis of this information to estimate risk. A convenient summary of environmental risk assessment/risk management frameworks used in The Netherlands, Australia and New Zealand, Canada, the United Kingdom, and the United States is offered by Power and McCarty (1998). Some of their features are discussed below.

This paper distinguishes between risk assessment and risk management. We restrict risk assessment to the activities that provide the scientific information to be used in the decision making process. Risk management is the use of this and other

Framework for the Integration of Health and Ecological Risk

kinds of information to select among possible alternatives and to implement the selected alternative. We maintain this distinction to focus attention on the scientific aspects of integrated risk assessment.

Recognizing the similarities in risk assessment frameworks currently in use, we used the U.S. Environmental Protection Agency's (USEPA's) framework for ecological risk assessment (USEPA 1992, 1998) and associated terminology as a starting point. The ecological risk assessment (ERA) framework has greater general applicability than do human health frameworks or those environmental frameworks derived directly from human health frameworks. The ecological frameworks are more inclusive because (1) they were developed to deal with a range of environmental stressors beyond toxic chemicals, (2) they must describe the nature and role of the environment in the risk process, and (3) they must explicitly deal with the identification of the endpoint to be assessed. A well-developed body of concepts and terminology exist in the literature treating ecological risk assessment (*e.g.*, Bartell *et al.* 1992; Suter 1993; Calabrese and Baldwin 1993; USEPA 1998).

Like the ERA framework, the integrated framework consists of three major components (Figure 1). During the first of these, Problem Formulation, the overall goals, objectives, scope, and activities of the assessment are delineated. The Analysis step consists of data collection and modeling exercises to characterize exposure in time and space, and to define the effects on humans and ecological systems resulting from exposure. The methods appropriate for the Analysis step may be stressor specific, but also depend upon the nature of the systems identified to be at risk. Exposure and effect information are synthesized as estimates of risk in the Risk Characterization step. Ideally, these estimates are quantitative, but, if information is lacking, only qualitative estimates of risk may be possible.

The integrated framework shown in Figure 1 treats the relationship of risk assessment to risk management, stakeholder input, and data collection activities in a general manner. The risk assessment is performed by experts termed risk assessors. Risk management is the process of deciding what actions should be taken and is performed by individuals who may not be technical experts. Stakeholders are individuals or groups who have interests in the risk management (industry, non-governmental organizations, and governmental organizations other than the regulator). They may convey their concerns and provide data or models. The integrated framework shows risk management and stakeholder activities as parallel and concurrent activities that may interact in various ways depending on the legal context and the assessment problem. The USEPA's ERA framework and many others prescribe inputs by the risk manager to the Problem Formulation through a planning process, which may also include stakeholders. Considerations of regulatory requirements and constraints (where appropriate), societal values, and of other issues relevant to the assessment enter the assessment process at this level. The results of the assessment ultimately are communicated to risk managers and stakeholders. In between the planning of the assessment and the communication of results, the scientists may work independently of the risk manager and stakeholder (as in the U.S.) or may accept input concerning the performance of the analysis and risk characterization. This framework allows for communication among these groups at any time, depending on the legal and cultural context.

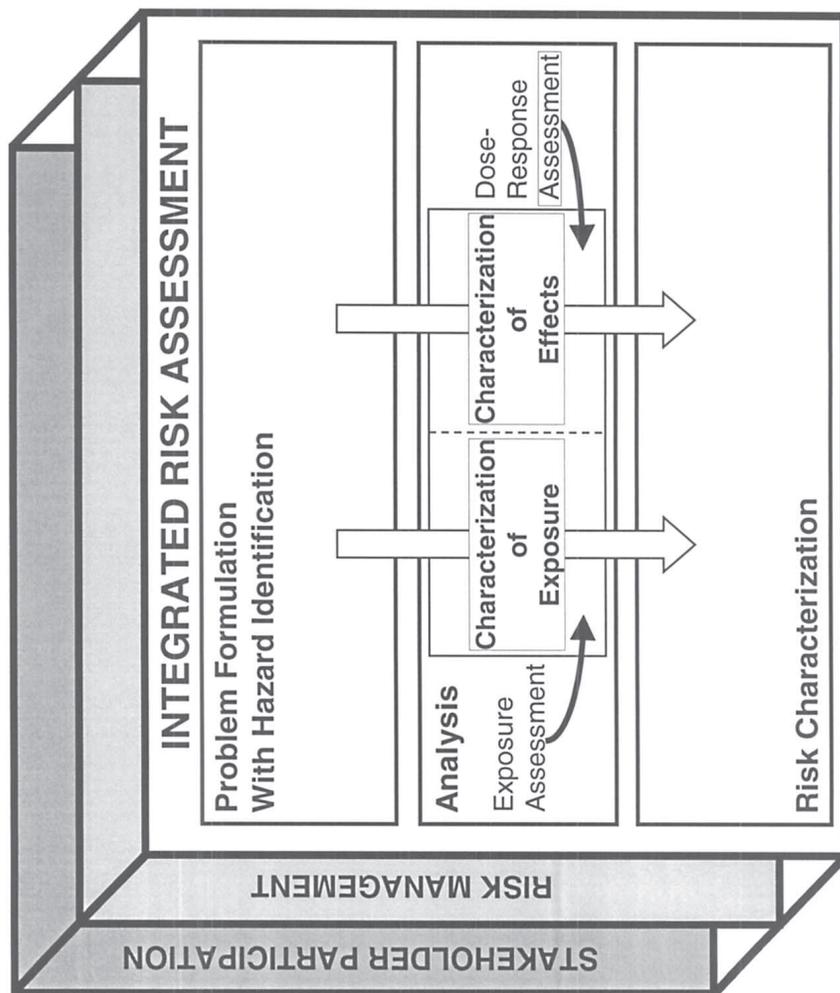


Figure 1. A framework for integrated human health and ecological risk assessment (modified from USEPA 1998). Risk assessors, risk managers, and stakeholders perform parallel activities that may interact at various stages.

Framework for the Integration of Health and Ecological Risk

Unlike some other frameworks, the integrated framework does not display the input of data, because data may enter from various sources at various points in the process. The risk assessors may collect existing data, and new data may be generated by the assessors or by stakeholders.

The integrated framework also does not explicitly represent or discuss iteration of the assessment process. The process may be iterated any number of times if additional data or analysis is needed to support the risk management process.

Relationship to Other Frameworks

Most, if not all, the frameworks for human and environmental risk assessment and management used today are based on the report "Risk Assessment in the Federal Government: Managing the Process," also called the "Red Book" by the U.S. National Research Council (NRC 1983). This framework was originally designed for human health assessment only, but was later adopted for ecological risk assessment (Barnthouse and Suter 1986; USEPA 1992; Barnthouse 1993).

All frameworks define the roles of science and political and societal values as essential parts of the process. They differ in the degree of separation of science from policy, the different roles of stakeholders in each stage of the process and the relative emphasis on risk management and risk assessment (Power and McCarty 1998).

The USEPA's ERA process separates science from the risk management process and mainly allows stakeholder consultations in risk management stages prior to and following risk assessment, which, itself, is considered a purely technical exercise. Other frameworks, including the redefined NRC framework (NRC 1996), the European Union's risk assessment framework for new and existing chemicals (EC 1996) and the FAO/WHO framework developed for risk management and risk assessment of food additives (FAO/WHO 1997) demand a greater role for risk managers or stakeholders in the risk assessment. The degree of participation of risk managers or stakeholders in the risk assessment process depends on the relative degree of concern about bias and relevance. If risk managers and stakeholders are intimately involved in the process, they may influence the selection of scenarios, models, and parameters to obtain desired results. On the other hand, if they are not involved, the risk assessment may not address issues that are critical to the decision. The proposed integrated framework (Figure 1) does not specify the timing or degree of involvement.

Leaving aside the degree of interaction with risk management and stakeholders, all risk assessment paradigms follow essentially the same logic. In some cases the stage of problem formulation, as described extensively in the U.S. Guidelines for ERA, is addressed, harmonized and laid down in advance of individual assessments. For example, assessments of individual chemicals within an agency or regulatory program may all use a common formulation of the assessment problem (EC 1996; FAO/WHO 1997). Procedures for human health and ecological risk assessment differ mainly in terminology. A significant difference is the use of "hazard identification" which is sometimes used to indicate the stage in which data are being evaluated and stressors of concern selected — and therefore part of "problem formulation" (*e.g.*, NRC 1983), whereas in other schemes hazard identification is

part of the characterization of effects (effects assessment), indicating the identification of adverse effects that a stressor has an inherent capacity to cause (*e.g.*, EC 1996; FAO/WHO 1997; OECD 1995). Other differences are considered minor for the purpose of this paper and generally will not lead to confusion.

III. PROBLEM FORMULATION

What Is Problem Formulation?

Problem formulation is the process by which the assessment is defined and the plan for analyzing and characterizing risk is developed (USEPA 1992, 1998). The first step is a planning dialog that clarifies the management goals, the purpose and scope of the assessment, and the resources available to conduct the assessment. The planning dialog considers whether a risk assessment is needed, and who should be involved in the assessment/risk management process. It also helps to ensure that the assessment will provide the information necessary to support the environmental decision-making process (*i.e.*, risk management). Risk managers, risk assessors, and stakeholders all bring valuable perspectives to assessment planning. This exchange may be based on the characteristics of recognized stressors (stressor-driven), direct observation of effects in the environment or in humans (effects-driven), or a desire to protect a valued resources (resource-driven).

Problem formulation requires that information concerning known or suspected stressors, observed or hypothesized effects, and systems at potential risk is integrated to generate assessment endpoints and conceptual models (Figure 2). Assessment endpoints are the specific attributes and entities to be assessed and protected (USEPA 1998). Criteria important for selecting appropriate assessment endpoints have been discussed by Suter (1989, 1990, 1993), USEPA (1992, 1998), and others. They generally include considerations of relevancy (with respect to the environmental systems, stressors, and societal values), applicability, and utility. The conceptual model is a representation of the relationships between the sources of the stressors and the assessment endpoints. It constitutes a hypothesis about how potentially significant risks arise. Ideally, the conceptual model should undergo rigorous review by risk managers, scientific peers, and stakeholders to ensure that all concerns have been addressed and that the assessment will yield a scientifically sound and credible characterization of risk. The methods to be used in the assessment to evaluate the risk hypotheses reflected in the conceptual model are described in the analysis plan, the final product of problem formulation (Figure 2). Analysis plans provide the information necessary for risk assessors and risk managers to determine that the assessment will provide the kinds and quality of information necessary to make environmental management decisions.

What Is Integrated?

Assessment Questions. An integrated approach offers the opportunity to develop and focus on assessment questions common to both health and environmental perspectives. It would ensure consistency in the spatial and temporal scopes of the two kinds of assessment, thereby enhancing the consistency of support information and processes used in environmental decision making. An integrated approach also

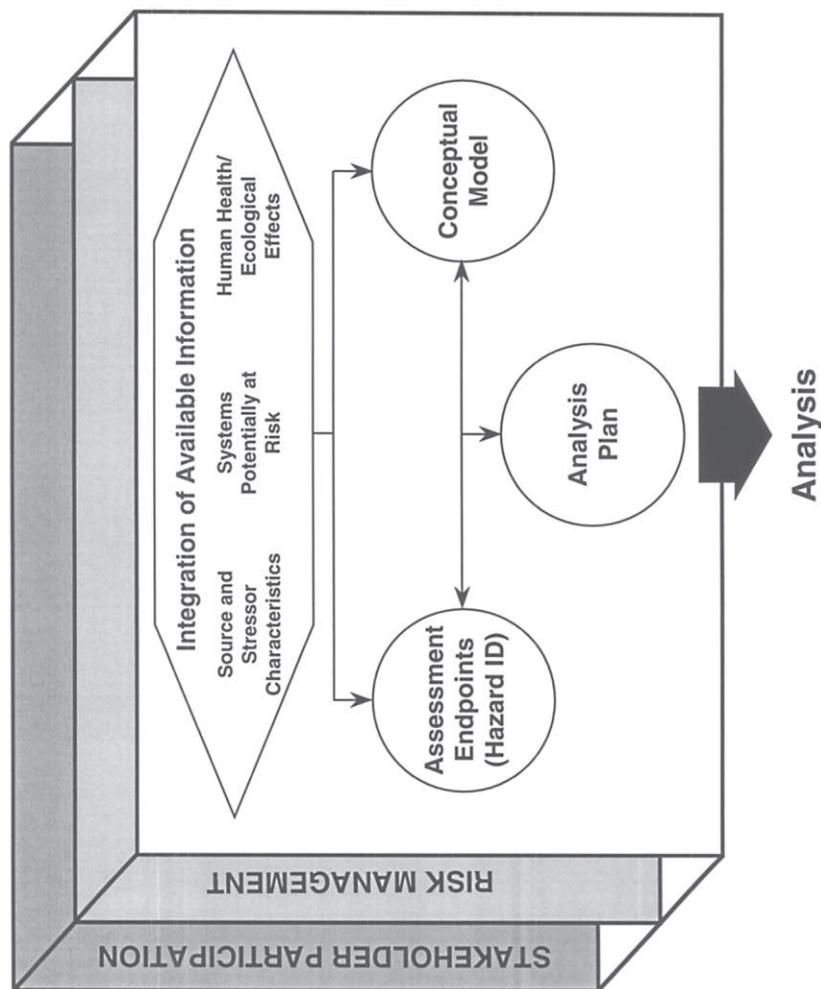


Figure 2. The problem formulation stage of an integrated risk assessment. Risk management and stakeholder activities are parallel and may interact with the problem formulation process to a greater or lesser extent depending on circumstances (modified from USEPA 1998).

helps to ensure adequate consideration of risks to humans through evaluation of risks to other organisms that influence human health and welfare.

Impetus for the Assessment. An integrated approach has obvious utility in stressor-driven assessments, which are assessments that evaluate risks associated with specific stressors (*e.g.*, new chemicals) in the environment. However, the impetus for an assessment may also be observed exposure (*e.g.*, mercury in fish) or effects (*e.g.*, mass mortality of birds). In those cases, the implications of those observations for both humans and nonhuman endpoints should be considered.

Assessment Endpoints. Integration would foster coherence in endpoints used to assess health and ecological risks. Knowledge of the environmental fate or mode of action of a stressor can elucidate the susceptibility of potential human and ecological endpoints. In addition, knowledge of ecological susceptibility can suggest what indirect effects on humans may be identified as endpoints.

Conceptual Models. Conceptual models in integrated assessments would reflect common sources and transport pathways of environmental stressors. Humans would be considered another potential receptor on these pathways. Such models would reflect a more complete list of risk hypotheses related to the environmental stressors, including incorporation of multiple sources, multiple exposure pathways, multiple direct effects, and the possibility of indirect effects.

Analysis Plan. An integrated approach offers substantial opportunity for enhanced efficiency of sample and analysis activities, as well as other data gathering activities. Models can be selected to describe exposure (transport and fate) and effects in a manner that maximizes utility in assessing risk to humans and the environment, and that have similar data needs. Assumptions supporting those models and other analysis approaches would be made in common, and results of planned analysis activities would be expressed in similar fashion. Sampling, analysis, testing, and other data generating activities can be conducted to ensure relevance to human and ecological risks at minimum cost. Finally, if the assessment will be iterated, an integrated approach might foster the development of parallel tiers, which use common data and models. For example, both health and ecological assessments may begin with a screening assessment that will use a common set of conservative assumptions and then move to a more focused and realistic assessment.

IV. CHARACTERIZATION OF EXPOSURE

What Is Characterization of Exposure?

Characterization of exposure is the estimation of the concentrations, doses, or degree of contact of chemical, physical or biological stressors to which human individuals or populations, nonhuman individuals, populations, or ecosystems are or may be exposed. The objective of exposure characterization is to measure or model exposure in terms of routes, intensity, exposure media, spatial scales and time scales, using units that can be combined with the characterization of effects. The spatial scale refers to the geographical dimension of the problem: examples include the area around a point source, a region, or the globe. The time scale has aspects of duration, frequency, and timing.

Exposure characterization requires the evaluation of:

Framework for the Integration of Health and Ecological Risk

- Data completeness, quality and relevance for the aim of the risk assessment.
- Stressor characteristics: the identity and properties of the chemical, physical or biological stressor.
- Sources and emissions: identification and quantification of all sources and a correct description of industry and use category.
- Distribution pathways: conversion of the conceptual model to a quantitative model of relevant distribution routes and routes of exposure for endpoint organisms and ecosystems.
- Transport and fate: quantification of important transport, transformation, and degradation processes within the distribution pathways.
- External and internal exposure models: external exposure is estimated in terms of contact between a stressor and an organism which can be estimated from transport and fate models and knowledge of the organism's behavior, whereas internal exposure is estimated as dose to target organs and requires consideration of toxicokinetic processes such as uptake, transport, and metabolism.

The uncertainty in the exposure estimates should be addressed. Tiered approaches are generally preferable, beginning with simple conservative screening models and proceeding to more realistic and complex models generating probability density functions of exposure.

What Is Integrated?

Sources and Emissions. In an integrated approach it is often useful to consider the whole life cycle of a stressor so as to identify all potential emission sources which may lead to exposure of humans or nonhuman organisms (Figure 3). Emissions may occur at all stages. Sources must be identified which lead directly or indirectly to exposure of both humans and non-human species.

Distribution Pathways. Having identified emission sources, exposure pathways from these sources to environmental compartments and finally to receptor organisms or ecosystems should be identified as well as the commonality of these routes for different receptors (Figure 4). While some pathways are unique to humans (*e.g.*, contamination of food packaging) or nonhuman organisms (drinking from waste sumps), there is much commonality of the pathways for environmental contaminants.

Transport and Fate Models. Exposure pathways common to two or more receptor organisms or ecosystems can be described by common transport and fate models, including aspects such as advection and diffusion, partitioning, bioaccumulation, and abiotic and biotic degradation (Lew *et al.* 1996). These processes are determined by the characteristics of the stressor, the receiving environmental compartment, and the receptor organism or ecosystem.

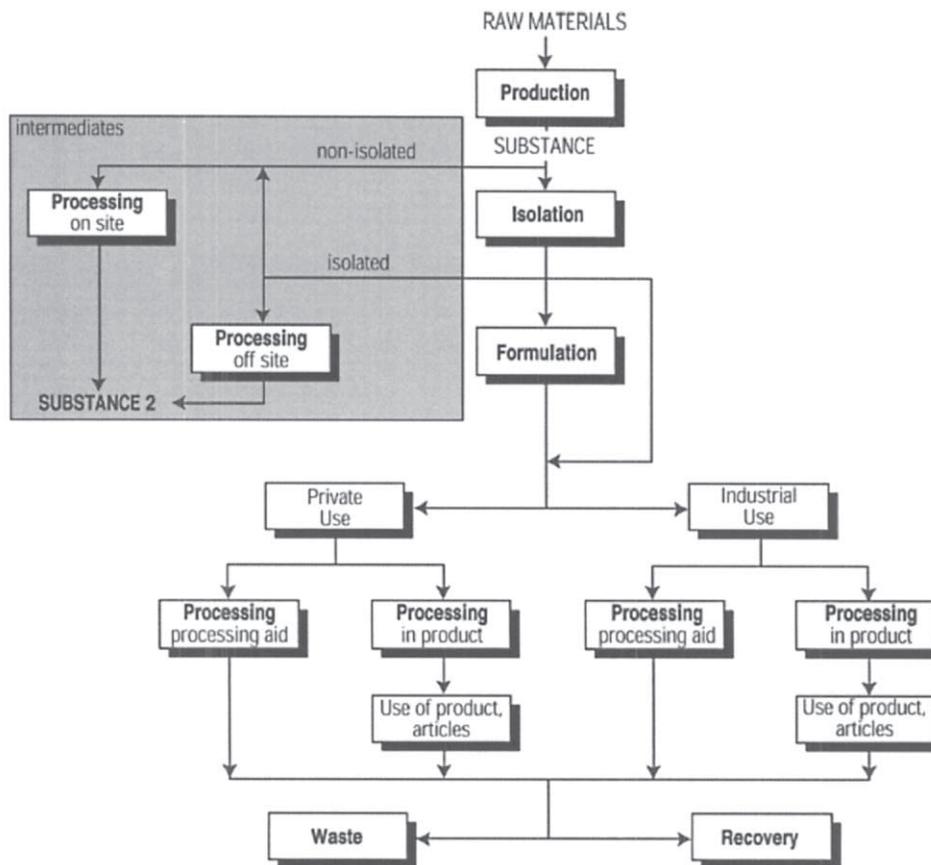


Figure 3. The life cycle of a chemical substance. Emissions to the environment can occur at any point in this cycle.

External and Internal Exposure Models. Most stressors must contact target organisms to cause an effect. Contact and internal transport and fate may be modeled similarly for different species.

Measures of Exposure Related Parameters. The application of common descriptions of sources and emissions and common models for transport, fate, contact and toxicokinetics implies that, for all parameters that are not receptor specific, the same value and units should be chosen. This applies to both measured parameters and parameters for which values must be estimated by expert judgement.

Analytical Tools. Integrated exposure assessment requires the application of the same quantitative methods such as methods for sensitivity and uncertainty analysis. Monitoring strategies should also consider aspects important for an integrative approach, particularly in relation to spatial scales and time scales.

Framework for the Integration of Health and Ecological Risk

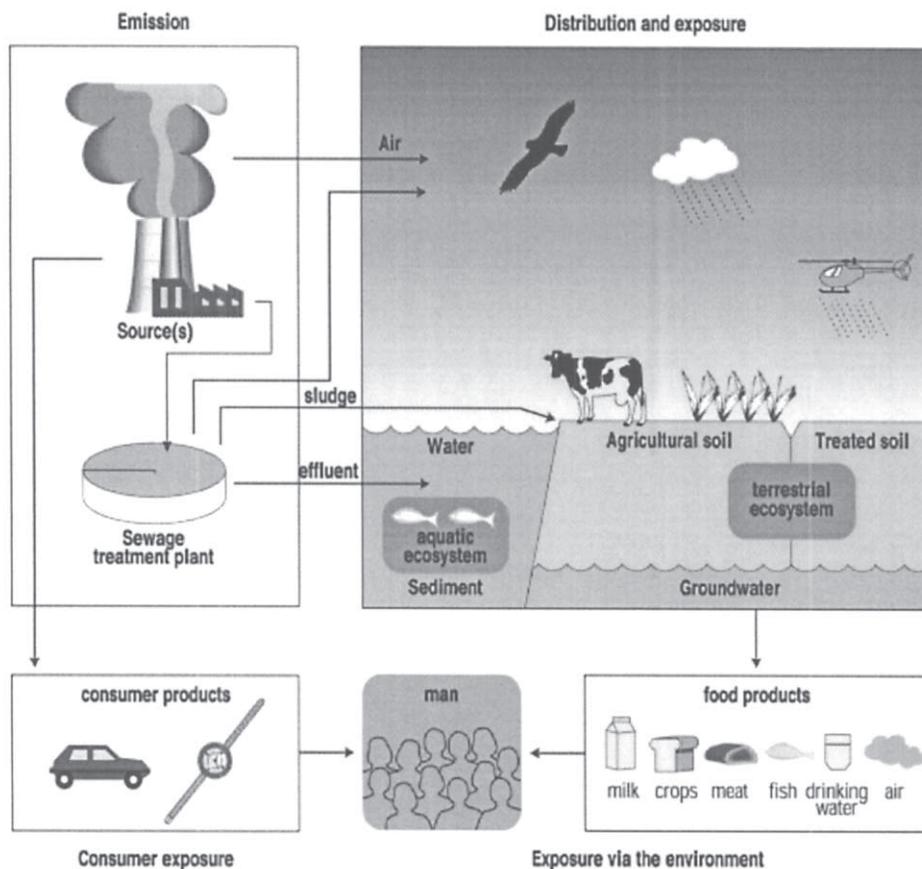


Figure 4. Routes of exposure of human and nonhuman organisms (van Leeuwen and Hermens 1995).

V. CHARACTERIZATION OF EFFECTS

What Is Characterization of Effects?

Characterization of effects (also termed hazard characterization) consists of two distinct stages:

1. Hazard identification: the identification of adverse effects that a stressor has an inherent capacity to cause to human individuals or populations, or environmental populations or ecosystems, or natural resources;
2. Exposure-response analysis: the estimation of the relationship between level of exposure to a stressor and the incidence and severity of an effect.

The hazard identification is normally part of the problem formulation in the USEPA frameworks, but it may be revisited during the characterization of effects if new data suggest additional hazards.

Characterization of effects requires:

- Evaluation of data completeness, reliability, and relevance for the aim of the risk assessment.
- Evaluation of the nature, intensity, and time scale of adverse effects with a causal relation to the stressor.
- Identification of the modes of action.
- Quantification of the relation between response to the stressor and exposure.
- Extrapolations relating experimental and observational data to the assessment endpoints including humans or ecosystem attributes.
- Evaluation of indirect effects.

What Is Integrated?

Reported Effects and Modes of Action. As appropriate, integration of the characterization of effects should be based on an understanding of the common modes of action of stressors in a range of organisms including humans. In addition, identification of similarities in the nature, intensity and time scale of effects among species allows a better understanding of the actual risk to these organisms and helps in the identification of issues of concern. Some common mechanisms might be found to explain complex toxicity profiles (IPCS 1999a,b). Essentially all of the effects of TCDD, as well as related PCDDs, PCDFs, and coplanar PCBs, are mediated by binding of the contaminants to a specific cellular protein, the Ah receptor. The Ah receptor is highly conserved, being present and functional in essentially all vertebrate species. It functions as a ligand activated transcription factor controlling proliferation, differentiation, and apoptosis in a tissue and developmental stage specific manner. The Ah receptor is a member of the PAS family of basic helix-loop-helix regulatory proteins, which can heterodimerize and control circadian rhythms, differentiation, and oxidative stress. This common mechanism results in related reproductive, developmental, immunotoxic, and neurotoxic effects in various species including domestic and laboratory animals, wildlife, and people.

Biomarkers and Indicators. Common mechanisms of action identified across species may lead to the identification and application of biomarkers and other indicators of effect common to humans and other ecological receptors. Knowledge of the applicability of such measures of effect will improve the ability to estimate effects on other species in the assessment. Additionally, standardization of such measures will enhance the ability to understand the relative magnitudes of effects across receptors.

Exposure-response Modeling. Making use of the commonalities of mechanisms of actions among humans and ecological receptors is a real strength of the integrated approach. Based on common mechanisms of action, stressor-response modeling for humans and other species in the environment would use the same prin-

principles. Ideally, such efforts would result in models of exposure-response (*e.g.*, benchmark dose models), as opposed to a hypothesis testing approach, which yields statistics like the No- or Lowest-Observed-Adverse- Effect Levels. This is important to integrated assessment because use of NOAELs and LOAELs does not allow comparison of the nature and magnitude of effects between human and ecological receptors. Toxicity equivalent factors and similar approaches used to combine or interconvert responses to stressors with common modes of action may be common to human and non-human species.

Extrapolations. Extrapolations bridge the gaps between observed effects on experimental or field-monitored organisms and the effects that must be estimated for assessment endpoints. Extrapolations are required between species, specific subpopulations, temporal and spatial scales, and modes of exposure. Common extrapolation procedures for humans and nonhuman species can be pursued including uncertainty factors, uncertainty distributions, allometric models, species sensitivity distributions, intertaxa regressions, and pharmacokinetic/pharmacodynamic models.

Direct and Indirect Effects. Integration of the characterization of effects should consider both direct and indirect effects resulting from exposure to the stressor. Indirect effects result from relationships among environmental processes. Integrated analyses of effect should recognize the potential cascading influences of one or more stressors. For example, direct toxicity to fish may result in loss of piscivorous wildlife and reductions in human welfare.

VI. RISK CHARACTERIZATION

What Is Risk Characterization?

Risk characterization is the phase of a risk assessment that: (1) combines the results of the characterizations of exposure and effects to estimate the risks to each endpoint, (2) estimates the uncertainties associated with the risks, and (3) summarizes the results for presentation to the risk manager and stakeholders.

What Is Integrated?

Combining Exposure and Effects. In the simplest case, an exposure estimate is used to estimate effects in an exposure-response model. Integration becomes more difficult when effects have been observed in the field and causation must be assigned or when multiple lines of evidence are available.

Determining Causation. Causation must be determined when apparent effects are associated with chemical contamination or some other hazardous agent. Examples of apparent effects include cancer clusters, fish kills, and reduced tree growth. Various criteria have been developed in human and ecological risk assessment for determining causation (Rothman 1988; Fox 1991; Suter *et al.* 2002). An integrated assessment would use a common set of evidence, common criteria, and common interpretations of those criteria to determine the cause of human and ecological effects that cooccur or are apparently associated with a common cause.

Combining Lines of Evidence. Risk characterizations often must derive a best estimate of risk from multiple lines of evidence. These may include results of toxicity

tests of different species, results of single chemical and mixtures toxicity tests, and exposure estimates derived from different fate models and from environmental measurements. These lines of evidence may be quantitatively weighted and combined, the highest quality line may be chosen subjectively, an inferential logic may be developed, or some other process may be chosen. In an integrated assessment a common approach would be used to integrate multiple lines of evidence, and, as far as is appropriate, the chosen approach would be implemented in a consistent manner. In addition, evidence from ecological and human health risks would be integrated when appropriate. As a simple example, observed effects on piscivorous wildlife would be considered when estimating health risks to humans who consume fish. In this case, body burden or critical organ burden of the contaminants could be a common measure between animals and humans, normalizing for the wide range of species difference in metabolic activity and rate of food consumption.

Uncertainty. Uncertainty is at the heart of risk assessment. Through uncertainty analysis, the risks of various stressors can be expressed in a common form (*e.g.*, the probability of occurrence of specified effects on human and ecological endpoints). However, the treatment of uncertainty in risk assessment is inconsistent, and the terminology is diverse. An integrated assessment should start with a common concept and terminology of uncertainty (*e.g.*, distinguish variance from true uncertainty), and as far as appropriate should use common analytical methods.

Presentation of Results. The results of risk characterizations must be presented in a form that is easily understood without losing their accuracy or diminishing their information content. This requires skillful use of text, graphic, and tabular presentation. To diminish confusion and to promote coherent decision making, the results of health and ecological risk assessments should be presented in a common format that allows comparison of results. For example, if health risks are presented as “the maximally exposed human will exceed a safe dose due to eating fish from the lake,” and the ecological risk is presented as “the probability of extinction of the local otter population is x ,” the results are both legitimate, but they are not comparable. An integrated assessment would use some common presentation of results (*e.g.*, proportions of human and otters in a region experiencing reproductive impairment) as well as any species-specific endpoints, and would explain differences in the magnitude of effects. Similarly, the uncertainties would be presented in a common form (*e.g.*, cumulative probability). This integrated risk characterization would greatly facilitate the task of communicating risks to risk managers and the public.

VII. RISK MANAGEMENT AND STAKEHOLDER PARTICIPATION

What Is Risk Management?

Risk management, in contrast to the scientific process of risk assessment, involves making decisions concerning actions in response to estimated risks to humans and ecological systems. A risk manager defines the issues to be addressed by a risk assessment, selects among alternative management options, and determines the acceptability of risks associated with decisions. The deliberations and decisions integral to risk management involve many kinds of information. In addition to consideration of potential adverse effects estimated by the risk assessment process, the sociopolitical and economic implications of alternative options may be consid-

Framework for the Integration of Health and Ecological Risk

ered in the decision making process. Legal mandates and regulatory constraints define the nature of decisions (as well as the focus of the risk assessment) and limit the range of management options available. Engineering feasibility may further constrain the implementation of various options. Thus, the understanding of risk to humans and ecological systems contributed by risk assessment is but one consideration in the overall risk management process.

What Is Integrated?

Ideally, the net benefit of the regulatory, remedial, or restoration decision to human health and the environment would be maximized. Given that there may be conflicts between human health and ecological goals and that economic and political considerations may mitigate against maximizing either health or ecological benefits, it is important, at minimum, to ensure that both health and ecological risks are fully and fairly considered. This requires that the results of health and ecological risk characterizations be presented in a manner that facilitates comparison and balancing.

Risk management decisions should be transparent and should use a clear and consistent logic. Integrated assessments should provide consistent expressions of health and ecological risks because they are needed for consistent decision logics.

What Is Stakeholder Participation?

Stakeholders in the risk assessment process are members of society who are concerned about the issues associated with the assessment and who may be affected by management decisions that use the results of the assessment. Potentially included as stakeholders in a risk assessment are representatives of industry, public interest groups, property owners, resource consumers, and other private citizens. Stakeholders can participate in risk assessments in a number of ways, including by assisting in development of management goals, by proposing assessment endpoints, by providing valuable insights and information, and by reviewing assessment results. Although the circumstances of stakeholder involvement vary widely among different risk assessments (depending on the regulatory and management context of the assessment), active stakeholder participation helps to ensure understanding of assessment results and the success of management actions.

What Is Integrated?

Stakeholder participation can be integrated during all phases of the risk assessment process. During problem formulation, stakeholders can provide input to development of management goals that address both ecological and human health issues. They also can help to identify ecological entities and human health issues that can become joint or complementary assessment endpoints. In both problem formulation and analyses phases, stakeholders can provide information and data useful to understanding exposures of humans and other receptors, possible effects resulting from exposures, and the possible interactions of humans and nonhumans that influence exposure and effects. Integration of stakeholder involvement during risk characterization and risk management can improve the description, interpretation, and understanding of risks estimated by the assessment. Stakeholders' input

can be used to help identify the relative importance of different risks to humans and ecological systems, thereby assisting the decision-making process and supporting management actions.

VIII. RISK COMMUNICATION

What Is Risk Communication?

Risk communication is an essential but difficult interactive process among risk assessors, risk managers, stakeholders, and other members of the public in which information about risks is exchanged (NRC 1989; Lundgren and McMakin 1998). Because ecological and human health risks are interdependent, there is a need for communication of health and ecological risks in an integrated manner.

Risk communication occurs first in the problem formulation when the risk manager explains the questions that he wants answered and the legal, policy, time, and resource constraints on the assessment. The assessors respond with the scientific and technical constraints on the assessment and provide scientific information to help clarify and sharpen the questions and define the scope of the assessment. After the assessment is completed, risk assessors communicate their results to the risk manager in a form that is useful for decision making including presenting the risks for alternative actions and uncertainties concerning risk estimates. Risk communication will also include stakeholders and the general public, but the timing and extent of this communication depends on the problem and context.

What Is Integrated?

Communication during the problem formulation should include the human health and ecological risk assessors, the risk manager and, as appropriate, the stakeholders. If decisions about the purpose and scope of the assessment are not coherent, it will not be possible integrate the sampling, analysis and assessment processes or to perform consistent analyses of human and ecological risks.

When the assessment is complete, the human and ecological risk assessors should present a coherent message concerning risks. Even when human and ecological risk assessments are performed in a consistent manner, apparent inconsistencies often occur and must be explained. Members of the public commonly assume that risks to non-human organisms are indicative of risks to humans. If this is not the case, the assessors must be prepared to explain the differences in diet, inherent sensitivity, route of exposure, or other factors that accounts for the difference.

One of the major sources of confusion in risk communication is inconsistency in the degree of conservatism. A way to avoid this confusion is for health and ecological risk assessors to present their best estimates of the consequences of the actions along with consistent estimates of uncertainty. Uncertainty is often difficult to communicate, and assessors should consider alternative forms appropriate to the audience.

IX. CONCLUSIONS AND RECOMMENDATIONS

Integration of health and ecological risk assessments has obvious advantages. The framework presented here should facilitate the processes of planning and perform-

Framework for the Integration of Health and Ecological Risk

ing integrated assessments. It should also facilitate environmental decision making by providing a consistent and coherent set of human and ecological risk estimates.

The implementation of this framework will require greater collaboration among risk assessors than is currently the case. For all risk assessments, an interdisciplinary team should perform the problem formulation. It should, in consultation with the risk manager, identify the stressors and sources, select the endpoints, define the environment, and develop a conceptual model. The team should then determine whether there are linkages between the sources of stressors and potentially significant responses of both human and ecological endpoints. If there are linkages to both types of endpoint receptors, the team should then plan and carry out an assessment that uses consistent data, exposure and effects models, and risk characterization. They should communicate their results in a consistent and integrated manner so that risk managers and stakeholders understand the implications of alternative actions. Finally, they should support the decision-making process by providing results in terms that are appropriate to the decision logic used by the risk manager.

ACKNOWLEDGMENTS AND DISCLAIMERS

The authors thank the other members of the working group for their comments and suggestions over the course of more than 3 years of meetings and reviews. They are: Linda Birnbaum, Terri Damstra, Jim Hart, Steve Hedtke, Robert Kroes, Robert MacPhail, Erminio Marafante, Peter Ross, Larry Reiter, Glen Van Der Kraak, Gil Veith, and Michael Waters. Special thanks to Terri Damstra for keeping us organized. This paper does not necessarily reflect the policies of the U.S. Environmental Protection Agency.

REFERENCES

- Barnthouse LW. 1993. Ecological risk assessment and the National Research Council. In: Bender ES and Jones FA (eds), *Applications of Ecological Risk Assessment to Hazardous Waste Site Remediation*. Water Environment Federation, Alexandria, VA, USA
- Barnthouse LW and Suter GW II. 1986. *Users Manual for Ecological Risk Assessment*. ORNL-6251. Oak Ridge National Laboratory, Oak Ridge, TN, USA
- Bartell SM, Gardner RH, and O'Neill RV. 1992. *Ecological Risk Estimation*. Lewis Publishers, Chelsea, MI, USA
- Burkhart JG and Gardner HS. 1997. Non-mammalian and environmental sentinels in human health: "Back to the future?" *Human Ecol Risk Assess* 3:309-28
- Calabrese EJ and Baldwin LA. 1993. *Performing Ecological Risk Assessments*. Lewis Publishers, Chelsea, MI, USA
- Colborn T and Thayer K. 2000. Aquatic ecosystems: harbingers of endocrine disruption. *Ecological Applications* 10(4):949-57
- Conway R A. 1999. A broader view. *Environ Toxicol Chem* 18(6):1077
- EC (European Community). 1994. Commission Regulation (EC) No 1488/94 of 28 June 1994 laying down the principles for the assessment of risks to man and the environment of existing substances in accordance with Council Regulation (EEC) No 793/93. Official J European Communities No L 161/3
- EC (European Community). 1996. Technical Guidance Document in support of Commission Directive 93/67/EEC on Risk Assessment for New Notified Substances and Commission Regulation (EC) No. 1488/94 on Risk Assessment for Existing Substances, Part I. Office for Official Publications of the European Communities, Luxembourg

- Enserink M. 2001. West Nile researchers get ready for round three. *Science* 292:1289-91
- FAO/WHO (World Health Organization). 1997. Risk Management and Food Safety. Report of a Joint FAO/WHO Expert Consultation, 27-31 January 1997, Paper 65. FAO Food and Nutrition, Rome, Italy
- Fox GA 1991. Practical causal inference for ecoepidemiologists. *J Toxicol Environ Health* 33:359-74
- IPCS (International Programme on Chemical Safety). 1990. Environmental Health Criteria 116, Tributyltin Compounds, pp 273. World Health Organization, Geneva, Switzerland
- IPCS (International Programme on Chemical Safety). 1999a. Concise International Chemical Assessment Documents for Triphenyltin Compounds. World Health Organization, Geneva, Switzerland
- IPCS (International Programme on Chemical Safety). 1999b. Concise International Chemical Assessment Documents for TBTO, World Health Organization, Geneva, Switzerland
- Kellert S. and Wilson EO. 1993. *The Biophilia Hypothesis*. Island Press, Washington, DC, USA
- Lew CS, Mills WB, Wilkinson KJ, *et al.* 1996. RIVRISK — A model to assess potential human health and ecological risks from chemical and thermal releases into rivers. *Water, Air and Soil Pollution* 90:123-32
- Lubchenco J. 1998. Entering the century of the environment: A new social contract for science. *Science* 279:491-5
- Lundgren R. and McMakin A. 1998. *Risk Communication: A Handbook for Communicating Environmental, Safety, and Health Risks*. Battelle Press, Columbus, OH, USA
- Munns, WR Jr., Kroes R, Veith G, Suter GW II, Damstra T, and Waters MD. 1993. Approaches to integrated risk assessment. (this issue)
- NRC (National Research Council). 1983. *Risk Assessment in the Federal Government: Managing the Process*. National Academy Press, Washington, DC, USA
- NRC (National Research Council). 1989. *Improving Risk Communication*. National Academy Press, Washington, DC, USA
- NRC (National Research Council). 1991. *Animals as Sentinels of Environmental Health Hazards*. National Academy Press, Washington, DC, USA
- NRC (National Research Council). 1996. *Understanding Risk. Informing Decisions in a Democratic Society*. National Academy Press, Washington, DC, USA
- OECD (Organization for Economic Cooperation and Development). 1995. Report of the OECD Workshop on Environmental Hazard/Risk Assessment. OECD Environment Monograph No. 105, OCDE/GD(95)134, Paris, France
- Power M and McCarty LS. 1998. A comparative analysis of environmental risk assessment/risk management frameworks. *Environ Sci Technol* 32:224A-31A
- Ross PS. 2000. Marine mammals as sentinels in ecological risk assessment. *Human Ecol Risk Assess* 6:29-46
- Ross P, Vos S, Birnbaum JG, *et al.* 2000. PCBs are a health risk for humans and wildlife. *Science* 289:1878-9
- Rothman KJ. 1988. *Causal Inference*. Epidemiology Resources Inc., Chestnut Hill, MA, USA
- Sheffield SR, Matter JM, Rattner BM, *et al.* 1998. Fish and wildlife species as sentinels of environmental endocrine disruptors. In: Kendall RJ (ed), *Principles and Processes for Evaluating Endocrine Disruption in Wildlife*, pp 369-430. SETAC Press, Pensacola, FL, USA
- Stahl RG Jr. 1997. Can mammalian and non-mammalian "sentinel species" data be used to evaluate the human health implications of environmental contaminants? *Human Ecol Risk Assess* 3:328-35
- Suter GW II. 1989. Ecological endpoints. In: Warren-Hicks W, Parkhurst BR, and Baker SS Jr (eds), *Ecological Assessments of Hazardous Waste Sites: a Field and Laboratory Refer-*

Framework for the Integration of Health and Ecological Risk

- ence Document. EPA/600/3-89/013. U.S. Environmental Protection Agency, Washington, DC, USA
- Suter GW II. 1990. Endpoints for regional ecological risk assessment. *Environ Manage* 14:19-23
- Suter GW II. 1993. *Ecological Risk Assessment*. Lewis Publishers, Boca Raton, FL, USA
- Suter GW II, Munns WR Jr., and Sekizawa J. 1993. Types of integration in risk assessment and risk management, and why they are needed. (this issue)
- Takahashi M, *et al.* 1998. Specific accumulation of butyltin compounds in marine and terrestrial mammals and their cytotoxic effect on mammalian lymphocytes. First Meeting of the Japan Society for Endocrine Disrupters Research, Kyoto, Japan
- USEPA (U.S. Environmental Protection Agency). 1992. *Framework for Ecological Risk Assessment*. EPA/630/R-92/001. Washington, DC, USA
- USEPA (U.S. Environmental Protection Agency). 1998. *Guidelines for Ecological Risk Assessment*. EPA/630/R-95/002F. Washington, DC, USA
- Van der Schalie WH, Gardner HS, Bantle JA, *et al.* 1999. Animals as sentinels of human health hazards of environmental chemicals. *Environ Health Perspect* 107(4):309-15
- Van Leeuwen CJ and Hermens JLM. 1995. *Risk Assessment of Chemicals: An Introduction*. Kluwer Academic Pub., Dordrecht, The Netherlands
- Vermeire TG, Jager DT, Bussian B. *et al.* 1997. European Union System for Evaluation of Substances (USES): Principles and structure. *Chemosphere* 34:1823-36
- Warren-Hicks WJ and Moore DRJ. 1998. *Uncertainty Analysis in Ecological Risk Assessment*. SETAC Press, Pensacola, FL, USA
- WHO(World Health Organization). 2001. *Report on Integrated Risk Assessment*. WHO/IPCS/IRA/10/12. Geneva, Switzerland (also available at http://www.who.int/pcs/emerg_site/integr/ra/ira_report.htm)
- Wilson EO. 1998. Integrated science and the coming century of the environment. *Science* 279:2048-9