ABSTRACT

KATHERINE M. SHEA M.D. Combined Ecological-Human Health Risk Assessment: At Case for Change. (Under the Direction of Dr. Mark Sobsey)

Current applications of quantitative human health risk assessment do not adequately consider end points important to long-term public health. Public health criteria absent from standard assessments include measurements of fertility rates, growth and development, and functional status during child-bearing years. Also absent is consideration of indirect adverse health effects from degradation of air, water, soil and food, habitat loss and climate change.

A potential remedy for this is to incorporate human health risk assessment into an ecological scheme like the EPA Framework for Ecological Risk Assessment (EPA/630/R-92/001 February 1992). Humans should be described as integral members of ecosystems with emphasis placed upon both short-term individual health and transgenerational population health. Ways in which the application of ecological concepts to risk assessment defines an enhanced public health orientation to environmental hazard are discussed. Barriers to a combined approach are identified. Interdisciplinary research must be supported to develop a combined ecological-human health risk assessment framework.

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This paper is dedicated to my children, Meg and Joe, and to their children and to their children's children. I embarked upon this challenging course because I felt called to try to provide a voice for the future of all children. I hope in some way that the ideas in this paper will help improve those futures for many generations to come.

Contents

INTRODUCTION

Quantitative human health risk assessment (QHHRA) has become the golden standard for setting environmental health regulations in the United States. Since the National Research Council's (NRC) 1983 publication of the formal four part paradigm[1], a large, multidisciplinary literature on the philosophy, methodology and policy use of this regulatory tool has evolved. Human health risk assessment is accepted by regulatory agencies as a legitimate and often indispensable vehicle for bringing scientific data to environmental policy making. The judiciary has further elevated this form of scientific analysis by stressing its importance in decisions on environmental litigation.[2] A journal is now devoted to risk assessment[3] and an international society has been established for the numerous practitioners in the field.[4] Academic institutions teach courses on human health risk assessment techniques,[5] and the field of comparative risk assessment is evolving from the parent discipline of risk assessment. It is a technique that is entrenched in the fields of environmental science and policy.

Through the application of QHHRA techniques, federal regulatory agencies have formulated rules which have stimulated improvements in the physical environment. These techniques have been applied to carcinogens, criteria air pollutants, and heavy metals with positive effects upon public health. Unleaded gas must be used in new cars, and the phase out of all unleaded gasoline has been accelerated because of the application of modern QHHRA techniques to non-cancer health outcomes.[6] Design alterations reducing exposure to refueling fumes are required on new automobiles as a result of application of QHHRA techniques to the health effects of ozone exposure.[7] Permissible occupational exposure to benzene has been successfully reduced to the 1978 recommended level of 1 ppm through use of modern QHHRA techniques.[8] QHHRA is an important and invaluable tool utilized to achieve the rational control of human exposure to environmental toxicants.

As QHHRA has been increasingly utilized, the limitations of the approach have become evident.[9] Problems exist with the single chemical-single disease application of QHHRA as well as with the use of standardized exposure scenarios and the overemphasis on chemical carcinogenesis as an assessment endpoint. Specific considerations which are often under-represented in the application of QHHRA are non-fatal endpoints, intrauterine and postnatal growth and development, and level of function in the child-bearing years of life. Theoretical approaches to obviate many of these problems have been developed,[10] yet, as human health risk assessment has evolved in practice, it has developed a rigidity which makes application of much of the current theory difficult. Consequently, the utility of the risk estimates derived from QHHRA has been questioned.[11]

Even if the most sophisticated scientific techniques within the QHHRA paradigm were to be applied, however, the current approach does not adequately consider protection of long-term population health. While the use of the individual as the unit of analysis, single human disease states as the endpoints of the assessment, and standard single lifetime exposure scenarios are potentially quite effective at protecting individuals from harm, analysis of these variables may not produce risk characterizations that are useful for evaluating environmental health effects on human populations across multiple generations. Also not addressed in standard risk assessments is consideration of recently recognized indirect threats to human health resulting from degradation of air, water, soil and food supply, habitat loss and climate change.

A potential remedy for these limitations is to incorporate human health risk assessment into a broader ecological scheme like the EPA Framework for Ecological Risk Assessment (Framework).[12] As with other forms of biota, humans should be described as integral members of ecosystems dependent upon environmental integrity, community interactions and energy flow dynamics with emphasis placed upon both short-term individual health and transgenerational population health. An ecological approach to health risk assessment would augment individual based QHHRA by the additional use of population parameters and community level interactions, the appropriate units of analysis for public health issues. An ecological approach would facilitate consideration of indirect adverse human health effects from environmental disruption. The addition of basic ecological concepts to the analysis of environmental risk to human health would insure a broad public health orientation to environmental risk assessment.

This paper explores ways in which the application of ecological concepts to human health risk assessment defines a more effective public health approach to environmental risk. Section I gives a brief review of the evolution and current approach to QHHRA as well as a description of the proposed United States Environmental Protection Agency (EPA) scheme for ecological risk assessment. Section II discusses how application of the ecological concepts to human health risk can be the next logical step in formal assessment of risk to human health from environmental hazard. Barriers to a combined ecological-human health approach are identified in Section III. Section IV offers some strategies for overcoming the barriers to a combined approach. Conclusions are offered in the final section.

SECTION I: BACKGROUND

Understanding the Language of Risk Assessment

In areas of controversy and change, it is critical to understand how words are used. Risk Assessment research and practice is such an area. Several of the terms used in this paper have different meanings to practitioners of different disciplines. Because they are central to the arguments presented in this paper, they are defined below. The word risk is used in this paper to represent the multidimensional concept including the quantifiable probability of the occurrence of an adverse event and the perceptions of the threat of that adverse event. Risk Assessment is used to describe the systematic collection and interpretation by experts of scientific information relating environmental hazard to adverse outcome. Quantitative Human Health Risk Assessment is that practice of generating a probability statement about the frequency at which a particular environmental toxicant can be expected to cause a particular disease state in humans. Ecological Risk Assessment is the process of evaluating the scientific information relating environmental stresses to adverse ecological outcomes, and is not strictly limited to a probability statement, single hazard or single outcome. Health is used to describe the "state of complete physical, mental and social well-being,...not merely the absence of disease or infirmity"[13], and is a definition which depends upon context.[14] The context of human health includes physical, social, political, temporal-spatial, historical, functional, spiritual, moral and aesthetic components. Population Health describes those conditions of mortality, growth and development, adaptability and reproductive capacity which result in the maintenance of a stable population.[15] Public Health is used to refer to the complex interactions between segments of a society which promote and protect the health and well being of the human population. Within this definition is nested the concept that determinants of health include political and societal structure as well as the more traditional elements of individual life-style, genetics and physical environmental elements.[16]

Origins of human health and ecological risk assessment

QHHRA: QHHRA has its roots in nineteenth century industrial toxicology and public health,[17] but has gained its form during the past thirty years of rapid expansion of environmental laws and regulatory agencies.[18] Several historical trends in key governmental agencies have converged to support the development of QHHRA. First, the FDA practice institutionalized in the 1950s of establishing acceptable human exposure levels by determining "no observed adverse effect levels" (NOAELs) in laboratory animal studies and dividing these levels by an arbitrary safety factor, established a precedent of providing a specific concentration of a specific chemical as the measure for safety. The safety factor approach is predicated upon the assumption that toxicants exhibit true threshold dose-response relationships such that a specific exposure dose exists below which no adverse health effects can be measured. This approach antedates the formalization of QHHRA and is still widely used throughout the world.

A second historical thread originates in the study and theory of human disease caused by ionizing radiation. The Atomic Energy Commission followed by the Nuclear Regulatory Commission developed "probabilistic risk analysis" as a way of addressing societal concerns about nuclear power plant failures.[19] The judgment by influential radiation biologists in the mid 1970s that ionizing radiation can induce genetic damage at any exposure level shaped subsequent development of carcinogen risk assessment.[20] The related theory that chemicals can induce carcinogenesis at all exposure levels led to the Delaney clauses in federal food and drug legislation which prohibit addition of animal or human carcinogenic chemicals to foods. Ensuing debates over *de minimis* (negligible) risk as a specific probability of increased cancer rate from a given exposure led to the acceptance of small, non zero cancer risks as standard. Thus, for both ionizing radiation and chemicals thought to be carcinogens, safety factor approaches to regulation of exposure were replaced by safety criteria framed as point estimates of tolerable increases in probability of cancers derived via risk assessment. The resulting broad application of carcinogen risk assessment techniques to both nuclear industry safety and food safety in the 1970s further strengthened the importance of QHHRA in federal environmental regulation.

Thirdly, the federal courts in adjudicating several cases involving the Occupational Safety and Health Administration (OSHA) regulation of toxins in the workplace elevated the use of scientific risk assessment to a requirement for any regulation to survive legal challenge.[21] The landmark cases in the 1970s and 1980s had equally profound impact on the practices of the Consumer Product Safety Commission (CPSC) and the EPA. This caused the EPA to step up its use of formal QHHRA following the 1983 National Research Council (NRC) "Red Book" publication which called for uniform use of a four part risk assessment approach across federal agencies. Despite active debate over the validity of QHHRA, EPA refined and distributed in computer software form a standardized approach to cancer risk assessment in the mid 1980s which has been utilized both inside and outside of the federal government.

Finally, the formation and institutionalization of the National Toxicology Program (NTP) in the 1980s fueled the legislative emphasis on carcinogenesis as the important endpoint of chemical exposure and generated chemical specific data on hundreds of chemicals and their carcinogenic potential in laboratory rodents. The NTP has also bolstered the mechanistic, pharmacokinetic approach to evaluation of chemical hazards using data intensive, chemical specific models.

The result of these developments is that as risk assessment has become required for justification of regulatory standards, the scientific flexibility often called for by serious proponents of QHHRA has been forced to give way to a much more rigid approach.[22] Publications on QHHRA routinely highlight points along the cascade from hazard identification through risk characterization where expert judgment, scientific assumptions, data inadequacies and uncertainties can substantively influence the final risk prediction.[23] Many risk analysts who advocate scientific flexibility within the broad outlines of the NRC paradigm are frustrated by the political and practical constraints placed upon the application of this scientific and regulatory tool.[24]

Ecological Risk Assessment: Ecological risk assessment has somewhat different origins. The modern environmental movement began in the United States with the passage of the National Environmental Protection Act (NEPA) of 1969. Among other major provisions in this law was the first Congressional requirement for completion of an environmental impact assessment prior to receipt of federal funding for significant projects. The decade following NEPA saw the passage of environmental laws concerned with air and water pollution, toxic and hazardous waste, occupational safety, consumer protection and endangered species. Out of this collection of laws and regulatory mandates came numerous approaches to assessing the impact of human activity upon the environment. No standardized method has developed for performing environmental impact assessments, and evaluation of the various techniques in use has been spotty. Nonetheless, the assessment process is considered useful by many, and provides background for more formal ecological risk assessment.[25]

The phrase ecological risk assessment begins to appear in the literature in the 1980s. Most of the development of risk assessment techniques, however, has occurred in the area of human health assessments. It was not until the 1987 EPA report entitled "Unfinished Business" which ranked active environmental problems hierarchically according to health, ecological and welfare aspects of risk that the push to develop a generally applicable methodology for ecological risk assessment intensified.[26] This resulted in the initiation of formal work inside of EPA in 1988 toward a general ecological risk assessment approach. In 1990, the Science Advisory Board published a report which endorsed the use of comparative risk ranking to set priorities for national environmental protection and stated that "EPA should attach as much importance to reducing ecological risk as it does to reducing human health risk."[27] This highlighted the need for more formal ecological risk assessment approaches. In 1992, the Framework for Ecological Risk Assessment was published as the first iteration of such an approach.

The simultaneous development of the field of ecotoxicology has also supported the trend toward formalization of approaches to ecological risk assessment. Ecotoxicology research provides data that can be substituted for the equivalent laboratory toxicological data into a paradigm similar to that of QHHRA using ecological endpoints of interest instead of human health endpoints.[28] The National Research Council has also been concerned in the past decade with improving the consistent use of ecological knowledge in environmental decision making and has published several volumes exploring related topics.[29] As risk assessment in general has gained regulatory prominence, the push to develop generally applicable ecological risk assessment techniques has increased. Several prominent ecologists have published books within the last few years discussing the complexities of ecological risk assessment.[30] The EPA Framework is the first major attempt to generate a unified paradigm comparable to the 1983 NRC paradigm for human health risk assessment.

The NRC Human Health Risk Assessment Paradigm

The landmark publication of the 1983 'Redbook' represented the formalization of the four part risk assessment paradigm commonly utilized in setting regulations today. (Figure 1) The NRC paradigm is presented here as it is currently used by the EPA to facilitate comparisons between the human health and ecological risk assessment approaches.[31]

The first component of QHHRA is hazard identification. It is a qualitative step which seeks to identify and review health effects data associated with exposure and determine whether a particular substance or chemical is causally linked to particular health effects. EPA has developed a "weight of evidence classification scheme" which gives guidelines to risk assessors for interpretation of data reviewed. The standard scheme assigns highest confidence to direct human exposure studies and laboratory animal studies followed in descending order by *in vitro* studies and structure activity relationships. The scope of hazard identification is limited to direct adverse health effects on individual humans. It can be performed by a single person, or small group with scientific training, but not necessarily training specific to the questions under consideration.[32] In general, if a toxicant is judged to be a carcinogen, the risk assessment is performed with carcinogenesis as the adverse health outcome regardless of the relative importance of other adverse health effects from that same toxicant. If it is not judged to be a carcinogen it is then evaluated for other adverse health effects such as reproductive toxicity, neurotoxicity or immunotoxicity according to severity of effect, portal of entry versus systemic effect and sensitive sub populations.

Hazard identification is followed by dose-response assessment. This stage seeks to determine the relationship between "the magnitude of administered, applied or absorbed dose and...the occurrence of health effect(s)."[33] This is the stage where sophisticated toxicology studies, extrapolation schemes and pharmacokinetic modeling are utilized to attempt to determine the maximal safe exposure of an individual to a specific chemical. EPA has adopted a no threshold model for calculating dose-response relationships for carcinogens and a threshold model for non-carcinogens. Default assumptions designed to build in conservative estimates have also been incorporated into EPA practice guidelines.

The third stage in the NRC paradigm is exposure assessment. Ideally this stage determines the magnitude, frequency, duration and route of exposure via integration of environmental models of source, transport and fate of toxicants

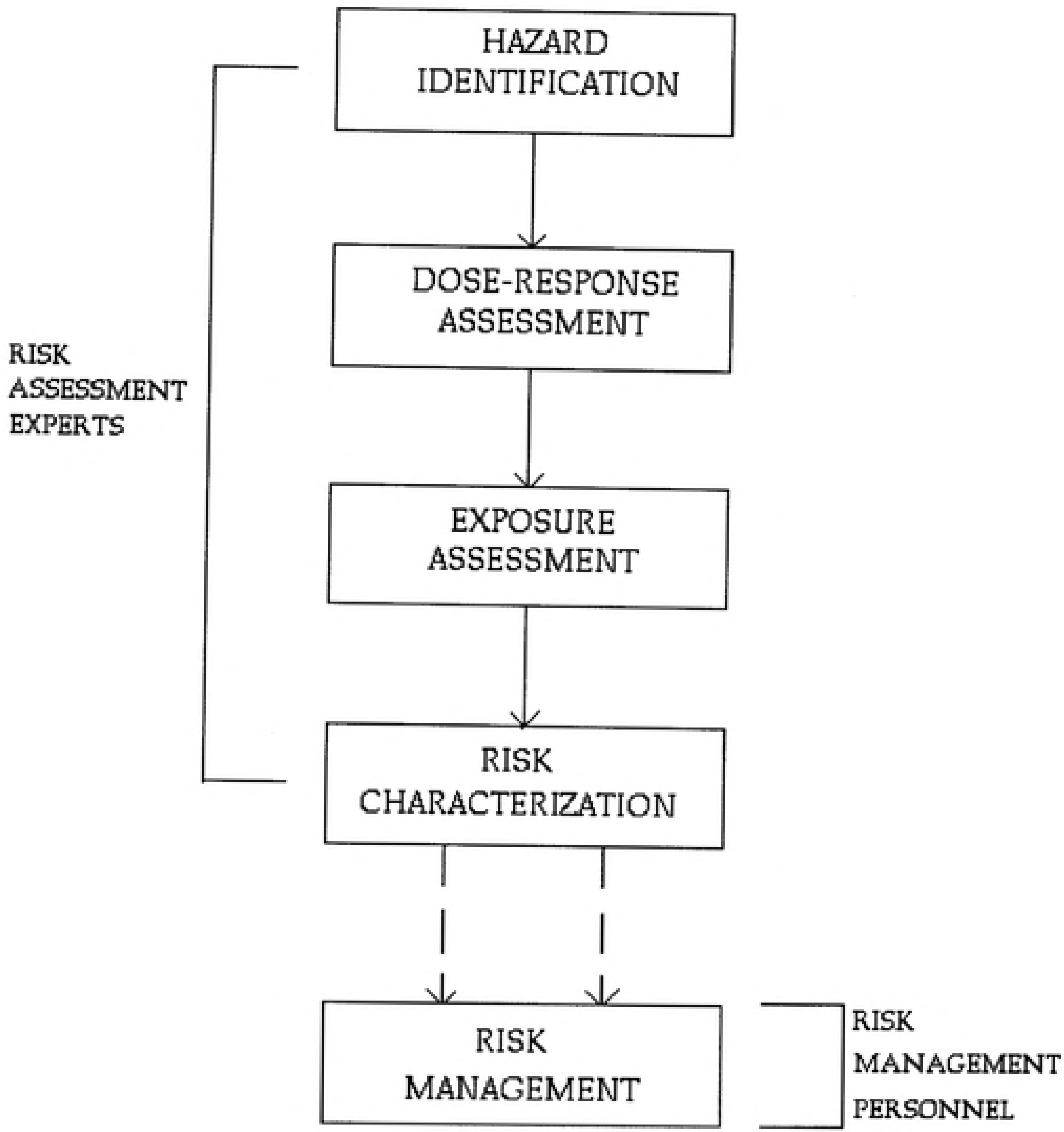


Figure 1: National Research Council Risk Assessment Paradigm

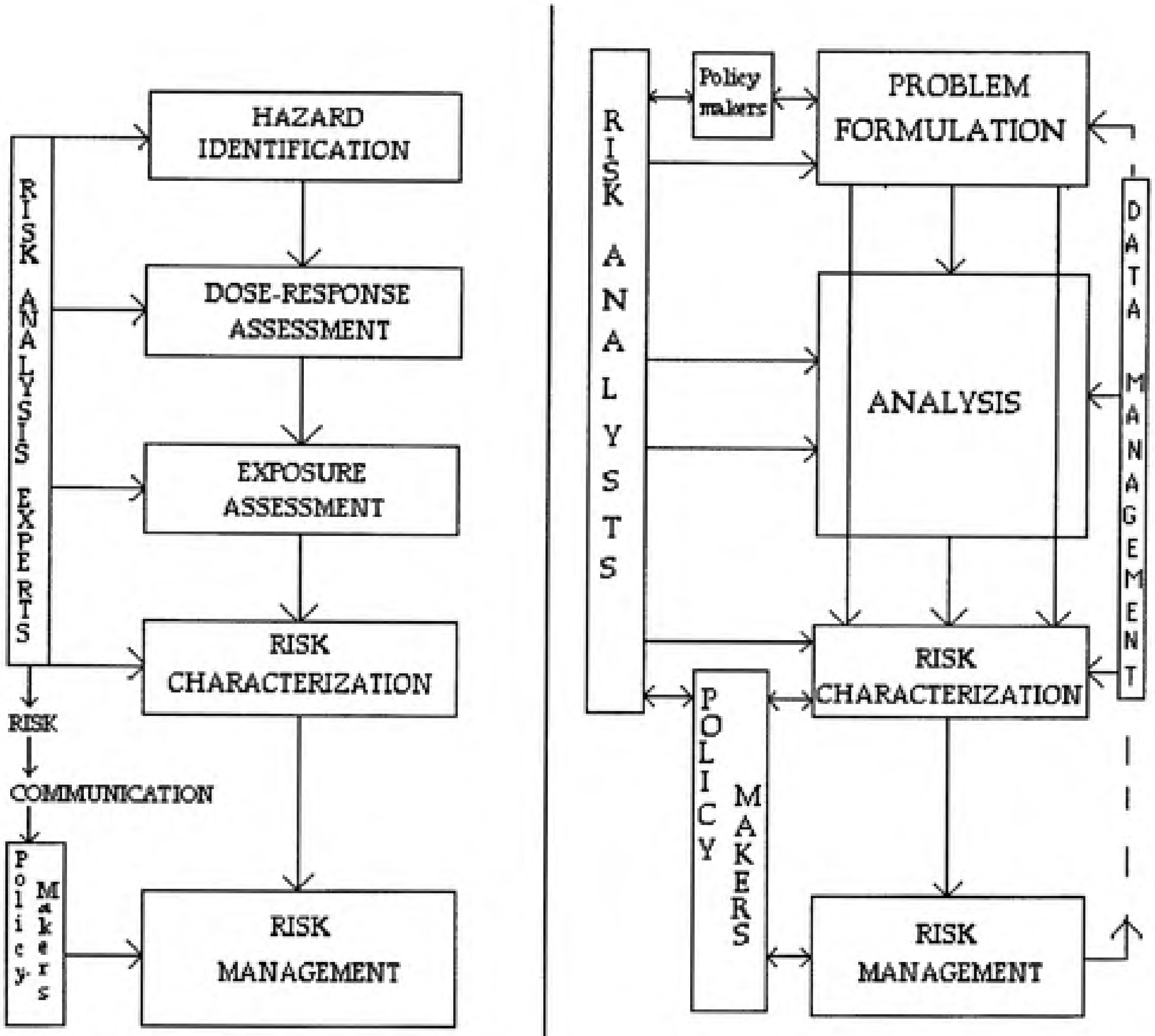
and population exposure characteristics. Again individual humans represent the unit of analysis and single human lifetimes determine the bounds of the exposures in most EPA risk assessments. The exposure is treated as a unidirectional phenomenon from source to individual human, though the models can be extremely complex including multiple routes of entry of the external dose and specific pharmacokinetic models of internal dose delivered to target organs.

The final stage of the four part paradigm is risk characterization which represents the integration of the preceding three stages. The output of this stage is the estimate of the type and magnitude of adverse health effects from an environmental toxicant as well as a statement of the probability of the occurrence of those effects at particular levels of exposure. Risk characterization is the least well developed component of the NRC paradigm. EPA defines individual lifetime risk as the product of dose and potency of the toxicant. Population risk is treated as the simple product of individual risk and number of exposed individuals. An explicit presentation of the sources and magnitude of uncertainty is recommended as part of the risk characterization, but in practice may be somewhat limited.

The 1983 NRC recommendation that the "regulatory agencies take steps to establish and maintain a clear conceptual distinction between assessment of risks and consideration of risk management alternatives"[34] is followed by EPA, though not without dissent.[35] Risk management is maintained as separately as possible from risk assessment in order to avoid theoretical distortion of risk estimates by political considerations.

<u>The USEPA Framework for Ecological Risk Assessment</u>

The Framework for Ecological Risk Assessment was published in February 1992 by the Risk Assessment Forum of the US EPA.[36] It is the product of efforts begun in 1988 to develop a framework for ecological risk assessment comparable to the 1983 NRC paradigm for human health risk assessment. In the introduction, the chair of the Forum is careful to emphasize that the published framework represents the starting point for an iterative process of developing ecological risk assessments. Also stated is the desired goal of ultimately developing a unified framework for ecological and human health risk assessment.



NRC HUMAN HEALTH RISK ASSESSMENT PARADIGM

US EPA ECOLOGICAL RISK ASSESSMENT FRAMEWORK

Figure 2: A Comparison of Human Health and Ecological Risk Assessment

The Framework is organized in three stages: problem formulation; analysis; and risk characterization. Figure 2 juxtaposes the four part NRC paradigm and the Framework. Several basic differences exist. First, while the NRC paradigm ideally separates risk assessment from risk management, the Framework explicitly integrates them. Second, the NRC paradigm implies a linear progression without feedback from hazard identification to risk characterization while the Framework incorporates interaction and internal modification. Third, the NRC paradigm does not explicitly consider data acquisition, verification and monitoring while the Framework integrates data management into all aspects of assessment. These broad differences represent lessons learned from QHHRA and its critics. The explicit inclusion of interaction between managers and assessors, data management, and iterative improvements in assessment techniques emphasizes the need to recognize that risk assessment is a policy tool for bringing science to regulations and must be flexible enough to respond to changes in scientific knowledge at the same time it is comprehensible to non scientist policy makers.

Figure 3 details the components of problem formulation in ecological risk assessment, the analog to hazard identification in the NRC paradigm. Of special note is that endpoint selection is determined by a process of analysis of the stressor characteristics, the ecosystem potentially at risk and the ecological effects of the stressor. The stressor characteristics which help determine the problem include the type of stressor (chemical or physical), the intensity of the stressor (concentration or magnitude), the duration the stressor remains in the environment (short or long), the frequency of release of the stressor (single event, episodic or continuous), the timing of exposure to the stressor (relative to biological cycles) and the scale of the stressor (spatial distribution). Endpoints are chosen based upon their ecological relevance, their susceptibility to the stressor and the policy and societal goals and values surrounding the stressor and the ecosystem under evaluation. This stands in contrast to the hazard identification stage in the NRC paradigm which seeks to determine "whether a particular substance or chemical is or is not causally linked to a particular [human] health effect."[37] The selection of the assessment endpoints in the Framework is thus a cooperative decision between scientists and policy makers based upon the actual environmental stressors for a specific time, place and ecosystem. The problem formulation stage culminates in a conceptual model which guides the analysis.

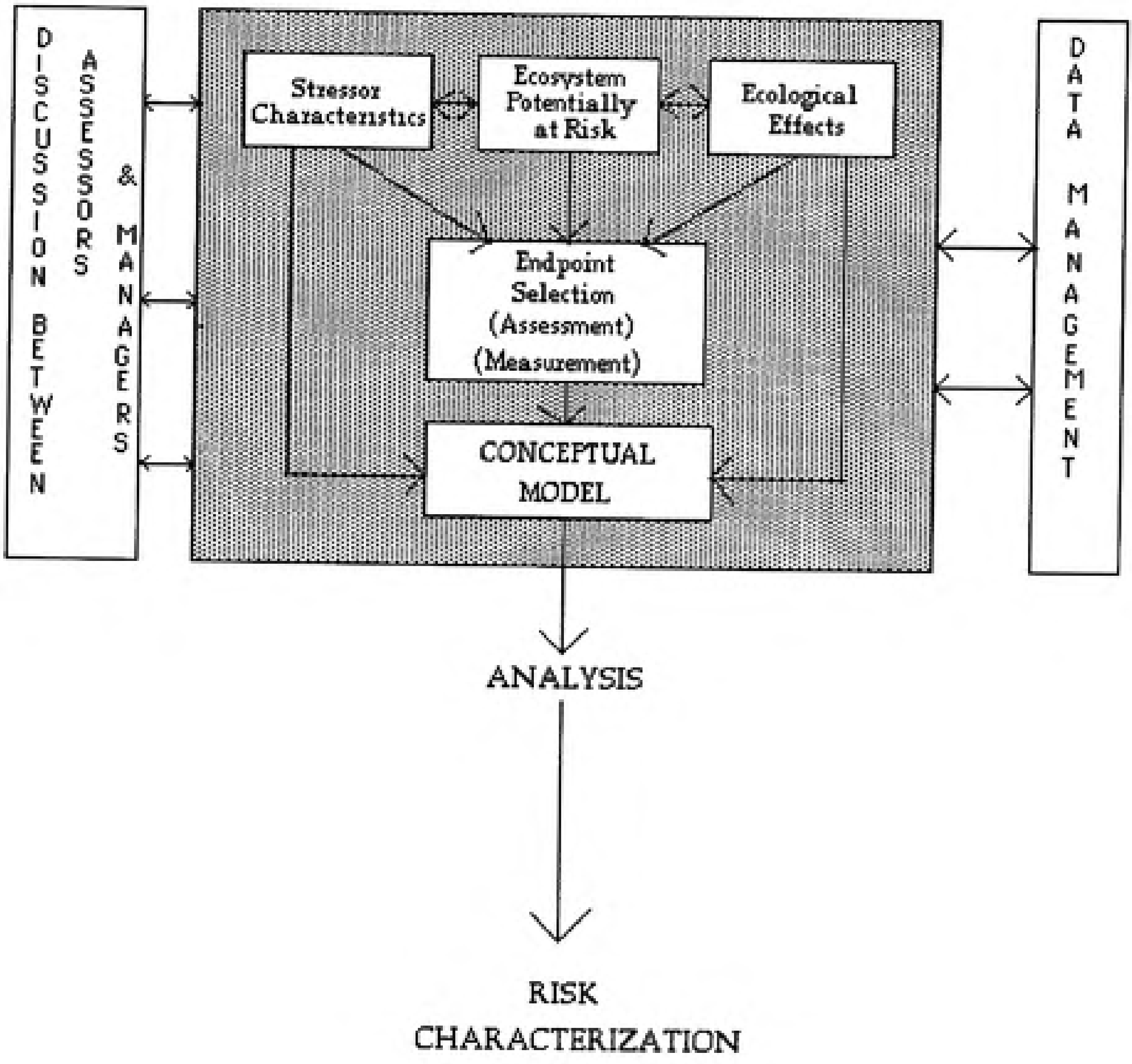


Figure 3: Problem Formulation

The NRC paradigm analog to the analysis phase of the Framework is exposure assessment combined with exposure response (Figure 4). The Framework attempts to define the internal interaction between exposure and response. By allowing multiple endpoints and broad scope it seeks to integrate ways in which the characteristics of the stressors and the systems they stress may modify both exposure profile and response characterization. This interactive approach acknowledges the reality that exposures often alter behavior which in turn alters exposure. Organisms adapt to stresses (e.g. decreasing intake, biochemical alternation) as well as amplify (e.g.. bioaccumulation, bioactivation) or change them (e.g.. migration). No parallel for this attempt to deal with interactions exists in the more linear human health NRC paradigm.

Figure 5 shows the components of risk characterization proposed for the Framework. Explicit discussion of uncertainty and the interpretation of ecological significance are integral to the Framework. The participation of policy makers in the risk characterization phase is embraced in this approach rather than minimized as it is in QHHRA. Full and formal disclosure of uncertainty and expert judgment are required rather than recommended. Further, the Framework permits non-quantitative techniques and results in both numerical and narrative characterization of the risk, recovery potential and significance of the risk within the body of the risk assessment. QHHRA, by definition, results in a numeric estimate of risk.

The EPA Framework is currently being applied for the first time to ecological problems. Determination of the feasibility of using such an approach awaits the outcome of current experiments in application. Nonetheless, the refinements in the Framework compared to the NRC paradigm are as promising for human health risk assessment as they are for ecological risk assessment. The next section will attempt to show how the ecological approach to risk assessment delineated in the Framework represents the next logical evolutionary step from strict QHHRA designed to protect individuals to a broader approach also capable of protecting populations and future generations.

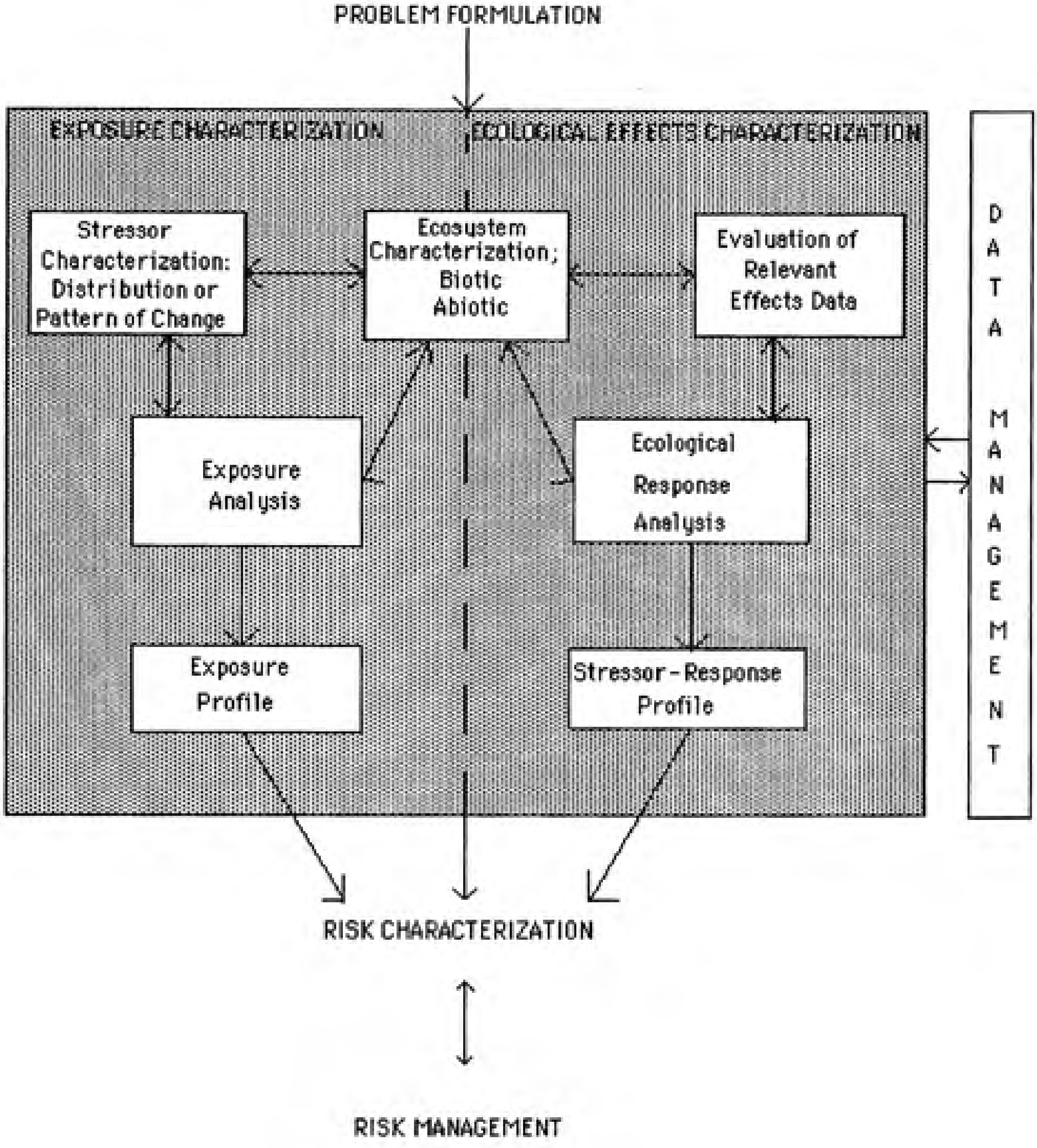


Figure 4: Analysis

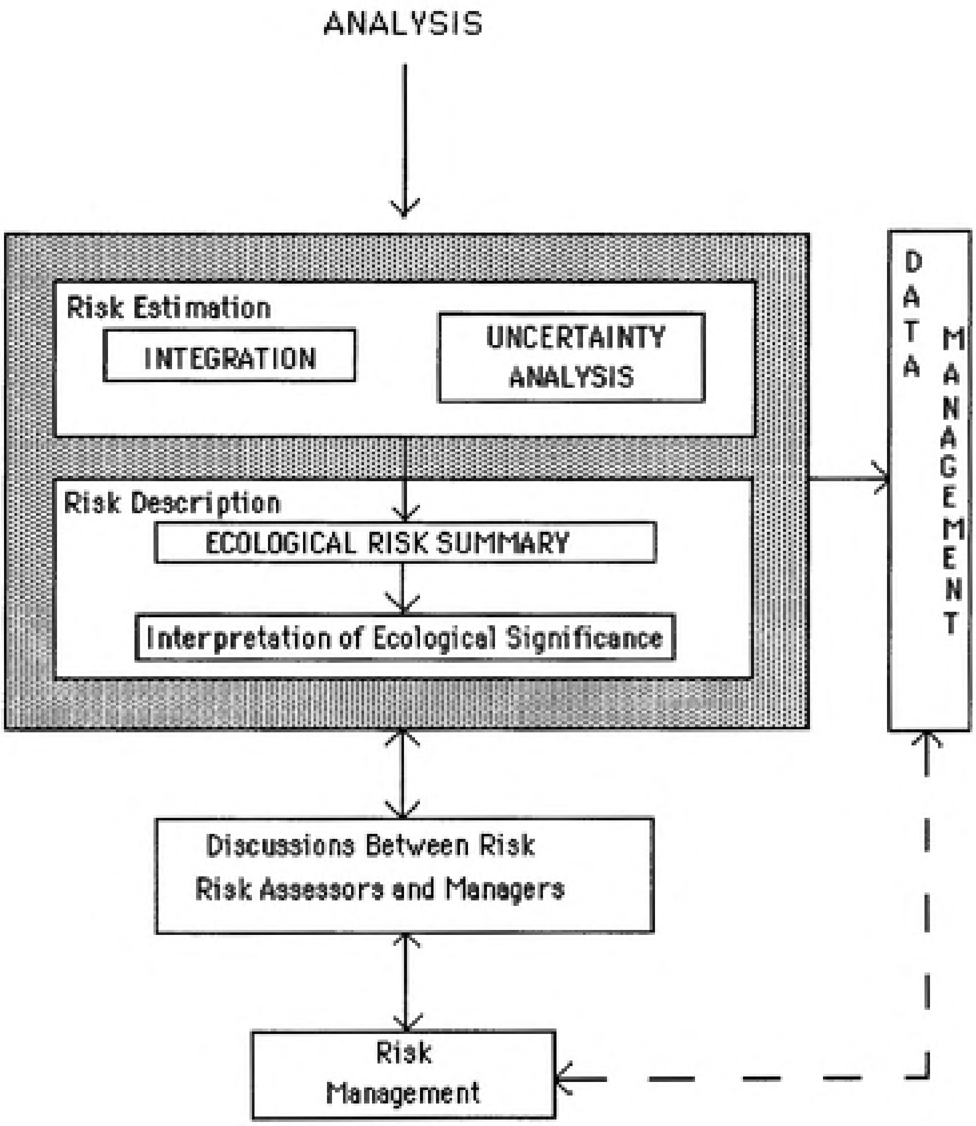


Figure 5: Risk Characterization

SECTION II: EXPANDING THE VISION OF HUMAN HEALTH RISK ASSESSMENT

Despite the wide acceptance and proven value of risk assessment, many prominent environmental scientists, ethicists, lawyers, lay advocates and regulators question the degree to which formally applied quantitative human health risk assessment can be expected to render practical guidance for those officials whose mission is ultimately the protection of public health. Despite sophisticated advances in quantitative techniques for modeling exposure, extrapolating laboratory data and describing uncertainty,[38] the restrictions placed upon regulatory agencies by legislation and case law have significantly impaired their ability to utilize these improved techniques. This leaves the practice of risk assessment vulnerable to criticism. Even if the restrictions on the practice of QHHRA were to be eliminated, however, the fundamental choice to use the individual human as the unit of analysis and specific disease states as the outcome measures limits the extent to which QHHRA can assist policy makers in making decisions which will protect long-term public health. The application of ecological risk assessment concepts to human health would introduce a broader population approach by extending concepts of risks from the individual to a transgenerational time frame incorporating direct and indirect threats to human health. In effect this expands the vision of health from that of an individual free from disease to populations with the potential of producing generations of healthy individuals. It is the next logical step in the attempt to modify environmental risk to human health.

Ecological study of populations, communities and ecosystems involves examination of the interactions and outcomes important to community viability and resilience.[39] The types of knowledge sought in ecological study include descriptions and understanding of complex linkages between species in ecosystems, the effects of nutrient and energy flow between the biotic and abiotic environment on population density, and the determination of the scales of time and space appropriate to the study of a given problem. While the ecological approach to population and community must always consider the viability of individuals (the object of QHHRA), it also requires consideration of interactions between individuals, groups of individuals within a species, and groups of different species. A glance at the table of contents of a textbook in ecology reveals topics like Resource Acquisition and Allocation, Population Growth and Regulation, Interactions Between Populations, The Interface between Climate and Vegetation, and Biotic Diversity and Community Stability.[40] These are the very considerations needed in order to extend the individual level approach of QHHRA to a population level public health approach to environmental risk assessment.

Expanding the Vision - Time

The assumption of QHHRA is that an acceptable individual lifetime risk translates into an acceptable population risk across generations. For toxicants with environmental residence times shorter than a human lifetime or toxicants with only acute toxicities, this is often true. For environmental toxicants with prolonged residence times, chronic effects, or developmental or reproductive toxicities, it becomes important to consider long-term, transgenerational health effects as well. Figure 6 schematically depicts that this is the point at which the concepts of individual QHHRA and ecological risk assessment tend to diverge. It also is meant to demonstrate that QHHRA should always provide the kernel of any human health risk assessment. It is clearly important to protect currently living humans from immediate threats to health from environmental hazards. In theory, QHHRA does that well. It is no less important to protect future generations from the same hazards. The time frame of reference for environmental risk needs to be extended to include future generations. These long term threats to human health must be conceptualized in several ways.

Transgenerational toxic effects can result from fetal exposures, bioaccumulation and biomagnification of toxicants in the food chain, or persistence of an environmental toxicant or stress over several generations. The importance of fetal exposures can be illustrated by the devastating effects of maternal ingestion of fish contaminated with methyl-mercury from Minamata Bay, Japan upon the neurologic development of their children. The transgenerational health consequences are both immediate and direct for the children permanently effected with cerebral palsy, and long-term and indirect for the families and society that must care for of those children.[41] Prenatal exposure to the indoor air pollutant, environmental tobacco smoke (ETS) has also been

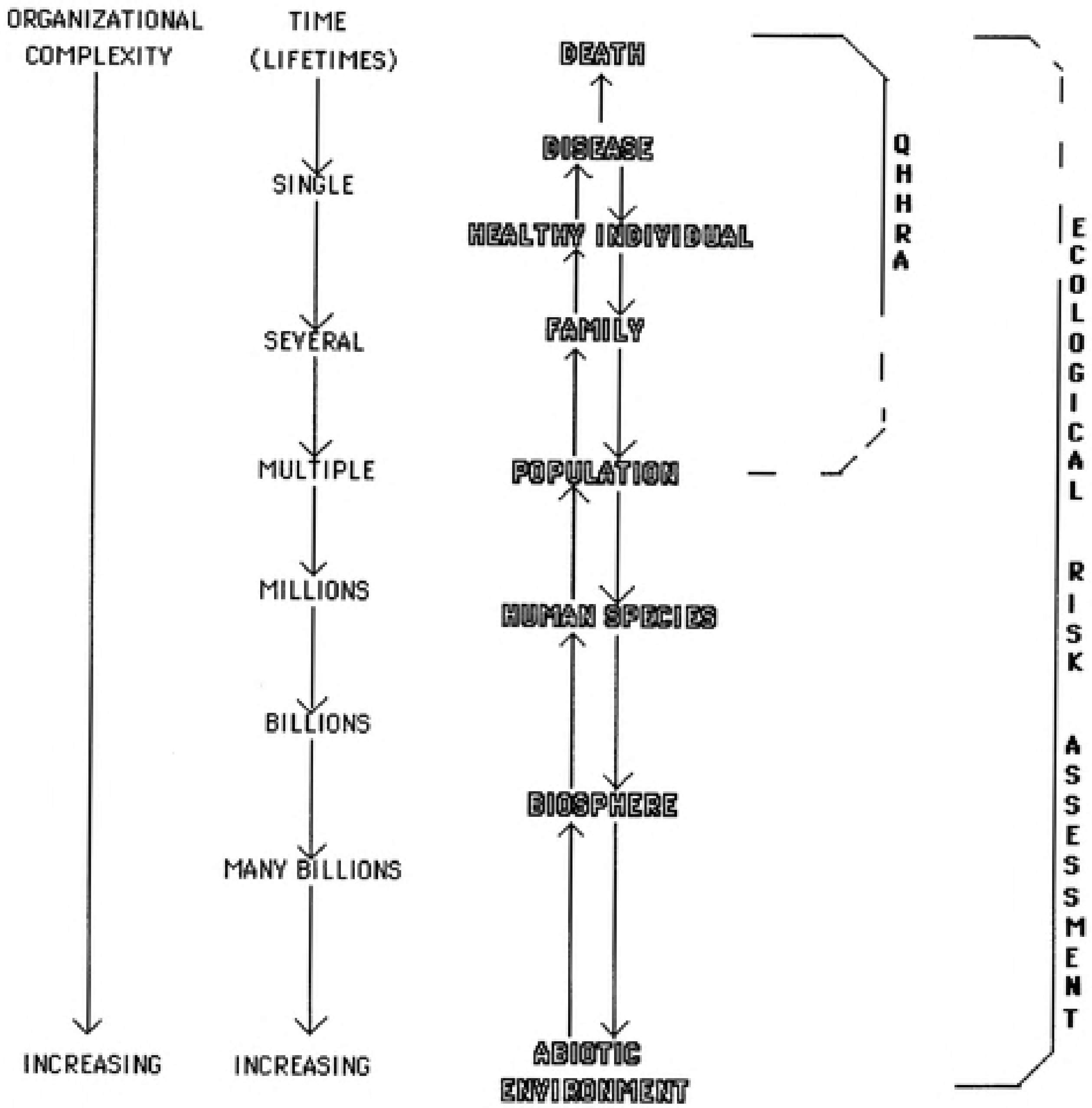


Figure 6: The Divergence of Ecological and Quantitative Human Health Risk Assessment
(QHHRA = quantitative human health risk assessment)

shown to retard intrauterine growth and impair postnatal lung function. Human studies show with increasing power that infants exposed *in utero* to ETS are more susceptible to respiratory infection and reactive airway disease throughout childhood compared to non exposed infants. This kind of illness is costly monetarily for parents, disrupts schooling for children and clearly has long-range implications for individuals effected directly and indirectly. ETS can be used as a model to speculate on other transgenerational effects of indoor and ambient air pollution. QHHRA is not designed to include these kinds of exposures in the analysis of health risks. An ecological approach to health risk assessment would be able to accommodate all of these effects via an expanded time frame and considerations of intraspecies interactions.

Transgenerational environmental risk can also occur postnatally. The realization that PCBs ingested by mothers eating contaminated fish are excreted in breast milk has lead to investigation of effects on nursing babies. Scientists have found a suite of neuro-developmental deficiencies statistically linked with early PCB exposure.[42] Although the results of these studies vary, it is clear that this is another important route which can have serious health consequences for humans and is not adequately addressed within the confines of standard QHHRA approaches.[43] Neurodevelopmental damage effects not just the children exposed, but potentially their offspring as well by altering parenting abilities to provide a healthy social and physical environment for the next generation. Again through the ecological consideration of intraspecies interaction and population dynamics, these health effects could be considered.

A more subtle type of transgenerational effect can be postulated by considering shifts in the population burden of ubiquitous pollutants. In contrast to the examples above representing transgenerational effects of exposures in index lifetimes upon subsequent generations, this type of transgenerational effect results from cumulative population exposures to ubiquitous toxicants. For example, it is now well recognized that lead levels as low as 10 mg/dl cause significant decrements in measurable I.Q. and motor development.[44] Despite the reduction of lead exposure achieved through the removal of lead from gasoline and paint (the kind of result to be expected from effective use of QHHRA), estimates suggest that low level lead intoxication continues to effect 17% of American children.[45] A significant shift to the left in the cumulative IQ distribution of exposed children with truncation at the high end of the distribution and attenuation at the low end may have profound societal

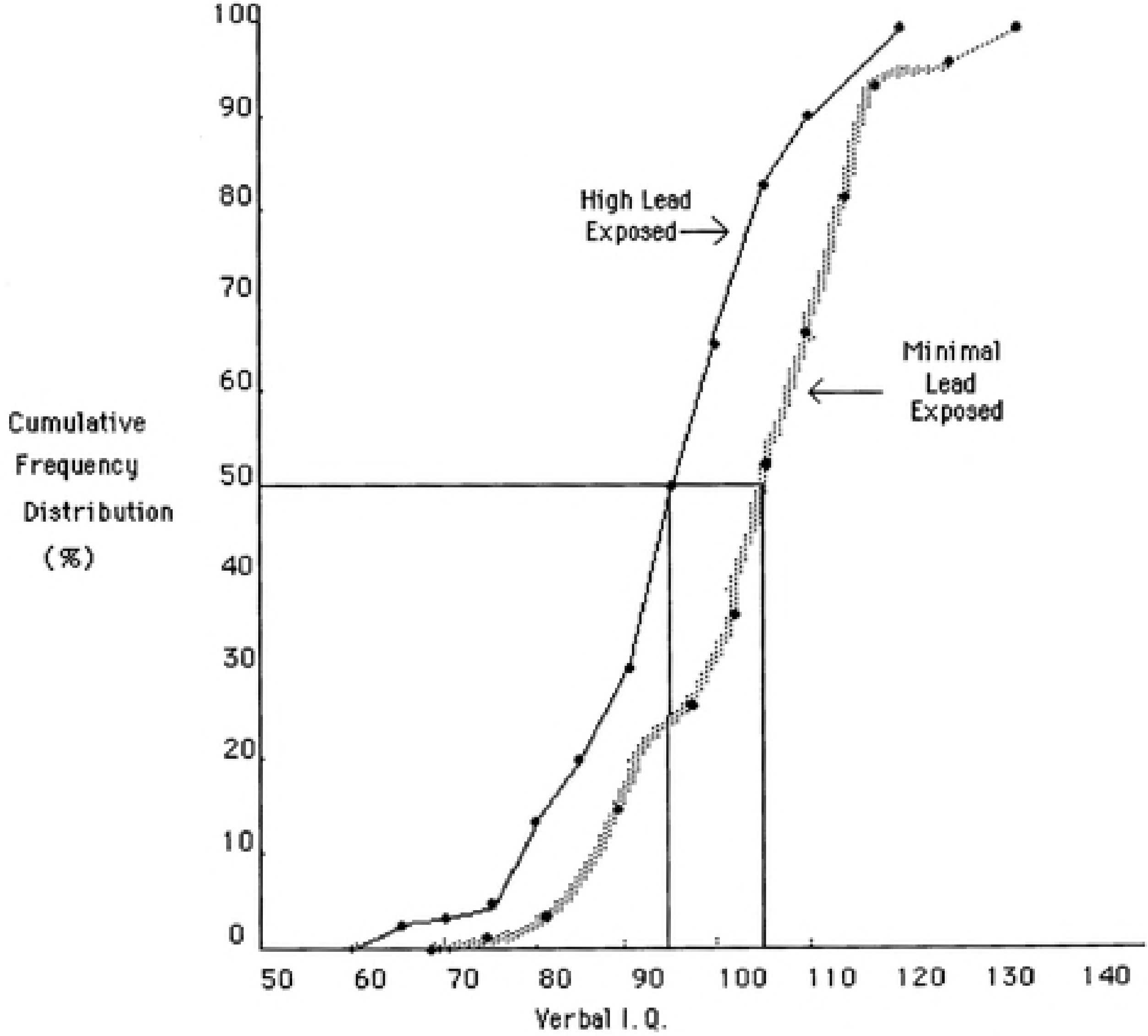


Figure 7: Negative Shift in Cumulative Distribution of Verbal I.Q. with increasing lead exposure. (Adapted from Needleman, H. L. and Landrigan, P. J. RAISING CHILDREN TOXIC FREE)

implications on population function. (Figure 7) Coupled with the behavioral correlates of lead intoxication, this population shift describes more than the likelihood of a finite increase in the incidence of the disease of lead poisoning. The shift represents a reduction of achievement potential for the entire exposed population. The ramifications for the health of future generations seems clear. Most of the determinants of health in modern society (e.g. sanitation, food quality, modern medicine, education) are directly linked to intellectual achievement.[46] By lowering intellectual potential across the population, lead pollution may also threaten human health across the population. Finally, lead is stored in bone, mobilized slowly and capable of passing through the placenta to the fetus. Babies are born with measurable lead in cord blood, setting the stage for transgenerational bioaccumulation and exaggerated effects in subsequent generations from continued exposure postnatally.[47] Ecological concepts which look at adverse effects over multiple generations added to human health risk assessment strategies would be able to elucidate these kind of effects. Standard QHHRA dose not offer this kind of scientific issue for policy consideration.

A second example of this kind of transgenerational effects may be postulated from the subtle immunotoxicity caused by polychlorinated biphenols (PCBs). These ubiquitous pollutants have been shown to be broadly distributed environmentally and measurable in increasing concentrations in rural and urban populations alike.[48] If environmental levels of exposure cause population-wide decrements in immune function, it may be that resistance to infectious agents, prevalence of immunologically mediated diseases and response to mutagens may also be altered across the population. Although these effects remain speculative,[49] the possibility must be considered. Standard QHHRA does not lend itself to consideration of population shifts in function but rather identifies levels of exposure above which overt illness occurs. The influential work of Geoffry Rose raises these same questions in more traditional human epidemiological study of hypertension and coronary heart disease. As with epidemiology, it seems that environmental health risk assessment should seek to identify and understand the population mean exposures to harmful substances as well as the prevalence of high end disease states.[50] The approach suggested by Rose applied to risk assessment, because it utilized the population as the unit of analysis, is more consistent with protection of public health and ecological risk assessment than with standard QHHRA.

Expanding the Vision - Health

The public health perspective requires utilization of population level outcome variables such as population rates of infant mortality, birth defects, prematurity, neurodevelopmental abnormalities, chronic disease in early life, infertility and sub fertility, and premature death.[51] That is, public health is concerned with population level parameters of health in real populations. QHHRA is generally limited to the analysis of individual level risk from isolated environmental exposures in single individuals. By combining QHHRA with an ecological approach to human health risk assessment, the ability to assess specific risks to individuals from specific exposures is preserved at the same time that a population level, public health component is added. Great overlap between to the two approaches exists. QHHRA can theoretically consider non-fatal endpoints, multiple exposures, and realistic exposure scenarios within the dictates of its structure. What is unique to the ecological approach is the attention to the interactions and outcomes at and beyond the population level, especially those having to do with whole population shifts of function and indirect effects on human health. It has the potential to be proactive in philosophy, seeking to promote health rather than merely to prevent disease. Application of the ecological theory to human health risk assessments would add these considerations and produce information important to public health decision making which is not possible with even the most sophisticated QHHRA techniques.

QHHRA was designed to protect against illness. Though contemporary work is seeking to expand on current practice, the endpoints used in risk assessments continue to be specific human disease states, most often cancer, but also forms of neurotoxicity, non cancer mutagenesis or excess mortality.[52] These are truly endpoints since once they occur they cannot be mitigated. Health, in contrast, is absence of illness in the presence of a certain high level of potential function. Alluded to above, prudence would dictate that consideration of impaired functional states be studied on a population basis as well as study of individual disease states at the individual level. Expanding the outcomes to which risk assessment is applied to include population indicators of reproductive potential, for example, might well lead to defining environmental harm more by population effect that by single agent-disease state units. Current debate on the issue of falling sperm counts postulated in industrial countries provides a case in point.[53] Though significant scientific difficulties surround determination of

Table 1. **Chemicals known to Disrupt Endocrine Function**

Herbicides
- 2,4-D
- 2,4,5-T
- Alachlor
- Atrazine
- Metribuzin
- Nitrofen
- Trifluralin

Fungicides
- Benomyl
- Hexachlorobenzene
- Mancozeb
- Maneb
- Metiram-complex
- Tributyltin
- Zineb
- Ziram

Insecticides
- Beta-HCH
- Carbarly
- Chlordane
- Dicofol
- Dieldrin
- DDT and metabolites
- Endosulfan
- Heptachlor and H-Epoxide
- Kepone
- Lindane
- Methomyl
- Methoxychlor
- Mirex
- Oxychlordane
- Parathion
- Synthetic pyrethroids
- Toxaphene
- Transnonachlor

Nematocides
- Aldicarb
- DBCP

Industrial chemicals
- Alkyl phenols
- Cadmium
- Diethylhexyl phthalate and its metabolites
- Dioxin (2,3,7,8-TCDD)
- Lead
- Mercury
- PBBs
- PCBs
- Pentachlorophenol
- Penta- to nonylphenols
- Phthalates
- Styrene dimers and trimers

From: Amdur, M. O., et. al.. Casarett and Doull's Toxicology 4th Edition, McGraw-Hill, Inc.: New York, 1991.
Colborn, T., et. al. Chemically-Induced Alternations in Sexual and Functional Development: The Wildlife/Human Connection. Princeton Scientific Publishing Co., Inc.: Princeton; 1992.
Colborn, T. et. al., "Developmental Effects of Endocrine-Disrupting Chemicals in Wildlife and Humans. Environmental Health Perspectives 101 (5): 1993.

re-evaluation of both how stresses are defined and what outcomes are most important. If the modulators of "Policy Goals and Societal Values"[66] are set to protect public health and future generations, the mechanism for achieving such protection is present within the design of ecological risk assessment which nests classic QHHRA within a broader conceptual framework.

Reducing, particulate air pollutants also offer the opportunity to look beyond direct human health effects. Acid particulates are known to have significant direct effects upon human health.[67] Particulates are also the antecedents of acid rain, a complicated interaction of emissions from burning of fossil fuels, air particulates and water. Acid rain is known to change the nutrient cycles in soil with the potential to disrupt both microbial and higher plant growth. By some calculations it has doubled the cycling of sulfur from the earth's crust and now anthropogenic activities dominate the sulfur cycle. It also accelerates rock weathering, acidifies lakes and even has the potential to effect ocean productivity.[68] Acid aerosols are also a powerful modulator of greenhouse gasses in the northern hemisphere. As with ozone, but perhaps more pervasive because of the mechanisms of formation and transport of this type of air pollution, the indirect effects to human health may be more dangerous in the long run to population health, than are the short term direct effects to individual health. An ecological perspective for health risk assessment which would simultaneously consider the relationship between human death rates and PM10 concentration , measures of lake pH and sport fish yield and evidence of changes in photoplankton blooms. This would provide an expanded view of threats to human health and a more public health oriented assessment of risks.

Another risk to human health which cannot be accommodated by current QHHRA techniques can be illustrated by examining the important ecological stressor, habitat loss. Believed to be the leading cause of extinctions and loss of biodiversity,[69] destruction of natural habitat by human expansion in the US and globally affects human health in several ways. First, by converting so called "undesirable" habitats like swamps to more desirable forms of land, like golf courses and housing developments, human expansion reduces the capacity of the biosphere to perform important natural regulatory functions such as water filtration and decomposition. Human substitutes, for example waste water treatment plants, are not as efficient and require addition of potentially dangerous chemicals to the environment to perform the function lost when the natural system is destroyed. Often this results in a less efficient and more toxic alternative to the missing system.[70] Secondly, habitat destruction results in changes in human disease patterns by changing the distribution of human pathogens. Well documented changes in malaria patterns in areas of rain forest destruction and schistosomiasis incidence in areas flooded by dams built on the Nile provide dramatic testimony to the health consequence of alterations in habitat.[71] It is not unreasonable to speculate that, for example, the rapid increase in Lyme disease in the past decade in the US might be due to changes in the habitat forcing deer along with their infesting ticks into closer contact with humans. Developed countries are no less likely to suffer these changes in disease pattern than less developed countries, but the changes are predictably more subtle and more easily missed without careful and pointed scrutiny. Thirdly, loss of biodiversity represents permanent loss of environmental capital. Despite modern technological advances in synthetic chemistry, much of our current biotechnology, agrotechnology, biologic pest control and biomedical therapeutics still find their origins in the naturally occurring genetic systems of organisms other than humans. Decreases in the richness of the DNA pool represent real long-term threats to human species adaptability and population health by depleting the raw materials from which research formulates new technologies for food, medicine and fibers.[72] The coral used as an implant which can accept attachment of eye muscles and blood vessels to permit a normally moving prosthetic eye in people who have undergone therapeutic or traumatic enucleation is harvested from currently endangered coral reefs.[73] Numerous cardiovascular, anti-neoplastic and anticoagulant drugs are derived from rain forest species threatened by aggressive deforestation.[74] The customary approach to human health risk assessment has no way to consider these important indirect threats to human health. An ecological approach to health risk assessment would do this by definition.

Expanding the Vision - a Concrete Suggestion

In the previous sections, I have attempted to illustrate how the addition of ecological considerations to the assessment of environmental threats to human health would expand the vision of risk assessment from the level of individual disease to the level of population health. Health risk assessment is one of the most important tools utilized by policy makers to insure that laws effecting environmental health protection are grounded in science. Scientists responsible for presenting the state of the art scientific understanding of risks to human health to policy makers should include as part of that presentation the transgenerational, population level and indirect ways in which pollution and environmental degradation can harm human health. The over emphasis on cancer endpoint in the last twenty years is beginning to give way to consideration of non-cancer disease states,[75] but the current failure to consider damage to future generations of humans, other species, ecosystems and the non-biologic environment may eventually make concentration on direct harm to human health seem foolish. Scientists could stimulate an expansion of the vision of human health risk assessment by applying the Framework for Ecological Risk Assessment by the EPA to the analysis of risks to human health.

The Framework is not yet tested but it has been drafted by ecologists who have incorporated lessons learned from over a decade of experience with formal QHHRA. Therefore, as the Framework is applied to environmental issues, it may avoid old problems as it elucidates new ones. It could be tested as effectively by application to ecosystems which include humans as by application to ecosystems from which humans are artificially excluded. Were this to be attempted, the iterative improvement of ecological risk assessment could benefit humans as well as non-human biota. Several potential benefits are sketched below.

First, the problem formulation phase of the Framework is a cooperative, interdisciplinary scoping process during which the whole spectrum of adverse effects caused by an environmental stress are considered. This would enable risk assessors to consider individual level disease states in humans and non-humans, as well as transgenerational adverse effects, interactions among humans and between humans and other species and potential human health consequences mediated indirectly through non-human endpoints. The scoping process permits everything that is considered in QHHRA plus the broader issues affecting long-term population and public health.

The dynamic nature of the analysis phase in the Framework lends itself well to consideration of intra and interspecies interactions which affect multiple generations as well as whole populations. This aspect of the Framework permits consideration of chronic, cyclic environmental ozone exposures like those documented for city dwellers who, rather than demonstrating acute health effects, show evidence of chronic adaptation in pulmonary function to moderate elevations in ambient ozone compared to unexposed rural dwellers.[76] It is also within this portion of the Framework analysis that indirect effects such as "interspecies interactions..., trophic-level relationships..., resource utilization... [and] ecological compensatory mechanisms" are considered.[77] Thus the Framework could accommodate consideration of the ramifications of population shifts in immune status, loss of biodiversity and environmental capital or depletion of primary production on human health whereas QHHRA alone could not.

Finally, the risk characterization phase is more flexible and accessible to policy makers in the Framework approach than the classic NRC paradigm. The Framework states that "discussions between risk assessor and risk manager are important. At the initiation of the risk assessment, the risk manager can help ensure that the risk assessment will ultimately provide information that is relevant to making decisions on the issues under consideration...Similar discussions of the results of the risk assessment are important to provide the risk manager with a full and complete understanding of the assessment's conclusions, assumptions and limitations."[78] The "risk can be expressed as a qualitative or quantitative estimate"[79] which makes the risk estimate less arcane and more accessible to policy makers. The direct and explicit identification of uncertainties incorporated into the "weight-of-evidence discussion provides the risk manager with insight about the confidence of the conclusions reached in the risk assessment"[80] and further increases the utility of the risk characterization for the policy maker.

It seems reasonable, then, to test the feasibility of the approach outlined in the Framework on systems which include humans as well as systems which do not. At the very least such a combined approach would delineate gaps in data and weaknesses in theory of how humans and human health interface with the rest of the biotic and abiotic world. Ultimately a unified approach is the only way to assure long-term human species health and survival. The testing of the Framework on systems which include humans is one concrete step toward such an approach.

SECTION III: BARRIERS TO COMBINED ECOLOGICAL-HUMAN HEALTH RISK ASSESSMENT

Barriers to a combined approach to ecological and human health risk assessment are many and varied. They derive from traditions of current practice, institutional structure, philosophical orientation, methodological gaps and the ambient political climate. Aspects of each type of barrier are discussed in the following paragraphs.

Barriers Deriving from Traditions of Current Practice

The overwhelming concentration in environmental regulation upon direct threats to human health is the first barrier to a combined approach deriving from current practice. The EPA was created by executive order in 1970 to perform environmental research, environmental monitoring and ensure "the enforcement of all federally mandated statutes concerning environmental health and protection."[81] Though EPA has a broad mandate to protect human health and the environment, Congress has chosen to emphasize direct consequences to human health in its legislation. NEPA clearly states its purpose "to promote efforts which will prevent or eliminate damage to the environment and biosphere and stimulate the health and welfare of man..." in order to "fulfill the responsibilities of each generation as trustee of the environment for succeeding generations" and "assure for all Americans, safe, healthful, productive and esthetically and culturally pleasing surroundings".[82] The Science Advisory Board of the EPA has re-evaluated the mission of the Agency and stated the need to elevate consideration of ecological issues to the same level as human health issues.[83] A recent draft document calls for the EPA to "task [a] work group to review legislative authorities to identify opportunities (e.g.. reinterpretations of existing law...) and barriers to ecosystem protection" and to "use opportunities to develop grant and statutory flexibility keyed to indicators of improved environmental results."[84] Though laws can ultimately be changed or added to increase the ability of the EPA to work toward ecological-human health protection simultaneously, the language of existing legislation may be interpretable in ways that permit more latitude to the agency than historical trends would indicate. It seems reasonable to seek legal ways to circumvent the constricting case laws governing human health risk assessment by seeking to protect human health within the larger mission of protecting the environment and the biosphere. Precedent for this exists in some of the decisions made under the Endangered Species Act where human economic interests have not been totally triumphant over non-human species survival.[85] What will overcome this barrier in the short run is EPA commitment to broadening its activities to satisfy all of the mandates of NEPA.[86] What will be required in the long run is new law, a slower and less sure result of the political processes in a representative government.

Secondly, the tradition of current practice is to perform human health risk assessment one substance at a time. This is largely also a result of legislative and judicial mandates. For example, Congress has delivered to the various regulatory agencies long lists of toxic chemicals for regulation.[87] The General Accounting Office noted in a 1990 report that EPA had identified less than one percent of the 60,000 drugs listed in Toxic Substances Control Act for testing and completed review of only 16 because of the difficulties inherent to the single agent approach to QHHRA.[88] The burden placed upon the regulatory agencies to deal with these agents using individual risk assessments is worsened as the numbers of man-made chemicals increases by an estimated 1500 per year.[89] Alternatives to single chemical-single effect risk analysis are certainly theoretically possible within traditional QHHRA. Yet, OSHA's attempted to regulate simultaneously 428 toxic substances in the 1989 Air Contaminants Standard could not survive industrial legal challenge.[90] A combined approach to human health and ecological risk assessment could well become entangled in the same legal and legislative trap. New congressional enabling legislation, or novel legal interpretation of environmental law would be needed to circumvent this major barrier to a combined approach.

Finally, current practice in human health risk assessment is to follow the EPA risk assessment guideline documents.[91] These employ conservative, linear extrapolation models, standardized average lifetime exposure scenarios and often emphasize cancer endpoints. In addition, the preferred form for risk characterization is a point estimate of the 'plausible upper bound' on the probability of increase in a single adverse event likely to result from a specific single agent exposure. Little explicit discussion of scientific assumptions, judgments or uncertainties may accompany this risk estimate.[91] In fact, attempts by risk analysts to incorporate modifying discussions of the risk estimate as part of the formal risk characterization may be discouraged by policy makers because of concerns over vulnerability to subsequent court challenge.[92] Therefore, policy makers, journalists and the public expect and may even prefer that risk characterizations will be delivered as a simple numeric probability statement. A combined approach to human health and ecological risk assessment would result in a much more complicated risk characterization including quantitative and qualitative components covering direct and indirect human health considerations. Significant reorientation of the consumers of risk characterizations would be required for successful implementation of a combined risk assessment approach.

Barriers Deriving from Institutional Structure

Institutional barriers exist within the regulatory agencies, the legislature, the legal system, the scientific community and funding organizations. Institutional inertia mediates against any philosophical change which would require radical reorganization.[93] Currently, risk assessment activities are distributed across twelve agencies and twenty eight programs all with different legislative mandates and agency missions[94] defined by hundreds of laws.[95] Combining human and ecological health risk assessment would require changes in the organization of many of these programs. The EPA is currently in the process of combining their human health and ecological risk assessment groups, traditionally separate, into a single unit housed at the EPA facility in Research Triangle Park, North Carolina. This is a major step toward overcoming institutional inertia within the most important federal environmental regulatory agency, and may foreshadow future interdisciplinary efforts which would ultimately permit combined human health and ecological risk assessments.

Institutional barriers exist between institutions as well as within institutions. An Office of Technology Assessment study on risk assessment drafted in the Fall of 1993 stressed the need to cross not only bureaucratic boundaries within government, but also institutional boundaries between government, academics and industry.[96] Because of its extreme complexity, without mutually shared information, methodologies and goals, a combined approach to human and ecological risk assessment is not likely to be successful.

Legal institutions are particularly prone to inertia problems because of the historical, cumulative nature of the development of case and legislative law. Most case law is based upon precedent and ultimately constrained by the Constitution and pertinent statutes. Many environmental and health laws are amendments of original enabling acts and similarly are historically defined. No simple mechanism exists to overcome this barrier, but a novel approach to environmental decision making would provide for more open interpretation of existing laws. A combined human health-ecological risk assessment approach to regulation like the Framework could offer such an unprecedented approach.

The scientific community is also plagued with institutional inertia. As human knowledge expands, successful scientists tend to specialize. In so doing, the organization of science becomes linearized and vertical. The reward system in science is designed to acknowledge highly specialized, mechanistic work to the exclusion of broader, interdisciplinary study. Yet, integrated, interdisciplinary thinking is necessary to long range planning in all areas of human endeavor, most dramatically in the branches of science which have to do with the environment and global systems.[97] If scientists continue to remain exclusively within their own major disciplines, rich opportunities for understanding of environmental systems may be neglected for years. A combined approach to human health and ecological risk assessment would stimulate interdisciplinary science.

Finally, funding institutions also suffer from institutional inertia. This is largely due to the need to allocate very limited resources. Interdisciplinary work is time consuming and expensive. Novel approaches to old problems are of unknown value until development, execution and testing are completed. Funding institutions are much less likely to support research that does not conform to traditional scientific practice with more or less predictable yield. So, researchers and regulators alike are unlikely to find financial support for untried, interdisciplinary work despite multiple calls for such work from respected bodies like the National Academy of Science and the Science Advisory Board of the USEPA. Combined ecological-human health risk assessment would be such an untested approach.

Barriers Deriving from Philosophical Orientation

The dominant philosophy of modern western science and culture is usually termed logical positivism. Born of the Cartesian image of man as machine, the ontology of logical positivism claims that understanding of a whole system demands and is guaranteed by understanding of the elemental parts of that system.[98] Quantitative human health risk assessment epitomizes this philosophy by defining subject (a specific disease state in an individual human) and object (single-agent environmental hazard), determining law-like general relationships (the dose-response curve and exposure scenario) and making a quantitative and theoretically testable statement of outcome (the probability of the disease state occurring in an individual). As in other technical and scientific fields, logical positivism as applied to quantitative human health risk assessment can provide precise and powerful understanding of disease resulting from environmental exposure. Its usefulness, however, does have limits which result from its epistemology. Processes framed by logical positivism may not, for example, consider the qualitative or indirect components of dangers to human health from environmental hazard because they cannot readily be quantified. Consideration of interaction and process which define population health rather than individual non disease are not in the equations. The context of health is removed in the interest of achieving control and objectivity. A combined ecological-human health approach to risk assessment would not fit within this philosophical system because it would require considerations of interactions and context which are explicitly rejected by logical positivism.

Logical positivism is so completely integrated into all aspects of our technical society, however, that to consider that it may not hold the answers to all societal problems can seem impossible. The limitations of the best theoretical applications of QHHRA are examples of the limitations of reductionist analysis. Many who criticize reductionist thinking seek to discard it totally as incorrect and replace it with some other ontology such as phenomenology, realism, or dialectical philosophy.[99] Such an all or nothing approach is self-defeating and unnecessary. The mechanistic understanding of disease and environmental damage produced via the practice of the scientific method is an invaluable component of any environmental solution and a direct result of applied logical positivism. Such understanding cannot and should not be discarded. It must, however, be complemented by a broader more integrated approach to investigation which incorporates dynamic ecological concepts into its application. Rather than discarding studies which suffer from the "ecological fallacy", scientists should explore ways to use ecological data and concepts.[100] An approach which uses both logical positivism and more ecological philosophies would be necessary to support a combined human health-ecological risk assessment framework. Because ecology is the study of interactions, it is complex and must admit the possibility that fundamental laws with predictive power may not exist at the macro level.[101] To date, no laws of ecology analogous to laws of physics have evolved. That is, laws in ecology may always be subject to the tyranny of context. In philosophical terms, this represents the limit of the logical positivist approach. If it is interactions between populations and species that ultimately determine the fitness and resilience of those populations and species, then, by eliminating the interactions from study as logical positivism requires, it becomes impossible to understand or predict outcomes from those interactions. The context determines the outcomes, but the context must be removed in order to achieve the scientific control required by logical positivism. Ecology by its failure to find universal laws is forced to consider the possibility of alternative epistemologies. With these alternative rules of evidence can come alternative methodologies and expanded ways of viewing the world and its environmental problems. Although philosophy is not considered explicitly within the Framework document, the softening of the requirements of logical positivism is evident in the insistence upon the use and value of expert judgment,[102] the importance of formal analysis and documentation of uncertainty,[103] and the admission of qualitative evidence within the formal risk assessment process.[104] Instead of seeing these modifications as temporary necessities pending full and complete mechanistic understanding of ecological units, they can be seen as the philosophical underpinnings of a more comprehensive way of examining the world. This different world view would expand upon the base of logical positivism by embracing the interactive world which modifies and is modified by its component parts.[105] To break through this philosophical barrier may be the most difficult requirement for successful application of a combined approach to ecological- human health risk assessment.

Barriers Deriving from Methodological Limitations

Methodological barriers to a combined approach to human health and ecological risk assessment are considerable. They can be divided into specific scientific problems defined by questions arising from the problem formulation, analysis and risk characterization phases of the Framework approach to risk assessment, and to larger problems arising from attempting interdisciplinary work. Both kinds of problems will be sketched below, but solutions to these problems are beyond the scope of this paper, and beyond the scope of any single individual's work.

The most obvious methodological requirement of a combined ecological-human health risk assessment approach is that humans would need to be described as part of ecosystems. To date, human health has been held aloof and considered in isolation from the rest of biota. Work begun within sociology and social psychology earlier this century would need to be revisited and extended in order to place humans within a larger schema which would enable joint consideration of human and non-human responses to environmental stress.[106] Contributions from medical geography, human ecology, cultural anthropology, economics and political science might also be required to achieve such a description. An anthropocentric orientation could be maintained, but explicit description of human interdependence with the rest of biota would be crucial to successful implementation of a combined approach.

Work would also be required to develop methodologies for identifying and balancing scientific and societal values. In the problem formulation stage of the Framework, even if human health considerations were always awarded highest priorities, many instances would arise requiring tradeoffs to be made between current and future generations, mild threat to human health in the face of major threat to other species, reversible vs permanent predicted outcomes, or economic vs non economic values. A systematic approach to the identification and methods for resolution of conflicting issues would be imperative.

Perhaps the most readily appreciated methodological needs can be found within the requirements of the analysis phase of the risk assessment. Realistic exposure scenarios which are dynamic and contain the ability to express the interactions between exposure and behavior would need to be adapted and refined to include humans as well as other members of ecosystems. Mixed exposures to multiple chemicals, and chemical and non-chemicals stressors would need to be characterized in more realistic and inclusive models. This could be begun by combining existing methodologies from theoretical ecology,[107] systems engineering[108] and risk assessment research,[109] but would require aggressive cross-disciplinary development.

The risk characterization phase of a combined approach like the Framework would require the development of methodologies for combining qualitative and quantitative data. It is unlikely that, even for those questions ultimately answerable by quantitative methods, adequate data will always be available to support all environmental decisions. Methods for combining the two kinds of data in a flexible way would be necessary in order to reach risk characterization conclusions in a combined approach. Similar improvements in uncertainty analysis would be necessary.

Filling all of the methodological gaps would involve a serious commitment to interdisciplinary methodological research. Experience with inter-disciplinary research is, however, quite limited. Consequently, methodologies must be developed for working within new interdisciplinary systems as well as for working on more complicated scientific problems. Looking to other sectors where systemic changes are being attempted can help elucidate some of the potential methodological needs of interdisciplinary work.[110] Major issues which must be addressed begin with the need to redefine roles to be more collaborative and less adversarial or hierarchical. Politicians, social scientists, scientists, jurists, advocates and unaligned citizens would need to develop working relationships unbounded by traditional societal constraints and prejudices. This admits that the risk assessment process is as much a political process in the most egalitarian, democratic sense possible as it is a scientific analysis. To achieve this level of awareness and cooperation would require a shared vision of a broader context of human health and human health risk assessment than is currently held. Methods for communicating that vision and incorporating it in new working relationships would need to be developed in an atmosphere of mutual respect and in the spirit of an iterative experiment. Methods of assessment which permit time for experimentation, thought, reorientation and re-experimentation would need to be fostered. All of these systemic issues are possible within the Framework document if the policy making community would permit it. The leadership for such a radical change could come from the scientific risk assessment community.[111]

Barriers Deriving from the Political Climate

When I started this project, the United States had just elected a new president and vice president, the houses of congress were divided between the two major political parties and the country seemed poised for change. The strong ecological interests of the vice president seemed to promise that the 1990s would be the decade of the environment. Yet, the 103rd Congress had the worst record in decades on environmental legislation and was rendered impotent by in fighting. The elections in November, 1994 dramatically changed the political landscape. The 104th Congress threatens to be ruthless in its handling of environmental law by threatening to reconsider the US participation in the Montreal Protocol banning chlorofluorohydrocarbons, freeze all federal regulation, dismantle the FDA and turn totally to market based solutions to environmental problems. The proposal to combine human health and ecological risk assessment has thus moved from an exciting, politically correct idea to an impossible dream because of the changing composition of the political landscape. Formal political barriers are currently enormous.

Fortunately, political balance is not fixed. New elections always hold the promise of change. An idea with scientific and societal merit should be developed as fully as possible in order to be ready for presentation and implementation at the politically opportune time. I believe that combined ecological-human health risk assessment is such an ideal.

SECTION IV: THE WINGSPREAD CONFERENCE AS A PROTOTYPE FOR CHANGE

The first step in overcoming the barriers to a combined ecological-human health approach to environmental risk assessment is to encourage interdisciplinary scientific interaction. The problem formulation stage within the Framework must be performed within an interdisciplinary scientific setting. The Work Session at the Wingspread Conference Center in Racine, Wisconsin in July 1991 is an example of such an interdisciplinary effort.[112] A group of experts from anthropology, ecology, comparative endocrinology, histopathology, immunology, mammalogy, medicine, law, psychiatry, psycho-neuroendocrinology, reproductive physiology, toxicology, wildlife management, tumor biology and zoology met there in retreat to discuss the problem of environmental endocrine disrupters.

Interest for the conference "stemmed from a comprehensive review of the literature on adverse health effects in wildlife in the Great Lakes region of North America and Europe, and in marine mammals in the Northern Hemisphere,"[113] and from conversations among basic scientists, toxicologists and wildlife scientists. Speculation about the potential effects upon humans of xenobiotic endocrine disruptors had begun to appear in the peer reviewed literature, but most "scientists were unable to support their suspicions with research from their disciplines alone."[114] When the opportunity for interdisciplinary discussion was created by the W. Alton Jones Foundation, the Charles Stewart Mott Foundation, the Joyce Foundation, the Keland Endowment fund of the Johnson Foundation and the World Wildlife Fund, scientists were eager to attend. From this conference emerged a very strong consensus statement which is entirely consistent with and can be used to support a change to a combined ecological-human health risk assessment approach to environmental risk assessment. The work session can also be used as a prototype for other interdisciplinary sessions designed to examine broad issues of environmental risk.

The Wingspread Consensus Statement, is described in the preface as "so shocking...that no scientist could have expressed the idea[s] using only the data from his or her discipline alone without losing the respect of his or her peers."[115] It is organized in six parts, and abstracted below is some detail to facilitate examination of parallels between the published results of the conference and parts of the Framework.

STATEMENT FROM THE WORK SESSION ON CHEMICALLY-INDUCED ALTERATIONS IN SEXUAL DEVELOPMENT: THE WILDLIFE/HUMAN CONNECTION

1. *We are certain of the following*

   * *A large number of man-made chemicals that have been released into the environment...have the potential to disrupt the endocrine system of animals including humans...*

   * *Many wildlife populations are already affected by these compounds.*

   * *The patterns of effects vary...Four general points can....be made. (1) the chemicals...may have entirely different effects on the embryo, fetus or perinatal organism than on the adult; (2) the effects are most often manifested in offspring, not in the exposed parent; (3)...timing of exposure...is crucial...; and (4)...obvious manifestations may not occur until maturity.*

   * *Laboratory studies corroborate the....observations in wildlife*

   * *...effects seen in in utero DES-exposed humans parallel those found in contaminated wildlife and laboratory animals, suggesting that humans may be at risk to the same environmental hazards as wildlife.*

2. *We estimate with confidence that:*

   * *Some of the developmental impairments reported in humans today are seen in adult offspring of parents exposed to synthetic hormone disruptors....released into the environment....*

   * *Unless the environmental load of synthetic hormone disruptors is abated and controlled, large scale dysfunction at the population level is possible...*

   * *As attention is focused on this problem, more parallels in the wildlife, laboratory, and human research will be revealed.*

3. *Current models predict that:*

   * *The mechanisms by which these compounds have their impact*

vary, but they share...general properties....

- *Both exogenous...and endogenous...androgens...and estrogens... can alter the development of brain function.*

- *Any perturbations of the endocrine system of a developing organism may alter the development of that organism: ... these effects are irreversible...*

- *Reproductive effects reported in wildlife should be of concern to humans dependent upon the same resources... because of similarities in the development of the... endocrine systems.*

4. *There are many uncertainties in our predictions because:*

- *...information is limited...lack of measurable endpoints... and lack of multi-generational exposure studies that simulate ambient concentrations. [in humans]*

- *...there are adequate...data concerning reduction in reproductive success in wildlife, data are less robust concerning changes in behavior...*

- *The potencies of many synthetic estrogenic compounds relative to natural estrogens have not been established...*

5. *Our judgment is that:*

- *Testing...for regulatory purposes should...include hormonal activity in vivo...*

- *...Regulations should require screening all new products and by-products for hormonal activity...*

- *It is urgent to move reproductive effects and functional teratogenicity to the forefront when evaluating health risks. The cancer paradigm is insufficient because chemicals can cause severe health effects other than cancer.*

- *....Rather than separately regulating contaminants in water, air, and land, regulatory agencies should focus on the ecosystem as a whole.*

- *...New approaches are needed to reduce exposure to synthetic chemicals already in the environment and prevent the release of new products with similar characteristics.*

- *Impacts on wildlife and laboratory animals as a result of exposure to these contaminants are of such a profound and insidious nature that a major research initiative on humans must be undertake.*

- *The scientific and public health communities' general lack of* *awareness concerning the presence of hormonally active environmental chemicals, functional teratogenicity, and the concept of transgenerational exposure must be addressed. Because functional deficits are not visible at birth and may not be fully manifested until adulthood, they are often missed by physicians, parents, and the regulatory community, and the causal agent is never identified.*

6. *To improve our predictive capacity:*

- *More basic research in the field of developmental biology of hormonally responsive organs is needed...*
- *Integrated cooperative research is needed to develop both wildlife and laboratory models for extrapolating risks to humans.*
- *The selection of a sentinel species at each trophic level in an ecosystem is needed for observing functional deficits...*
- *Measurable endpoints (biologic markers)...are needed*
- *...exposure assessments are needed...that describe concentrations...in an egg...*
- *More descriptive field research is needed...*
- *...reevaluation of the in utero DES-exposed population... will lead the investigation in humans following possible ambient exposures*
- *The effects of endocrine disruptors on longer-lived humans may not be as easily discerned as in shorter-lived laboratory or wildlife species...New methods...should be accompanied by more and better biomarkers of social and behavioral development the use of multigenerational histories of individuals and their progeny, and ...chemical analysis of reproductive tissues and products...*[116]

This powerful statement is endorsed by experts in the sciences, social sciences and medicine from four countries, working in private and public institutions, academic and governmental. The statement of the problem (points 1 and 2), analysis of existing research (3 and 4) and proposal for research directions (5 and 6) provide striking parallels to the approach to risk assessment outlined in the Framework.

By concentrating on the human/wildlife connection, this work session in essence performed the problem formulation stage of a combined human health-ecological risk assessment. Beginning with observed endocrine disruption of known cause in wildlife populations, experts pooled research findings on related topics across disciplines and were able to come to firm consensus on the biologically relevant problem and it's relative importance. The group tackled the disparate collection of chemicals known to produce the broad effect of disruption of the reproductive endocrine system in various wildlife and laboratory populations. Research done on humans exposed to the therapeutic agent, diethylstilbestrol (DES) *in utero* demonstrate that the causal mechanisms offered as explanations for reproductive failures of environmentally exposed wildlife populations are also operational in humans. By beginning with assessments endpoints of reproductive potential, the work session circumvented the common emphasis on the carcinogenic actions of the chemicals under scrutiny. It also defined the chemicals of concern by their endocrine disrupting effects rather than their chemical structure or technological use. This approach applied to human health would result, for example, in the examination of the range and severity of toxic reproductive effects of herbicides upon non targeted animal species, humans included, rather than determination of the human carcinogenic effect of 2,3,7,8-tetrachloro-dibenzo-*p*-dioxin. The problem was formulated in the work session in a fashion consistent with the problem formulation phase described in the Framework.

An analytic structure for evaluating these effects would be very different from the standard QHHRA approach and very similar to the approach discussed in the Framework. In the analysis of existing research, the experts identified important endpoints for study, issues of exposure requiring definition and modeling and specific gaps in data and theory requiring immediate research. This is consistent with the analysis step of the Framework, although not comprehensive. The purpose of the work session was to identify the problems and suggest research needs, not to formulate the research approach. Nonetheless, the skeleton of the research approach is present and is similar to what would be required in a ecological-human health stressor-response analysis. The recommendations in the Consensus Statement address a number of the scope issues which make the ecological approach to risk assessment more consistent with public health goals. For example, the call for multi-generational exposure studies, regulation by ecosystem effect rather than standard environmental compartments and more direct longitudinal human study all highlight the scope limitations of standard QHHRA and elegantly support the Framework approach.

Finally, the recommendations of the Wingspread Conference reflect the same dynamic philosophical spirit of the Framework document. The statement proceeds from a discussion of uncertainties, to proposing a regulatory and research agenda embodying many of the ecological concepts discussed throughout this paper. Included are recommendations for developing more complete mechanistic understanding of how endocrine disrupters work at the molecular level as well as support for finding more and better biomarkers which can be interpreted as supporting a traditional logical positivist approach to science. Equally strongly, however, the participants called for more descriptive field research, narrative, multigenerational histories of families and investigation into social and behavioral development which are in harmony with a much more dynamic, contextual philosophy of describing human population health. It is interesting that by gathering experts from multiple disciplines to consider an environmental problem, the resultant recommendations are enlivened philosophically by more than traditional logical positivism. It seems that when professionals from different scientific disciplines (populations) begin to interact, the effect may be the elucidation of the limits of the philosophy which defines their disciplines. This is the classic ecological dilemma described by Schrader-Frachette and McCoy in their examination of the scientific viability of general ecological theory.[117] Its appearance within this very different context further supports the need to expand the philosophical basis of many activities of modern society, health risk assessment included.

The Wingspread conference is one current example of interdisciplinary problem identification. Many other forms of interdisciplinary collaboration can be used to address environmental risk assessment issues. These can range from information sharing on electronic clipboards, to multidisciplinary publications and scientific meetings, to formal work sessions and research. If, as I have tried to demonstrate, a combined approach to human health-ecological risk assessment is the preferred method for communicating scientific data to policy makers charged with protecting human health, then the absolute prerequisite is interdisciplinary cooperation in all aspects of the risk assessment process. The apparent success of Wingspread is quite encouraging.

CONCLUSIONS

In this paper I have tried to make a case for expanding the practice of human health risk assessment to incorporate transgenerational and indirect threats to human health. I wish to re-emphasize that standard quantitative human health risk assessment theory and practice are invaluable tools used to support rational environmental policy decisions and must be retained. QHHRA is restricted, however, to analysis of direct risk to individuals and represents consideration of only one category of environmental risk to human health. Great potential value exists in a combined approach to human health and ecological risk assessment which applies the 1992 EPA Framework for Ecological Risk Assessment to human health assessment endpoints. Population level considerations, transgenerational threats and indirect threats to human health could be captured without sacrifice of individual risk considerations. Barriers to a combined approach are many, but the trend toward interdisciplinary science as exemplified by the Wingspread conference supports the concept of combined ecological-human health risk assessment. Expanding QHHRA with the ecological concepts outlined in the Framework is a logical next step in the development of tools used to bring science to policy.

Much work, many talented people and years would be required to accomplish such a step. It would require a new vision, excellent and compelling leadership, systemic change among strongly defined scientific disciplines, great curiosity and a sense of adventure. No single individual paper or charismatic spokesman can force such a change. Many of the authors referenced in this paper have expressed concerns related to the need for change. These sentiments are consistent with a broadening of current risk assessment practice by addition of ecological concepts. The unrest in the scientific and regulatory communities evident in peer review publications, newspapers and popular publications seems to indicate that change is desired. Certainly, the current political climate makes change likely. Those scientists, regulators, risk analysts and academics who share parts of this vision should advocate for change which is scientifically sound separately and cooperatively in hopes of encouraging change which will result in durable and positive solutions supporting long-term human health and environmental integrity.

Steps toward these kind of changes are different for different disciplines. The key is for all institutions and all scientific specialties to allow and encourage interested individuals the freedom to step off of the traditional paths defining success and security. Interested individuals need time to experiment with ideas, time to read and talk to experts outside of their specialty areas, and time to write ground breaking papers and books within the formal structure of their disciplines and their jobs. Those same individuals need to be courageous in voicing their interests and demanding recognition of the legitimacy of innovative approaches to old and new problems. Institutions will not change if change is not demanded from within. Similarly, individuals cannot implement change within the confines of rigid institutions. Academic, governmental and industrial institutions need to respond to the growing number of scientists demanding support for interdisciplinary research. The solutions to our growing environmental problems which will protect the health of future generations will only be found through multidisciplinary approaches.

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