

ENVIRONMENTAL HEALTH SCIENCES DECISION MAKING

Risk Management, Evidence, and Ethics

W O R K S H O P S U M M A R Y

Yank Coble, Christine Coussens, and Kathleen Quinn, *Rapporteurs*

Roundtable on Environmental Health Sciences, Research, and Medicine

Board on Population Health and Public Health Practice

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

THE NATIONAL ACADEMIES PRESS
Washington, D.C.
www.nap.edu

NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

Support for this project was provided by the National Institute of Environmental Health Sciences, National Institutes of Health (Contract N01-OD-4-2193, TO#43); National Center for Environmental Health and the Agency for Toxic Substances and Disease Registry, Centers for Disease Control and Prevention (Contract No. 200-2000-00629, TO#7); National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention (Contract 0000166930); National Health and Environment Effects Research Laboratory and the National Center for Environmental Research, U.S. Environmental Protection Agency (Contract 282-99-0045, TO#5); American Chemistry Council (unnumbered grant); ExxonMobil Corporation (unnumbered grant); and Institute of Public Health and Water Research (unnumbered grant). The views presented in this book are those of the individual presenters and are not necessarily those of the funding agencies or the Institute of Medicine.

International Standard Book Number-13: 978-0-309-12454-6

International Standard Book Number-10: 0-309-12454-9

Additional copies of this report are available from the National Academies Press, 500 Fifth Street, N.W., Lockbox 285, Washington, DC 20055; (800) 624-6242 or (202) 334-3313 (in the Washington metropolitan area); Internet, <http://www.nap.edu>.

For more information about the Institute of Medicine, visit the IOM home page at: **www.iom.edu**.

Copyright 2009 by the National Academy of Sciences. All rights reserved.

Printed in the United States of America

The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The serpent adopted as a logotype by the Institute of Medicine is a relief carving from ancient Greece, now held by the Staatliche Museen in Berlin.

Suggested citation: IOM (Institute of Medicine). 2009. *Environmental Health Sciences Decision Making: Risk Management, Evidence, and Ethics: Workshop Summary*. Washington, DC: The National Academies Press.

*“Knowing is not enough; we must apply.
Willing is not enough; we must do.”*

—Goethe



INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

Advising the Nation. Improving Health.

THE NATIONAL ACADEMIES

Advisers to the Nation on Science, Engineering, and Medicine

The **National Academy of Sciences** is a private, nonprofit, self-perpetuating society of distinguished scholars engaged in scientific and engineering research, dedicated to the furtherance of science and technology and to their use for the general welfare. Upon the authority of the charter granted to it by the Congress in 1863, the Academy has a mandate that requires it to advise the federal government on scientific and technical matters. Dr. Ralph J. Cicerone is president of the National Academy of Sciences.

The **National Academy of Engineering** was established in 1964, under the charter of the National Academy of Sciences, as a parallel organization of outstanding engineers. It is autonomous in its administration and in the selection of its members, sharing with the National Academy of Sciences the responsibility for advising the federal government. The National Academy of Engineering also sponsors engineering programs aimed at meeting national needs, encourages education and research, and recognizes the superior achievements of engineers. Dr. Wm. A. Wulf is president of the National Academy of Engineering.

The **Institute of Medicine** was established in 1970 by the National Academy of Sciences to secure the services of eminent members of appropriate professions in the examination of policy matters pertaining to the health of the public. The Institute acts under the responsibility given to the National Academy of Sciences by its congressional charter to be an adviser to the federal government and, upon its own initiative, to identify issues of medical care, research, and education. Dr. Harvey V. Fineberg is president of the Institute of Medicine.

The **National Research Council** was organized by the National Academy of Sciences in 1916 to associate the broad community of science and technology with the Academy's purposes of furthering knowledge and advising the federal government. Functioning in accordance with general policies determined by the Academy, the Council has become the principal operating agency of both the National Academy of Sciences and the National Academy of Engineering in providing services to the government, the public, and the scientific and engineering communities. The Council is administered jointly by both Academies and the Institute of Medicine. Dr. Ralph J. Cicerone and Dr. Wm. A. Wulf are chair and vice chair, respectively, of the National Research Council.

www.national-academies.org

ROUNDTABLE ON ENVIRONMENTAL HEALTH SCIENCES, RESEARCH, AND MEDICINE

Paul Grant Rogers, deceased, (*Chair*), Partner, Hogan & Hartson,
Washington, DC

Lynn Goldman (*Vice Chair*), Professor, Bloomberg School of Public Health,
The Johns Hopkins University, Baltimore, MD

John M. Balbus, Director of Environmental Health Program, Environmental
Defense Fund, Washington, DC

Yank D. Coble, Immediate Past President, World Medical Association,
Neptune Beach, FL

Susan Dentzer, Health Correspondent and Head of the Health Policy Unit, The
News Hour with Jim Lehrer, Public Broadcasting Station, Arlington, VA

Henry Falk, Director, Coordinating Center for Environmental and
Occupational Health and Injury Prevention, National Center for
Environmental Health/Agency for Toxic Substances and Disease Registry,
Centers for Disease Control and Prevention, Atlanta, GA

Richard Fenske, Professor, Department of Environmental Health, University
of Washington School of Public Health and Community Medicine, Seattle

Howard Frumkin, Director, National Center for Environmental Health/
Agency for Toxic Substances and Disease Registry, Centers for Disease
Control and Prevention, Atlanta, GA

Peggy Geimer, Corporate Medical Director, Arch Chemicals, Inc., Greenwich, CT

Bernard Goldstein, Professor, Department of Environmental and Occupational
Health, Graduate School of Public Health, University of Pittsburgh,
Pittsburgh, PA

Myron Harrison, Senior Health Adviser, ExxonMobil, Inc., Irving, TX

Carol Henry, Retired Vice President for Industry Performance Programs,
American Chemistry Council, Arlington, VA

John Howard, Director, National Institute of Occupational Safety and Health,
Centers for Disease Control and Prevention, Washington, DC

Sharon Hrynkow, Associate Director, National Institute of Environmental
Health Sciences, National Institutes of Health, Bethesda, MD

Richard Jackson, Graham Family Professor, School of Public Health, Director
of the Graham Environmental Sustainability Institute, University of
Michigan, Ann Arbor

Floyd Malveaux, Executive Director, Merck Childhood Asthma Network, Inc.,
Washington, DC

Michael McCally, Executive Director, Physicians for Social Responsibility,
Washington, DC

Mark Myers, Director, United States Geological Survey, Reston, VA

Martin Philbert, Associate Dean for Research, School of Public Health,
University of Michigan, Ann Arbor

Lawrence Reiter, Director, National Exposure Research Laboratory, U.S. Environmental Protection Agency, Research Triangle Park, NC

Leona Samson, Professor, Center for Environmental Health Sciences, Massachusetts Institute of Technology, Cambridge

Paul Sandifer, Senior Scientist for Coastal Ecology, National Ocean Service, National Oceanic and Atmospheric Administration, Charleston, SC

Carlos Santos-Burgoa, General Director for Equity and Health, Secretaria de Salud de Mexico, Mexico D.F.

John Spengler, Professor, Department of Environmental Health, Harvard School of Public Health, Cambridge, MA

William Suk, Acting Deputy Director, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC

Louis Sullivan, President Emeritus, Morehouse School of Medicine, Atlanta, GA

William Sullivan, Director, Department of Natural Resources and Environmental Sciences, University of Illinois at Urbana-Champaign, Urbana, IL

Jennie Ward-Robinson, Executive Director, Institute for Public Health and Water Research, Chicago, IL

Samuel Wilson, Acting Director, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC

Harold Zenick, Director, Office of Research and Development, U.S. Environmental Protection Agency, National Health and Environmental Effects Research Laboratory, Research Triangle Park, NC

Roundtable Staff

Christine M. Coussens, Study Director

Nora Hennessy, Senior Program Associate

Tia Carter, Senior Program Assistant (until February 2008)

Louise Jordan, Senior Program Assistant (from February 2008)

Rose Marie Martinez, Board Director

Hope Hare, Administrative Assistant

Christie Bell, Financial Associate

Kathleen Quinn, Intern (Spring 2008)

*The members of the Roundtable on Environmental Health Sciences oversaw the planning of the workshop but were not involved in the writing of the workshop summary.

Reviewers

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council's (NRC's) Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

George Corcoran, Society of Toxicology, Wayne State University, Detroit, MI

Betty Dabney, Maryland Institute for Applied Environmental Health,

University of Maryland School of Public Health, College Park

Stephen Lester, Center for Health, Environment, and Justice, Falls Church, VA

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the final draft of the report before its release. The review of this report was overseen by **Melvin Worth**, Sun City, FL. Appointed by the NRC and the Institute of Medicine, he was responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authors and the institution.

Contents

PREFACE	xi
SUMMARY	1
1 APPROACHES TO DECISION MAKING	9
Human–Environment Network: Challenges to Environmental Health, 9	
Alternatives Assessment as a Strategy for Decision Making, 14	
Beyond Precaution, 16	
2 SCIENTIFIC ISSUES IN ENVIRONMENTAL HEALTH DECISION MAKING	21
Evaluating Weights of Evidence for Decision Making, 21	
The Role of Uncertainty and Susceptible Populations in Environmental Health Decision Making, 24	
The Use and Misuse of Science in Decision Making, 28	
Rationale for Revisiting an Environmental Health Decision: The National Toxicology Program, 29	
Session Discussion: Weight of the Evidence in Science Versus Law, 32	
3 CONFLICTS OF INTEREST, BIAS, AND ETHICS	35
General Observations Regarding Conflicts of Interest, 35	
Managing Conflicts of Interest: The International Agency for Research on Cancer, 38	
Session Discussion: Conflicts of Interest in the Current Research Climate, 42	

4	STAKEHOLDER PERSPECTIVES ON ENVIRONMENTAL HEALTH SCIENCES DECISION MAKING	45
	Full Disclosure of Conflicts of Interest, 45	
	The Credibility of Science, 46	
	Asymmetry in Decision Making, 47	
	Data Development for Risk Assessment, 47	
5	GENERAL WORKSHOP DISCUSSION	49
	Transparency, 49	
	The Context Around Conflict and Evidence, 49	
	Code of Ethics, 50	
	Future Directions, 50	
6	CLOSING COMMENTS	53
	REFERENCES	57
	APPENDIXES	
A	Workshop Agenda	59
B	Speakers and Panelists	63
C	Workshop Participants	75

Preface

Environmental health decision making can be a complex undertaking, as there is the need to navigate and find balance among three core elements: science, policy, and the needs of the American public. Much of environmental health decision making started in the 1950s and 1960s and was focused on health effects of simple environmental exposures. However, scientific knowledge has rapidly changed as new technologies and new insights into the complexity of environment–health interactions have emerged. Furthermore, while much of environmental health has focused on population research, there is a call from the public for more individualized and tailored science. Incorporating these new evolutions means there is a greater need to make evidence-based decisions in a careful, considerate, yet timely manner. The ability to do so can, at times, be complicated and therefore dictates the constant exploration and reevaluation of the decision-making process.

The 1960s and 1970s saw a strengthening of the nation’s commitment to environmental health sciences with the establishment of a number of agencies, such as the Environmental Protection Agency (EPA), the National Institute of Environmental Health Sciences, the National Toxicology Program, and the National Center for Environmental Health at the Centers for Disease Control and Prevention (CDC). These governmental agencies formed the core environmental health science programs and, in collaboration with other partners in the government, addressed the problems of the day by identifying the state of the science and the research gaps to better inform policy decisions.

A more complete scientific picture enables policies that can help prevent harmful exposure and promote beneficial environments. The goal of sound decision making is to ensure that science is the underlying backbone of policy. However, there are a number of unanswered questions about how to appropriately use science, including how much science is needed in order to take action, which chemicals should be subjected to further scrutiny, and how conflicts in

the research literature should be resolved. At times, these unanswered questions result in a gulf between research and policy due to uncertainty, for example in extrapolating from evidence derived at high doses to determine low-dose risks.

As a former policy maker, I know that science, risk, and policy are intertwined. In the 1970s, the House Committee on Health and the Environment was debating the safety of saccharin as an artificial sweetener. The initial reports at the time designated saccharin as a carcinogen, but only if an individual consumed between 150 and 300 bottles of soda pop a day. Well, the committee decided that was not very likely and delisted it. What this example illustrates is the need for policy to be based on science, but the science needs to be interpreted in the appropriate context that incorporates public use or exposure. It is interesting that this one example continued to be debated in the scientific and policy arenas into the late 1990s. Even at this workshop (held in 2008), the roundtable discussed how the science evolved to more fully understand the carcinogenicity of saccharin. Scientists have a more complete understanding of this one chemical based on a number of research studies to elucidate cellular mechanisms.

Policy makers often grapple with how to make appropriate decisions when the research is uncertain. For example, when the Clean Air Act was being drafted, various groups of scientists had conflicting positions about whether to include carbon dioxide or ozone as air pollutants, but the House committee partially based its decisions on the death rates and hospital admission rates from pollution in such places as California and Denver. The legislators did not want to wait to count bodies and instead made a judgment to remove the impurities that were causing adverse health effects. The challenge for the policy maker is to make the right decision with the best available data in a transparent process.

The Institute of Medicine's Roundtable on Environmental Health Sciences, Research, and Medicine was established in 1988 as a mechanism for bringing various stakeholders together to discuss environmental health issues in a neutral setting. Roundtable members represent the academic community, industry, non-governmental organizations, governmental agencies, and health professions. The roundtable provides an environment that fosters scientific dialogue on current and emerging issues in the field of environmental health. The purpose is to illuminate ideas and facilitate discussion. However, the members do not resolve issues or make recommendations.

The workshop on which this volume is based was held on January 15, 2008, in Washington, DC. This workshop was designed to address the scientific and ethical foundation of environmental health decision making. It included an overview of the principles underlying decision making, the role of evidence and challenges for vulnerable populations, and ethical issues of conflict of interest, scientific integrity, and transparency. The workshop engaged science interest groups, industry, government, and the academic sector through three sessions of speaker presentations, with each session being concluded with a general discus-

sion. The reader can find the workshop agenda, as well as speaker information and a list of attendees in the appendixes at the end of this summary.

This workshop summary which was written by the named rapporteurs, captures the discussions and presentations by the speakers and panelists. The information expressed here is the views of the individuals and should not be perceived as a consensus of the participants or the views of the roundtable, the Institute of Medicine, or its sponsors.

Paul G. Rogers, J.D., *Chair*
Roundtable on Environmental
Health Sciences, Research, and Medicine

Summary

The workshop on Environmental Health Sciences Decision Making was convened to inform the Roundtable on Environmental Health Sciences, Research, and Medicine on emerging issues in risk management, “weight of evidence,” and ethics that influence environmental health decision making. This is the first in a series of discussions for the roundtable to better understand the science needs in this area. The remarks in the workshop summary are the views of the individual presenters, panelists, or members and do not reflect a consensus of those attending or the roundtable.

This workshop focused on the strategies used to make decisions, whether they are based on the precautionary principle or cost-benefit analysis. During the initial session of the workshop (reflected in Chapter 1), the focus was on how complex decisions could incorporate new technologies and the need for a more interdisciplinary approach. The second session (Chapter 2) shifted the focus to the weights of scientific evidence and how this information is used in the decision-making process. The last session (Chapter 3) focused on the ethics and value of scientific information that is used for decision making. Speakers and participants discussed the issues of conflict of interest, bias, and transparency.

For the field of public health, identification of a hazard is only the first step in protecting individuals and the population at risk against its harmful effects. Earlier strategies focused on one chemical at a time and often assumed that individuals are static in the environment, so that their behaviors and lifestyle choices were not taken into account. However, as understanding of toxicology and epidemiology has evolved, so has scientific understanding of the complexity of environmental hazards. Risk assessment has moved beyond the general assumption that a major cause of a problem (exposure) can easily be identified and a solution generated. Thus, according to some of the workshop participants, society is currently at a crossroads in environmental health decision making, and there is a need to look

at the paradigm very carefully and think about what science can do to improve the way those decisions are made.

HOLISTIC APPROACH TO ENVIRONMENTAL HEALTH DECISION MAKING

During the workshop, Christopher Portier from the National Institute of Environmental Health Sciences stressed that complex human–environment interactions require a systems approach to understanding environmental health and implementing environmental health decisions. Such environmental components as basic needs, shelter factors, and endogenous factors interact with each other to determine a person's health status. He suggested that the general assumption about risk assessment—the major cause of a problem can easily be identified and a solution generated—is an outdated approach. Furthermore, he noted that with regard to the human system and how science addresses its exposure to hazards, there is a large amount of research and testing being performed, from the population and clinical levels to the molecular level. Although all of this science contributes to understanding the impact of the environment on health, most risk assessment is based on toxicological and epidemiological evidence and not on emerging sciences, such as genetics and toxicogenomics. Scientists and policy makers therefore need to look at the emerging areas of science to find ways to incorporate this research into the environmental health decision-making process.

ALTERNATIVE VIEW TO ENVIRONMENTAL HEALTH

Mary O'Brien from the Oregon Toxics Alliance furthered the discussion by noting that the presumed goal of environmental health science decision making is to produce less harm to human health and the environment. However, she stressed there is a fundamental disconnect between environmental health science and decision making for environmental health. Too often in the scientific community, among many other professions, there are many obstacles to good decision making, including a narrow power base that leads to narrow decision making and the fact that human nature is habit based and decisions are made in ways that stifle creativity and ingenuity. She noted that environmental health is fraught with examples of this disconnect in the decision-making process. An example is the substitution of one chemical for another to achieve a desired goal without careful thought and consideration given to the impact the new chemical may have on the environment.

One approach to overcome these limitations is to use alternatives decision making, which has ability to take diverse perspectives to examine reasonable alternatives for producing fewer harms. By bringing to the table parties with different views and positions, the discussions can lead to the generation of more

ideas, which may offer environmentally sound solid solutions to problems not seen without those views. However, to arrive at such solutions, there must be transparency as well as a level playing field based on equal representation on all sides of an issue, concluded O'Brien.

BEYOND PRECAUTION

Bernard Goldstein of the University of Pittsburgh Graduate School of Public Health noted that many environmental health decisions have been made from a fragmented, narrow, reductionist approach that can often create secondary problems. He echoed the call for a holistic approach for science, but at the same time cautioned about decision making under uncertainty. The precautionary principle is a moral and political principle that was developed as a result of the need for action in the face of scientific uncertainty. According to the European Commission, this principle should be applied whenever the “scientific data are insufficient, inconclusive, or uncertain and where a preliminary scientific evaluation shows that potentially dangerous effects for the environment and human, animal or plant health can be reasonably feared” (EU, 2008). The argument for using the precautionary principle in order to act in the face of uncertainty implies that without this principle there is an absence of action in the face of uncertainty. While attention should be paid to the premise of the principle, there is also the need to step back and examine what it means to the overall practice of public health, asserted Goldstein. If policy makers are going to rely on precaution, then they need to authorize research to ensure that a precautionary approach is needed. The research agenda should be linked to objectives of data need and data quality and involve the public.

The Nature of Evidence

The first step in understanding how evidence relates to scientific decision making is to look at evidence as science, noted Michael McGinnis of the Institute of Medicine. It is widely understood in the scientific community that evidence is science; however, there is another point to consider, which is the utility of evidence as science. Science may be a tool less for finding the answer than for revealing the next question to study and research; evidence may be a tool less for making the decision than for informing the context in which the decision is to be made, noted McGinnis. Evidence is not static or formulaic. Evidence is not binary in nature, but rather is a spectrum that ranges from a finding of no evidence available to one of irrefutable evidence. This view of evidence presents a challenge in determining the decision rules along the path to stronger evidence—in particular, how scientists form and agree to the standards used to inform the decision-making process, with the understanding that evidence has many forms, and the context in which those decisions are made.

While the evidence spectrum is clear in clinical medicine, such a spectrum is needed for interventions in population health, noted McGinnis. These interventions range from ones that originate from a purely physical or environmental process, such as fluoride in the water supply, to individual interventions, such as behavioral change interventions designed to encourage smoking cessation, increased physical activity, or change in dietary habits. In population health, effectiveness is often a function more of the nature of the intervention than the nature of the evidence; this suggests that the intervention is of such power that it carries with it an additional obligation to consider other aspects of the issues involved. Making decisions at the population level may require fewer points to consider, but their powerful impact requires understanding several factors: the potential health, economic, and social consequences of inaction; the potential health, economic, and social consequences of action; the characterization of uncertainties and mapping strategies as uncertainties resolve; and the systematic assessment and feedback factored into the approach of an intervention, concluded McGinnis.

Evidence and Uncertainty

Ultimately, there is a need to define variability and uncertainty distributions and to have both analysts and managers as an integral part of risk analyses, noted Dale Hattis of Clark University. Methods for estimating variability and uncertainty should ideally be based on causal mechanisms. During the workshop, Hattis outlined four implications that are important to understand as society moves forward in making risk management decisions. First, legal cases involving environmental issues are increasingly calling for the recognition that some finite rates of adverse effects will remain even after implementation of reasonably feasible control measures. Second, societal reverence for life and health means making the best decision with available resources to reduce harmful effects. Third, responsible social decision making requires making estimates of how many people are likely to experience how much harm and determining with what degree of confidence. Fourth, the traditional multiple-single uncertainty factor system cannot yield estimates of health protection benefit that can be juxtaposed with the costs of health protection measures.

WEIGHING EVIDENCE

A central tenet in scientific decision making is that any decision rendered needs to be based on the best available science, which “depends upon a disinterested and transparent scientific process” (Steinzor and Shudtz, 2007, p. 1). In other words, scientific decisions should be made using the weight of the evidence, yet in today’s world, scientific decisions are often called into question by the legal profession, seeking to influence an outcome, noted Rena Steinzor of the Univer-

sity of Maryland School of Law. The pathway from science to science policy is often perceived by scientists and the public as a straightforward one, as the merits of the science have been vetted during peer review in the publication process (Wagner and Steinzor, 2006). However, Steinzor suggested that this is not always true. The culture of law and science are vastly different and at times clash with one another, which puts pressure on science when it is applied in the legal setting. The difference between the legal and scientific processes are most profound in the regulatory arena, where, once a scientific decision has been reached, it can then be subjected to extreme scrutiny and deconstruction by the legal profession, observed Steinzor. This deconstruction can create important data gaps and is in stark contrast to the weight of the evidence approach used by scientists (Wagner and Steinzor, 2006).

REVISITING ENVIRONMENTAL HEALTH DECISIONS

Drawing from his experience at the National Institute of Environmental Health Sciences (NIEHS) and the National Toxicology Program (NTP), Kenneth Olden of the NIEHS discussed the need for revisiting scientific decisions. The *Report on Carcinogens* is a congressionally mandated document “prepared by the NTP for the purpose of identifying substances, mixtures of chemicals, or exposure circumstances associated with technological processes that cause or might cause cancer and to which a significant number of persons in the United States are exposed. Listed in the RoC are a wide range of substances, including metals, pesticides, drugs, and natural and synthetic chemicals” (NTP, 2005). Olden noted that the chemicals on the list go through an extensive public review and that additions are made after careful scrutiny and consideration of all available science. A decision to list a chemical in the RoC does not mean that it cannot be reconsidered. As science evolves and new information is discovered about the harmful, or not harmful, effects of a chemical, there may be circumstances for reevaluating. The case of saccharin is one example where the decision for revisiting the listing was based on the evolution of science.

ETHICS OF CONFLICTS OF INTEREST

Conflicts of interest are ubiquitous, noted Thomas Murray of The Hastings Center. They are usually based on situations in which there is reliance on the judgment of an outside party with some very specific professional expertise. Exercise of that judgment should promote the interest of a loyal party, which can range from the individual level (e.g., the patient in a doctor–patient relationship) to a broader level (e.g., institutions). The judgment that the professional owes the client, patient, or institution may include specific recommendations, but often it includes just interpretation of information for the receiver (loyal party), who

lacks the expertise necessary to understand the information without assistance, noted Murray.

To say that someone has a conflict of interest is not a moral criticism, but rather a description of a set of circumstances, observed Murray. That person has a primary interest that he or she needs to fulfill, although other interests may push or pull the person in different directions. A moral failure would be if the person neglected their primary interest and allowed these other interests to rule.

The many challenges in correctly identifying conflicting interests include variation in individual interpretations of what is considered to be conflict. This can range from not recognizing an issue as a potential for conflict to assuming impartiality because the monetary outcome is the same no matter which position is decided. Having criteria to determine the nature of conflict is therefore necessary in any scientific organization, noted Murray. Several steps are key to detecting, managing, and addressing all types of conflict of interest, including those financial in nature: clarity, simplicity, fairness, and predictability.

Different organizations have different techniques for addressing conflicts of interest, observed Vincent Coglianò of the International Agency for Research on Cancer (IARC). One such technique is to actually ignore the issue altogether. However, most organizations are choosing to implement some type of mechanism for addressing conflict, such as opting for a simple disclosure policy. Other organizations have chosen to build on a disclosure policy by adding a system of checks and balances to limit the number of experts involved if they have conflicts. In other words, the experts with conflicts are diluted by the experts who have no conflicts. While some organizations try to actively balance experts who have a conflicting interest with someone with an opposing interest, another strategy is striving to avoid conflicts of interest altogether. Using a case study, Coglianò illustrated the IARC strategy for addressing conflicts of interest that addressed the issues of best versus impartial experts, and maintain inference as they produce their monographs.

PERSPECTIVES ON ENVIRONMENTAL HEALTH DECISION MAKING

Throughout the workshop, both during the presentations and discussion periods, a variety of viewpoints were expressed on how to balance issues of conflict of interest and bias and to ensure weighting of evidence for decision making. In a panel discussion, four stakeholders shared their views on how best to ensure that decision making was based on sound, credible science.

Drawing from the preliminary studies of Rofecoxib (Vioxx), where there were conflicting interpretation of the same sets of data, David Michaels of George Washington University suggested the public overall may have been served better if an independent review had been conducted. He further asserted that a central tenet of the process to ensure that decisions are based on credible science would

include full disclosure and publication of conflicts, whether it was publicly or privately supported science. This disclosure would need to encompass the entire research enterprise and be applied equally to the publishing of research and the regulatory setting.

Myron Harrison of ExxonMobil Corporation stated that ultimately all scientific findings must be judged on their merits, whatever the source of funding. He noted that in reality, the science used in public health is particularly unstable and uncertain, and therefore scientific disagreement and controversy should be expected. In the face of this uncertainty, other human factors, such as personal beliefs and values, often play a large role. He noted that in order for an agency to optimize the credibility of science used in rule making, they can strengthen the science's credibility by using good lab practices, protecting human subjects, applying rigorous peer review, disclosing potential conflicts of interests, and implementing strong management systems.

The final two speakers addressed issues related to how the science is directly used in environmental health decision making. John Balbus of the Environmental Defense Fund asserted that due to the challenges of a very high burden of proof faced by many regulatory agencies, too few environmental health decisions are actually made and the supporting (safety) data are not often required. This makes the regulatory process challenging. He further stated that peer review of data is not uniformly applied throughout the rule-making process and called for equally rigorous review of all data that may be incorporated into the rule-making process.

William Farland of Colorado State University ended the panel discussion by noting that in order to move the environmental health decision-making process forward, there is a need to think strategically about how data can inform risk. Science is a moving target, and it is essential to think about what information is needed to inform decision making. He noted that focusing on basic instead of applied research and on disease-based instead of topic-based research creates an inability to generate the type of data necessary for rigorous assessment of chemicals. One idea to move the process forward is to develop a systematic approach to working with data and weighing the evidence. Finally, the paradigm should incorporate evaluation into the decision-making process, as assessing the impact of a decision is vital to the success of future decision making.

Approaches to Decision Making

When risk assessment was in its infancy in the 1950s and 1960s, the general assumption was that the major cause of a problem could easily be identified and a solution generated. As time has progressed and society and science have faced new problems, this assumption is no longer applicable to the decision-making process. Thus, society is currently at a crossroads in environmental health decision making, and there is a need to carefully examine the current paradigm and think about what science can do to improve the way decisions are made. This chapter highlights current approaches to environmental health decision making and opportunities to improve decision making under complex problems.

HUMAN-ENVIRONMENT NETWORK: CHALLENGES TO ENVIRONMENTAL HEALTH

*Christopher J. Portier, Ph.D., Director,
Office of Risk Assessment Research, NIEHS*

Risk analysis and risk decision making consist of balancing the needs of science, economics, and society. Science and economics conduct research based on hypotheses and interpret the results for societal application. Society, through government, balances the various scientific and economic outcomes to ultimately decide policy. It is the role of risk analysis to translate among these groups, evaluate the literature so that decisions can be made and implemented, and communicate to all the stakeholders (Figure 1-1). In most risk analyses, it is assumed that one can manage each risk independently and preserve the public's health. As time has progressed and society and science have faced new problems, this assumption is no longer applicable to the decision-making process.

Humans are not independent of their environments; rather, their interactions affect the environment, and the changes they make to the environment can

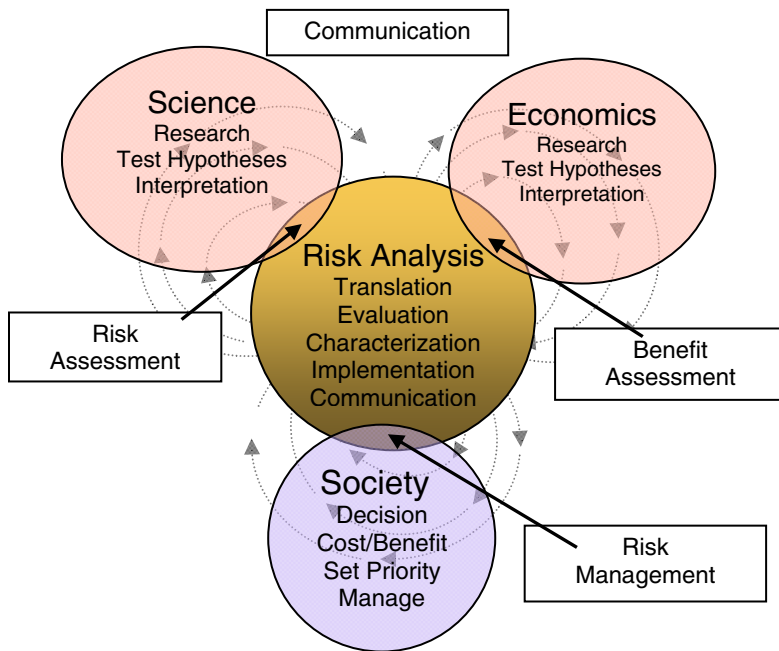


FIGURE 1-1 A risk decision-making approach is a function of evaluating science and economic information and effectively communicating the outcome to society.
SOURCE: Portier, unpublished.

affect their health. Taking complex human–environment interactions into account requires a new systems approach to environmental health decision making. With regard to human health and the factors that impact it, four overarching categories are basic needs, shelter factors, personal factors, and endogenous factors. All four are social determinants of health and play an interactive role in environmental health, yet only endogenous factors cannot be changed by individuals (Figure 1-2).

Basic factors are needs that are crucial to survival: having food to eat, water to drink, and clean air to breathe. At the most basic level of human functioning, these factors are the foundation for everything human beings do. The next level—shelter factors—includes items that, although not directly needed to live, can improve the quality of life, such as physical surroundings, like homes and schools; community; access to health care and hospitals; clean water for recreation; and the ability to be employed and earn a living. Personal factors, the third category, are less tangible in nature, such as exerting control over one’s life and making choices or decisions, the feeling of social cohesion, and establishing rela-

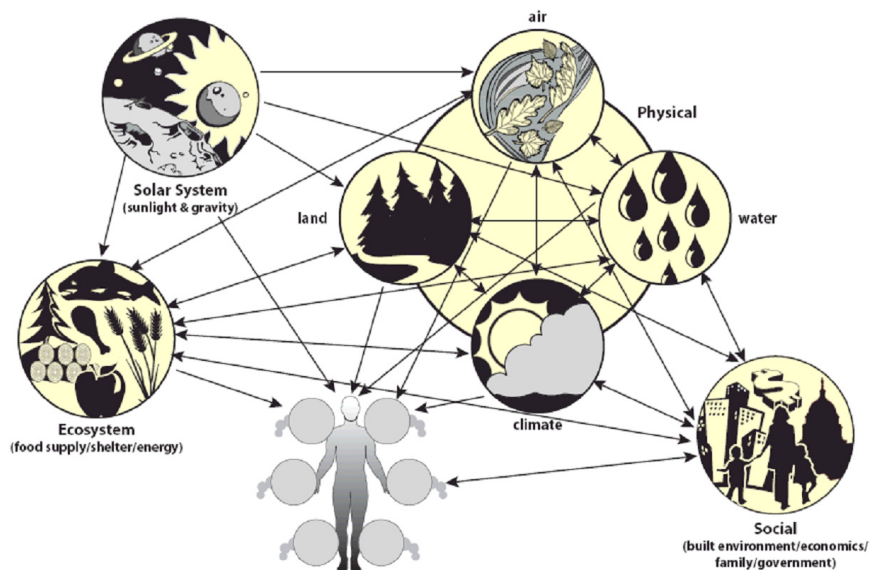


FIGURE 1-2 Basic needs, shelter factors, personal factors, and endogenous factors interact in a holistic network to determine health outcomes.

SOURCE: Reproduced with permission from *Environmental Health Perspectives*. Gohlke, J., and C. Portier. 2007. The forest for the trees: A systems approach to human health research. *Environmental Health Perspectives* 115(9):1261–1263.

tionships. Last are the endogenous determinants, such as genetics, race, ethnicity, and life history, which cannot be changed by individuals themselves.

All of these components, whether they are basic needs, shelter factors, personal factors, or endogenous factors, interact with each other, which creates a snapshot in time to determine a person's health status. The categories are further affected by the state of the physical environment and ultimately impact the health of an individual and his or her relationship with the environment. They need to be looked at from a holistic point of view, not a fragmented one, which is how environmental health decisions have historically been made.

The Need for a Holistic Approach to Decision Making

What people do in one aspect of the environment can greatly impact other aspects. For example, air quality and climate change impact human health through their interactions. Scientists and doctors have begun to see the earth's temperatures rise and, along with that, a direct effect on human and environmental health. With increases in climate change, the quality of the air may change, resulting in an impact on the ozone level and a reduction in smog clearance. In turn, such

chronic diseases as asthma may become more prevalent, a situation that places increased burden on the health care system. In addition, higher temperatures play a role in extreme weather events and natural disasters, which can wreak havoc, such as with Hurricane Katrina and Hurricane Rita as well as during the record heat wave in Europe in 2003, which resulted in significant mortality.

In the past, scientists and researchers would look for a single cause to account for global climate change, characterize it, and try to find a solution. That approach is no longer sufficient for making an assessment of risk and, in the end, an environmental health decision. Global climate change, as with many other environmental health issues, is not caused by a single factor; rather, a number of different factors will play an important role in the severity of the health impacts of climate change over the next century. Each factor will have its own set of associated risks.

Looking at the complexity of the environment on a global scale, one begins to realize that environmental health decisions have been made in a fragmented way. For example, different types of regulations for chemicals in the air contribute to air quality and climate change. Methyl mercury is regulated differently depending on the context and uses. Carbon dioxide, particulate matter, sulfur dioxide, and other chemicals are regulated independently, without assessing whether making a change to the regulation of one chemical may impact another chemical. Finally, there is the larger question of the impact of these individual regulations on air quality and climate change overall. Risk decision making for environmental health in the future will need to be based on a holistic view of the global network and its interactions.

The Global Network

What occurs in one environment or country can greatly impact another environment or country. The United States is not a solitary country immune to the decisions made in other countries—and the converse is also true. The world is becoming increasingly interdependent and, as a result, there are direct impacts of the environment on health. For example, the growing demand by U.S. consumers to have access to all types of fresh fruits and vegetables throughout the year carries with it many of the vulnerabilities of greater globalization of the U.S. food supply. Food manufacturing is also taking place in conditions that are possibly raising the risk of zoonotic diseases, which move from animals to humans (Hastein et al., 2006). In addition, while coal consumption is projected to stay static in countries of the Organisation for Economic Co-operation and Development (OECD), coal use in non-OECD states is projected to increase over the next 50 years (EIA, 2004). Yet OECD states are a contributing factor to the trend, as the manufacturing of goods is being shifted to these countries (EIA, 2007). There is growing recognition that environmental health is global. Environmental issues

in every part of the world can therefore have repercussions for the entire planet. If policy makers do not consider this broad picture, they risk making decisions that may be inappropriate to the overall goal of trying to improve human health on the planet.

Scientific Direction

With regard to the human system and how science addresses its exposure to hazards, a large body of research and testing is being performed, from the population and clinical levels to the molecular level. Although all of this science contributes to understanding the impact of the environment on health, most risk assessment is based on toxicological and epidemiological evidence and not on emerging sciences, such as genetics and toxicogenomics. Scientists and policy makers therefore need to look at the emerging areas of science to find ways to incorporate this research into the environmental health decision-making process. The ultimate goal would be to use scientific evidence to guide exploration into the environmental causes of disease and remove these hazards from the environment.

Through the use of an environment–disease interaction network, Portier's laboratory has taken approximately 500 compounds and, using genetics, created a linkage system to see how disease and environmental factors may match. Targeting the metabolic syndrome cluster illustrates the complexity involved in looking at disease and shows how closely related diseases have common etiologies. In these linkages, the chemicals and pharmaceuticals that one expects to cluster do. This type of activity and analysis focuses on genetics in relation to disease, targeting ideas for research in terms of looking at environmental diseases. Use of these types of networks and the overall use of more tailored, personalized medicine are beginning to guide scientific research.

This development is evidenced in the study of biomarkers, which are essentially indicators of disease or therapeutic effects that can be measured through dynamic imaging tests, as well as tests on blood, tissue, and other biological samples (FDA, 2006) by the federal government, including the National Institutes of Health, the Environmental Protection Agency (EPA), and the Food and Drug Administration. Furthermore, the National Toxicology Program and the EPA are using high throughput screening to set priorities and move forward with their testing program. However, without applications to the risk assessment field, these new scientific areas may lose funding priority. Science needs to continue to make strides in new research areas and to focus decision making by looking at risks in a global networked capacity that will strengthen the ability to protect public health.

ALTERNATIVES ASSESSMENT AS A STRATEGY FOR DECISION MAKING

Mary O'Brien, Ph.D., Oregon Toxics Alliance

The Need to Overcome Obstacles

The presumed goal of environmental health science decision making is to produce fewer harms to human health and the environment. However, there is a disconnect between environmental health science and decision making for environmental health. The field has made advances in knowledge of toxicology, structure activity relationships, cumulative impacts, animal and human development, and the nature and amount of toxic chemicals to which all living beings on earth are being exposed, but there is not a clear transformation of that science into health outcomes. The disconnect may be directly attributable to decision-making processes. Too often in the scientific community, among many other professions, there are many obstacles to good decision making, including a narrow power base that leads to narrow decision making and the fact that human nature is often strongly habit based, and decisions are made in ways that stifle creativity and ingenuity.

Several key elements in current environmental health decision-making processes contribute to less than optimal environmental health outcomes:

- The assumption that lack of toxicological evidence equals lack of risk. An example is the ongoing substitution of one brominated fire retardant for another, each of which has presented different environmental health problems.
- Lack of training of chemists and engineers in innovation for green engineering rather than merely for function and cost.
- The permitting of technologies and chemicals without consideration of alternatives.
- Lack of permitter training or authority to help or require the applicant to consider greener, even life saving alternatives.

Decision Making Using Alternatives Assessment

In contrast to many current environmental health decision-making processes, alternatives assessment involves four essential elements:

1. The first element is responsiveness to early warnings of health damage. There is no shortage of toxicologists, epidemiologists, physicians, neighborhood residents, or workers who have offered early warnings of environmental health damage. But some policy makers have too often justified "no responsive action," claiming that the risk has not been fully characterized. One compelling example has been the weak response of the United States to climate change despite envi-

ronmental health scientists' warnings of its trajectory toward massive species extinction, resource wars, starvation, and disease.

In order to move past this and work toward producing fewer harms, several questions are useful to ask in the face of the uncertainty surrounding early warnings. For example, is the uncertainty about the degree of harm or the existence of the harm? In other words, is the argument in a given situation truly about no harm resulting or about the precise amount or acceptability of harm? Does a claim of "no harm and therefore no change needed" seem warranted on the basis of past analogous experiences? And if health impacts are acknowledged, are pronouncements of acceptable risk resulting in a failure to search for or implement reasonable alternatives?

2. A second element is the engagement of diverse perspectives in the development and examination of reasonable alternatives for producing fewer harms. Joint examination of reasonable options is the most scientific process for decision making because the science brought by one sector will be held to the light of replicability or accuracy by other sectors. It is democratic, including both those who stand to gain money or health or both under particular options and those who stand to lose health or money or both under those same options; those who defend; and those who innovate.

The human tendency to centralize and retain power resists transparent, equitable, innovative decision making. This is precisely why diverse participation and transparency need to be mandated, as they are, for example, in the nation's National Environmental Policy Act regulations.

3. A third essential element is giving the benefit of the doubt to nature and public health. Different types of doubt exist for different types of environmental health decisions, so it is important to ask some questions about perceived or claimed uncertainty. For example, who is the beneficiary or beneficiaries of continued uncertainty? What incentives exist to resolve uncertainty in favor of the status quo? Alternatively, can incentives be offered to favor environmental health advances in the midst of uncertainty about the precise nature of harms?

One strategy is imposing a deadline when alternatives must be instituted for a given technology to be put in place or milestones when a particular issue or decision has to come under review again. For example, the goal of a 90 percent reduction in auto emissions from pre-1968 levels by 1975 led to the development of the catalytic converter, which has been considered one of the greatest environmental successes of the past century (Palucka, 2004).

4. A fourth critical element is the monitoring of results for successes and new early warnings, which becomes the foundation for improvements in decisions. Monitoring should be a central and early component of decision making. If the likelihood of monitoring for an outcome is low but the environmental stakes are high, then the initial decision should build in time-certain reevaluation in response to monitoring.

Incorporating responsiveness to early scientific warnings, entertainment of

diverse solutions, the favoring of environmental health amid uncertainty, and monitoring into environmental health decision making will increase the odds of optimal human health outcomes.

BEYOND PRECAUTION

*Bernard D. Goldstein, M.D., Professor,
Department of Environmental and Occupational Health,
University of Pittsburgh Graduate School of Public Health*

Public Health Approach

Many environmental health decisions have been made from what others have described as fragmented, narrow, “reductionist” approaches. With the recent resurgence of awareness in many environmental areas, such as global climate change, the timing is right to refocus efforts on making decisions that benefit the health of the public by addressing issues holistically. Three approaches are necessary to make environmental health decisions from a holistic or public health perspective: bipartisan or global environmental policy, a systems-based approach, and science that is focused on answering the most important questions.

A holistic decision making process can be best achieved by implementing a public health approach, which is defined by three key factors. First, policy makers need to take responsibility for all outcomes, whether good or bad. Second, they must utilize the core public health functions of assessment, assurance, and policy development. Third, the right target needs to be set to link the research agenda to the data needs, so that the research is relevant to both the scientist and the policy maker.

Trying to solve a problem without using a systems or public health approach often creates a secondary problem or unintended consequence. For example, most people in public health are familiar with the replacement of microbially contaminated surface drinking water with arsenic-contaminated groundwater in Bangladesh. Furthermore, central to a public health approach is engagement of the public, as solutions need to be relevant from a community perspective. Failure to provide the public with reasons to care about an environmental issue can therefore result in a policy failure.

Caution in Applying the Precautionary Principle

The precautionary principle, developed as a result of the need for action in the face of scientific uncertainty, is an important part of environmental health decision making that is advocated by the European Union (EU). Through their adoption of this principle, the EU is currently undertaking a reevaluation of the relationship between individuals and their community and, in a broader sense,

their consortium of nations. The main tenet of this principle, the need to act in the face of scientific uncertainty, is articulated in the Rio Declaration on Environment and Development (United Nations, 1992). According to the European Commission, this principle should be applied whenever the “scientific data are insufficient, inconclusive, or uncertain and where a preliminary scientific evaluation shows that potentially dangerous effects for the environment and human, animal or plant health can be reasonably feared” (EU, 2008). While attention should be paid to this idea, there is also the need to step back and examine what the implementation of the precautionary principle means to the overall practice of public health. If policy makers are going to rely on precaution, then they need to authorize research to monitor and ensure that a precautionary approach is necessary and has succeeded. Furthermore, the research agenda should be linked to objectives of data needs and data quality.

One of the primary arguments for using the precautionary principle in order to act in the face of uncertainty implies that without this principle there is an absence of action in the face of scientific uncertainty. This, however, is not the case. For example, in the 1970s, the United States banned the manufacture of polychlorinated biphenyls (PCBs) despite strong opposition by industry and clamor that there was no scientific evidence showing harm caused by these chemicals. Industry continues to take this position, yet because of the ban, humans and the environment have much lower levels of PCBs than they did at the time of the ban. The lower levels of PCBs are a result of actions taken despite scientific uncertainty, but without stated recourse to the precautionary principle. One therefore needs to question what this principle adds to already existing public health concepts. Supporters of the precautionary principle sometimes assume that scientists speak with one voice about environmental policy decisions. This is also not the case—nor, in U.S. society, do scientists unilaterally make policy decisions.

The EU actions on aflatoxins illustrate why the precautionary principle may not always be used for its appropriate purpose of protecting public health and the environment. It is scientifically accepted that aflatoxins are a family of toxins capable of producing liver disease and liver cancer. The fungus producing aflatoxins is widely distributed in foods, particularly among groundnuts and cereals, and is known to grow in wet climates and places with delayed harvesting. The EU has used the precautionary principle to enforce the most stringent standard in the world for aflatoxin. This standard has resulted in favoring European growers to the exclusion of \$700 million a year worth of sub-Saharan African products (Majone, 2002). A less stringent standard, whose public health significance has been rejected by the Joint Expert Committee on Food Additives of the World Health Organization/Food and Agriculture Organization of the United Nations, would result in a difference in risk of developing liver cancer of less than one case a year in Europe (Majone, 2002). This example and many others from the agriculture sector, including greenhouse implications of noncompetitive farming

and methane production, call into question the primary motives for using the precautionary principle. The question could be asked if it is really preventing or reducing risk in the face of uncertainty, or if it is being used to build trade protection walls around Europe. The use of precautionary principle also calls into question how society determines what a significant health benefit is as well as which issue has priority over another. All of these questions need careful analysis and exploration before applying the precautionary principle.

Connecting Science and Policy

A systems approach is critical to addressing environmental justice. Three truisms are that there are more environmental hazards in disadvantaged communities, that there are more individuals with poor health in disadvantaged communities, and that individuals with poor health tend to be more susceptible to environmental pollutants. To scientifically evaluate the potential for environmental health problems, the focus should be on the people who are most at risk from environmental pollutants, in whom effects are most likely to be seen. Performing such studies requires community involvement and a new approach to environmental health research and decision making—one that looks at the entire system and not just the individual chemical. Ultimately, such an approach connects science and policy.

Session Discussion: Applying a Systems Approach

There can be a fundamental conflict between science and society. The scientist wants to make decisions using all the available evidence in as rigorous and objective a manner as possible; society is constantly grappling with ways to express what is an acceptable and unacceptable risk. The fundamental trade-off that is occurring between what society wants and what science wants is one that challenges the decision-making process. Some participants suggested that new approaches or understandings of the conflict may help improve risk assessment and environmental health decision making.

The central theme of the three presentations was the need for a systems approach to environmental health decision making that encompasses the increasing complexity of the environment and avoids overburdening the thought process behind decisions. This theme generated ample discussion by the panel and participants about how to implement such an approach. O'Brien suggested that in order to avoid some of the complexities and not get bogged down, policy makers need to think much more broadly about a decision. Goldstein suggested that additional attention needs to focus on the data quality objective and that complexity can be reduced, as can the overall length of the decision-making process, if the research has an objective and is not being undertaken just because a topic can be researched. Taking this a step further, Portier added that there may be a need to

revisit certain issues and decisions in order to see whether the scientific process is using information in a way that addresses the complexity.

While many participants echoed the usefulness of a systems approach to decision making, questions arose regarding the implementation of such an approach. For example, does a systems approach include additional steps or further data analysis in the decision-making process compared with the original method? Participants questioned what criteria need to be developed to determine how to incorporate this new information. Is there a standard, and if so, what is it? Portier countered that it wasn't necessary to quantify all the data and links in the systems approach, but rather it is sufficient to know qualitatively what the links may be and how they could impact the decision-making process. Goldstein simplified this even more by explaining that a systems approach does not need to include complexity unless it adds value to the decision.

A second challenge to the systems approach is whether the use of complexity itself as a tool to obfuscate and thwart a particular argument could occur by various stakeholders. While this is possible, O'Brien noted that a systems approach should engage many diverse sectors in an ongoing conversation on a particular problem, essentially a collaborative process. To this point and based on his experience, Goldstein raised questions as to how to make the outcome a consensus that moves the science forward. He also pointed out the importance of a policy maker or science agency deciding that there has been sufficient input solicited and adequate data gathered to make a decision. O'Brien countered that the collaborative group itself needs to be linked to action and that there is a need to put limits on the data process. She further suggested that milestones could be set for revisiting decisions, if needed.

Scientific Issues in Environmental Health Decision Making

Good environmental health decisions require using all available scientific information. One part of this process includes a thorough and rigorous examination of all scientific evidence, including the consideration of the type of research (i.e., case study; cohort study; double blind, randomized control), and understanding the uncertainty in the existing data. Furthermore, science is a dynamic process and not static. There will always be new information to consider once a decision is made, which in some instances may alter the landscape for making decisions based on science. This chapter captured the presentations and discussion on how to weigh evidence in decision making, working with variability and uncertainty in the data, the use and misuse of science in decision making, and when policy makers should revisit decisions based on advancing science.

EVALUATING WEIGHTS OF EVIDENCE FOR DECISION MAKING

*J. Michael McGinnis, M.D., M.P.P., Senior Scholar,
Roundtable on Evidence-Based Medicine, Institute of Medicine*

Evidence as Science Along a Spectrum

The first step in understanding how evidence relates to scientific decision making is to reflect on the nature of evidence as science. In this respect, just as science may be a tool less for finding the answer than for revealing the next question, so may evidence be a tool less for making a decision than for informing its context.

Evidence is neither static nor formulaic. Its character is not binary, but evolutionary in nature. McGinnis's current area of focus, evidence-based medicine, may be described as a systematic march to care that is most effective, personal, and appropriately tailored to circumstance—in effect, a march down an evidence

spectrum in which the opposite poles represent, on one end, the nonexistence of evidence and, on the other, the evidence that is irrefutable. The challenge is therefore to determine the decision rules at play at various points along the path to ever stronger evidence.

Forms and Standards of Evidence: A Hierarchy

The decision rules will be forged by the forms of the evidence and the standards applied. In the biological sciences, both the forms and the standards take on a certain generally accepted character. The forms of evidence include biochemical data, animal studies, population studies, and individual studies. The standards of evidence relate to such issues as the consistency, strength, specificity, response of the association, and the biological plausibility. Together, these serve as a general framework for assessing health interventions.

In the case of medical care, for example, evidence is usually information from clinical experience that has met an established test of validity, with the appropriate standard determined according to the requirements of the intervention and the clinical circumstance. Typically, evidence of clinical effectiveness is conceptualized as a pyramid, in which the base of the pyramid contains the least scientifically sound type of evidence formation—professional ideas and opinions (Figure 2-1). Moving up the pyramid are ever-stronger types of evidence: case reports and case series; case-control studies and cohort studies; toward the top of the pyramid, randomized controlled studies; and, at the apex, randomized, double-blind, placebo-controlled studies—often called “the gold standard.”

While this hierarchy of evidence has been widely accepted and used in the medical community for more than a decade, its real-world application is less than perfect. It is important to look at the nature of evidence needed in the context of whether the motivating question focuses on safety, efficacy, effectiveness, or efficiency. Does the intervention under study cause harm? Does it work? Does it work in context? Is it a sound use of resources?

There is a growing recognition of the need to view evidence in a more nuanced and detailed fashion. Rather than a pyramid or hierarchy, a more comprehensive and systematic view of clinical evidence emerges when evidence is viewed through an evidence matrix, which is structured according to levels of certainty juxtaposed with levels of likely benefit, in order to provide a framework for better understanding which interventions would provide the greatest impact or greatest likelihood of impact (Pearson et al., 2003). Insight into the possible levels of impact can then be used to inform, in variable fashion, the many different types of decision-making challenges often faced in health care, such as regulation, medical coverage, guidelines, indicators used in quality care assessment, and even individual-level decisions (Teutsch, 2008). Considering the multifaceted dimensions of the application of evidence in medical care offers a sense of the complex nature of factors involved in using evidence for decision making.

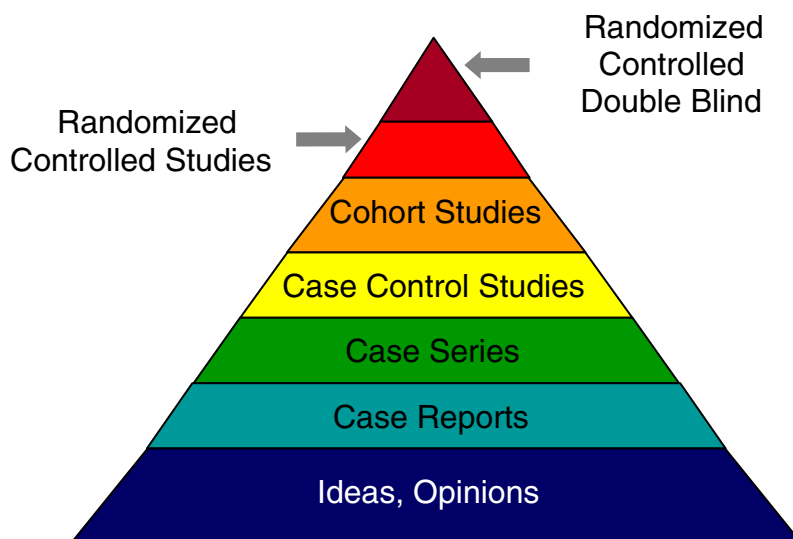


FIGURE 2-1 Evidentiary hierarchy of weighing evidence.

SOURCE: Copyright SUNY (State University of New York). 2004. Guide to research methods: The evidence pyramid. <http://library.downstate.edu/EBM2/2100.htm> (accessed November 11, 2008).

Evidence in Population Health

In population health matters (compared with personal medical care decisions), considering the roles and nature of evidence in policy decision making can be even more complicated. Because in population health, effectiveness is more a function of the nature of the intervention than the nature of the evidence, the evidence standard will vary dramatically according to the nature of the intervention. There is also a spectrum of factors at work in the decision making for population health, but that spectrum relates to the nature of the intervention—with purely environmental interventions at one pole (e.g., water supply fluoridation) and purely individual interventions at the other (e.g., behavioral change interventions designed to encourage smoking cessation, increased physical activity, a change in dietary habits).

Making decisions at the population level may require juggling fewer data points, but their powerful impact requires that particular consideration be given to understanding several other factors: the potential health, economic, and social consequences of inaction; the potential health, economic, and social consequences of action; the formal characterization of uncertainties and mapping strategies as uncertainties resolve; and the design of systematic assessment and feedback as part of the intervention.

Although population health and clinical medicine are two very different disciplines, there are certain commonalities between the approach to evidence in clinical arenas and in population health arenas. Both gravitate toward simple answers in complex circumstances and the need to consider the overall context in which the evidence or intervention would apply. The interventions need to be transparent about the decision rules at various points along the evidence spectrum, and at the same time communicate meaningfully and constantly about the state of the evidence. As seen throughout science, evidence is dynamic in nature and therefore needs a strategy to accommodate new insights. Perhaps the most important commonality related to the interpretation of evidence in both clinical and population health settings is the centrality of effective communication. Too often the concept of risk communication is not well understood, yet the ability to explain the nature of risk and the evolving nature of the scientific process is vital to enabling the public to understand how decisions are made in a scientific context.

There is an inherent tension between an individual's natural desire for the definitive answer and the nature of the scientific process, in which it is well known that nothing is foolproof. Communicating this tension effectively on both an individual and a population basis is fundamental. Although teaching institutions and other avenues have not yet been able to engage society in learning the theory behind risk, there is a need to continue to improve how the evolutionary and dynamic nature of evidence is communicated so that the public can better understand the workings behind a decision. With the continual challenge of misinterpretation of evidence by media and others, an effective communication strategy is vital to moving evidence to the point of decision making, whether for individual, clinical, or population-wide interventions.

THE ROLE OF UNCERTAINTY AND SUSCEPTIBLE POPULATIONS IN ENVIRONMENTAL HEALTH DECISION MAKING

*Dale B. Hattis, Ph.D., Research Professor,
George Perkins Marsh Institute, Clark University*

Problematic Concepts: Uncertainty and Variability

Starting in the 1980s, two probabilistic concepts, variability and uncertainty, began to be associated with the science of risk analysis. These two concepts can account for differences made in technical assessments and have different implications for policy decisions. Variability consists of the real differences among people or among cases in some parameter that affects risk. For example, how much exposure one individual may have to a chemical or substance, how much of a chemical or substance one person may intake compared with another person, and how much of that chemical or substance is activated by metabolic enzymes

all contribute to individual risks. The concept of uncertainty is the imperfection in knowledge of the true value of a parameter for either an individual or a group. Both of these concepts should be taken into consideration for purposes of risk management decision making, but for very different reasons, as they have different implications for both information gathering and analysis (see below).

Uncertainty and Variability: Different Yet Important

In order to understand the implications for the future of risk management decision making, the underappreciated features of both concepts need to be explained and understood. First, variability, the standard statistical descriptions of data (e.g., the standard deviation), tends to overstate real variability by including measurement errors. These measurement errors spread the observations out further from each other than the underlying reality of the differences among individuals. Currently, there are not many well understood or commonly used statistical methods to disentangle the measurement errors from the real variability. A second underappreciated feature of variability is seen during priority setting for interventions. Here, the more predictable variability there is among a number of categories for intervention, the more benefit can be derived by focusing resources on high-scoring categories for intervention.

In both the application of standard statistics and priority setting, the concept of uncertainty works in the opposite manner. First, standard statistical descriptions of data—for example, standard errors—tend to radically understate the actual level of uncertainty by excluding unsuspected systematic errors that affect all data points in common. Such systematic errors include the unrepresentativeness of population samples or error resulting from a miscalibrated instrument, among a number of other sampling inaccuracies. In addition, incomplete assessment of model errors is an important threat to the accuracy of uncertainty assessment. In a priority-setting system, greater uncertainty in priority scores suggests greater spreading of resources to lower scoring categories or interventions. Essentially, better data on lower priority categories improve information for later decision making, and the value of that information is greater if there is greater uncertainty initially.

Tied into the concepts of uncertainty and variability is the idea that uncertainty can be quantitatively characterized by reducing it to an observable variability among putatively analogous cases. Many times scientists claim they do not have information about a certain aspect of a chemical or substance, yet information can be assembled on similar chemicals or substances to then extrapolate to the original chemical in question. This approach is not without difficulty, however, as there is a need for rules for making the analogies—for example, defining the reference groups to derive uncertainty distributions for particular cases. While this may be a challenge, it does provide a way forward for health scientists to learn to reason quantitatively from available evidence relevant to specific uncer-

tainties. Doing so requires the creation of databases and applying the information derived from these databases to the risk analysis process.

Evolution and Implications of Concepts and Practices: Susceptible Populations

There has been an evolution of concepts and practices in the representation of variability (Hattis, 2004), especially for the study of susceptible populations. The older, obsolete view is a categorical representation of variability only in the form of discrete susceptible subgroups. This is problematic as it does not account for the variability within a susceptible group. Using the example of asthmatics, it often happens that, for example, an air pollution study makes measurements of susceptibility compared with nonasthmatics but reports the data only in the form of group means. One may say that individuals with this problem have been studied and therefore information is known about their sensitivities, but that view does not take into account the variation from one asthmatic to another. The current or usual practice for mathematical representation of variability is a simple application of assumed distribution of form without assessment of fit. As science moves forward, the best practice for this would be distributional forms chosen on the basis of mechanistic theories about how the differences among people or cases arise. Without such, one is more or less making a decision using measures that do not reflect the causal processes producing the differences of interest. Making projections beyond the data at hand is much more reasonable if it reflects some mechanistic theory.

This has large implications for the information used in policy making. Using the older, obsolete view can cause the dismissal of “hypersensitive” populations. While current practice does allow for susceptible subgroups with a defined safety threshold, there is no single factor that can capture a distributional response. Therefore, what is needed and obtained by using best practice is the quantitative analysis of how many people and which groups of people are at how much risk from various policies—ideally with some statement of associated confidence (Hattis, 2004).

In terms of technical aspects of variability measurement and analysis, the older, obsolete view is to deliberately restrict the sample and not have it correspond to what would truly be representative of the population. For example, it has been common for initial drug studies to have only young, healthy white men instead of an older, diverse population. This does little to tell the public how a particular drug will affect a wider population. A more current usual practice is to use observations in haphazard or convenience samples to include all readily available subjects but without attention to factors that could affect the primary parameter under study. As for the foreseeable best practices, they would include a stratified random sampling, with the strata constructed to represent groups expected to

be different in the studied parameter. This would also include oversampling of relatively rare subpopulations of special interest.

Future Direction and Motivation

Ultimately, there is a need to define variability and uncertainty distributions as integral parts of risk analyses for both analysts and managers. Four considerations will make this increasingly important in the future. First, legal cases involving environmental issues are increasingly calling for the recognition that some finite rates of adverse effects will remain even after implementation of reasonably feasible control measures. Second, societal reverence for life and health means making the best decision with available resources to reduce harmful effects. Third, responsible social decision making requires making estimates of how many people are likely to experience how much harm for effects of specific degrees of severity and with what degree of confidence. Last, the traditional multiple-single uncertainty factor system cannot yield estimates of health protection benefit that can be juxtaposed with the costs of health protection measures. It should be expected that a younger generation of analysts will not accept the older, obsolete procedures that fail to provide a coherent way to use distributional information that is clearly relevant to factual and policy issues. Also, this generation will have greater mathematical and computational facility, particularly as biology becomes quantitative systems biology. In addition, the legal process will demand the use of best science, and newer information and communication tools will foster increasing habits and demands for democratic accountability and transparency.

Hattis and Anderson (1999) proposed some risk management criteria for environmental health decision making that draw on considerations of uncertainty and variability. First is fair process—open disclosure and, to the extent practicable, voluntary acceptance of risks. The second is equity in the distribution of risks in relation to the benefits derived from accepting the risk—ideally, redefining criteria of significant risk in terms of individual variability and uncertainty (no more than x probability of harm for the y th percentile of the population with z degree of confidence). Third is a goal for government agencies to achieve the greatest possible effectiveness to reach health and safety goals using limited resources. And fourth is the ethical principle in medicine of “First, do no harm.” This means there is an obligation to assess the likely comparative consequences of policy prescriptions for environmental problems, selecting only interventions that have a reasonably high probability of producing overall benefits.

THE USE AND MISUSE OF SCIENCE IN DECISION MAKING

*Rena Steinzor, J.D., Jacob A. France Research Professor of Law,
University of Maryland School of Law*

The Intersection of Science and Law

A central tenet in scientific decision making is that any decision rendered needs to be based on the best available science, which “depends upon a disinterested and transparent scientific process” (Steinzor and Shudtz, 2007). Scientific decisions should be made using the weight of the evidence, yet in today’s world, scientific decisions are often called into question by the legal profession, seeking to influence an outcome. The pathway from science to science policy is often perceived by scientists and the public as a straightforward one, as the merits of the science have been vetted during peer review in the publication process (Wagner and Steinzor, 2006). However, this is not always true.

The cultures of law and science are vastly different and at times clash with one another, which puts pressure on science when it is applied in a legal setting. On one side is science, which involves a quest for truth through the collection of evidence. That version of the truth is developed through a largely collaborative process, which has a built-in incentive to more deeply explore and test a hypothesis due to the nature of the scientific process itself. After careful, and at times repeated, testing, scientists ideally arrive at a particular explanation or propose a line of reasoning, which is based on the weight of the evidence. In the environmental field, this analysis often involves applying evidence from chemical structures and animal studies to human epidemiological evidence. Data are collected and reviewed by a multidisciplinary team of subject matter experts, who, after taking into account confounding factors and scientific error, try to reach a consensus on a particular scientific issue, which may then be accepted by the larger scientific community and the public.

On the other side is law, which trains individuals to be primarily concerned with winning and losing. Wagner and Steinzor (2006) have argued that “rather than incorporating science into policy dispassionately and using research to further a quest for truth, the legal system makes most decisions through an adversarial process driven by affected parties who interpret and re-interpret the science to prove that they should ‘win’” (p. 4). In fact, the legal profession instructs lawyers to take an issue and look for a version of the truth to present to a decision maker that contrasts with an opposing side’s version of the truth on that same issue.

The differences between these two processes are most profound in the regulatory arena, where, once a scientific decision has been reached, it can then be subject to extreme scrutiny and deconstruction by the legal profession in its quest to argue for one policy position over another. Lawyers often use a technique referred to as “corpuscularization,” which undermines a body of evidence by disassembling each individual study in order to discredit it from inclusion in the

overall data set. This clash presents a threat to achieving clean and independent science, as each component of scientific study is dissected to the point that the entire premise on which a decision was based is undermined. This technique can create important data gaps and is in stark contrast to the weight of the evidence approach used by scientists (Wagner and Steinzor, 2006).

Another threat to the integrity of scientific decision making is the conflation of risk assessment and risk management. The Office of Management and Budget's attempt to combine these stages in decision making has largely failed because it is a "one size fits all" approach to the widely different missions and goals of the federal government agencies (OMB, 2006). It is a transparent attempt to ensure that scientists consider the economic impact of a decision to control risk at the beginning, rather than at the end, of the decision-making process, at the same time that they describe and characterize the risk, raising the specter that some risks will never be deemed significant because they would cost too much to control.

The issue of perchlorate is one example. Perchlorate is a highly soluble type of rocket fuel that has been found in the drinking supply in certain sections of the United States. Economic estimates for environmental cleanup are quite high, resulting in the scientific research agenda being subverted and crucial research left undone. The military has argued that scientists should take national security into account in assessing risk, since this chemical is used by the military. What this means is that the use of economics to undermine objective scientific evaluation is inappropriate. The only truly scientific decisions are ones reached on the basis of the weight of the evidence.

RATIONALE FOR REVISITING AN ENVIRONMENTAL HEALTH DECISION: THE NATIONAL TOXICOLOGY PROGRAM

*Kenneth Olden, Ph.D., Sc.D., Principal Investigator,
The Metastasis Group, Laboratory of Molecular Carcinogenesis, NIEHS*

Four Fundamental Decisions

The National Toxicology Program (NTP) is charged with overseeing four fundamental decisions on the health effects of chemicals. First is what research exists and what research is needed to support the nation's toxicity testing program. The NTP has made great progress in developing transgenic animal models as well as furthering the understanding of toxicogenomics, that is, the genetic basis for differences in response to a toxic chemical. Second is which specific exposures should be studied and what are the best testing systems. One way the NTP has approached this is through the creation of the Interagency Coordinating Committee on Validation of Alternative Methods, which "promotes the scientific validation and regulatory acceptance of toxicological test methods that more

accurately assess the safety or hazards of chemicals and products and that reduce, refine (decrease or eliminate pain and distress), and/or replace animal use” (NTP, 2008). Third is which exposures to evaluate and report as risks to human reproduction and development. Fourth is the decision about what should be included in the *Report on Carcinogens*—a congressionally mandated document. All of these decisions are made using a public and prescriptive process that is attentive to the input received from the scientific community, policy makers, the American public, and other stakeholders.

Report on Carcinogens: Criteria and Process for Listing

The *Report on Carcinogens* (RoC) is a congressionally mandated document “prepared by the NTP for the purpose of identifying substances, mixtures of chemicals, or exposure circumstances associated with technological processes that cause or might cause cancer and to which a significant number of persons in the United States are exposed. Listed in the RoC are a wide range of substances, including metals, pesticides, drugs, and natural and synthetic chemicals” (NTP, 2005). The chemicals on this list go through a very extensive public review, and additions are made after careful scrutiny and consideration of all available science (Table 2-1). Specifically, in order for a chemical to be listed in the RoC, it would either be a known human carcinogen or is reasonably anticipated to be a human carcinogen.

TABLE 2-1 *Report on Carcinogens* Listings

RoC Edition	Year	Number of Substances Listed		Number of Substances Delisted
		<u>Known</u>	<u>Reasonably Anticipated</u>	
			Chemicals or Industrial Processes	
First	1980	26		
Second	1981	25	63	
Third	1983	23	98	
Fourth	1985	30	119	
Fifth	1989	23	140	4
Sixth	1991	26	148	2
Seventh	1994	27	156	
Eighth	1998	29	169	
Ninth	2000	48	170	2
Tenth	2002	52	176	
Eleventh	2004	58	188	

SOURCE: Olden, unpublished.

The process of listing a chemical in the RoC has gone through several revisions to ensure that the criteria used for such categorization are accurate. Starting in 1985, the RoC process itself began to allow for larger public input and increased transparency. The most significant changes resulted in the 1994 and 1996 reviews. In fact, the strength of the NTP is a direct result of the amount of public input factored into the decision-making process. Two other important changes to the RoC are a change in publication times, from annually to every 2 years, and the decision to use all of the available science as the criteria for inclusion in the report—for example, the allowance for the utilization of knowledge of mechanisms and structure/activity relationships in assessing risk. This change provided a set of criteria to determine that if a chemical or substance has a structure or activity comparable to a chemical already listed in the report, it is reasonable to assume that the chemical in question would also be a known or reasonably anticipated human carcinogen, even if all of the data needed to draw such a conclusion are still not accessible. Other criteria or kinds of evidence used in making the listing decision include experimental studies in animals, epidemiological studies in animals, and mechanistic studies. Essentially all available science is used to make a decision regarding the listing of a chemical in the RoC.

Reasons to Revisit

A decision to list a chemical in the RoC does not mean that it cannot be reconsidered. As science evolves and new information is discovered about the harmful, or not harmful, effects of a chemical, there may be circumstances for reevaluating it (see the saccharin case study below). First and foremost, it is the evolution of new science that may provide evidence in support of either upgrading a chemical from one that is reasonably likely to be a carcinogen to one that is a known carcinogen, or downgrading or removing it altogether from the RoC. A second circumstance is if the exposure has been eliminated because of removal from the market or to effective environmental control, so that a significant number of people are no longer being exposed to an environmental agent. Through constant revision and public evaluation of the science and evidence, the decision to delist a chemical has been made nine times since 1980. Since the original listing of these chemicals, the science evolved over the intervening years to show that the evidence was not substantial enough to continue to include the chemical in the RoC as a reasonably anticipated human carcinogen. Chemicals have also been removed from the list because they went out of commercial use, such as aramite and cycasin, thus eliminating exposure. Finally, there have been chemicals reviewed but not recommended for listing in the RoC. All of these decisions were made taking into account the evolving nature of science and discovery of new evidence to trigger a reassessment of data.

Case Study: Saccharin

One example of the use of evolving science and evidence to call for, and ultimately inform, the decision-making process for chemicals in the RoC is that of the artificial sweetener saccharin. The original reasoning behind the listing of saccharin on the RoC was based on the weight of the scientific evidence at the time. There was evidence, in the form of experimental animal data, demonstrating that use of this chemical caused urinary bladder cancer in male rats (HHS and NTP, 2005). This chemical was therefore listed as reasonably anticipated to be a human carcinogen. Over the intervening years, evidence came to light that led the scientific community to call into question the carcinogenic effects of saccharin, and a decision was made to reassess its listing (HHS and NTP, 2005).

After careful review, several pieces of evidence were considered in the delisting of saccharin from the RoC. First, although there was evidence for the carcinogenesis of saccharin in male rats, there was less convincing evidence in female rats and mice (Arnold et al., 1980; Taylor et al., 1980). Second, studies indicated that the observed urinary bladder cancers in rats were related to the physiology of the rat's urinary system and that the damage to epithelial cells lining the bladder led to an increase in cell growth in the rat (Sweatman and Renwick, 1979). Third, results of several human epidemiological studies showed no clear association between saccharin consumption and urinary bladder cancer in the general population compared with diabetics, who presumably consume greater amounts of artificial sweeteners (Armstrong and Doll, 1975). Fourth, saccharin is essentially nonmutagenic in conventional bacterial assays and does not bind to DNA (Ashby, 1985; IARC, 1987; Whysner and Williams, 1996), both of which are important predictors of carcinogenicity. This example illustrates the reasons for revisiting decisions based on the evolution of science.

SESSION DISCUSSION: WEIGHT OF THE EVIDENCE IN SCIENCE VERSUS LAW

Evaluating the weight of the evidence in order to make credible decisions based on a full set of data is in the interest of all scientists as well as the public. However, how to evaluate and ultimately incorporate the weight of the evidence in the scientific decision-making process is an issue of current debate in the scientific community. Making a decision based on the totality of the evidence should be the standard for the decision-making process, argued Hattis and Olden. However, there is concern about the growing disconnect between the legal process and the scientific process, even to the point at which science is under attack and the use of widely accepted scientific criteria, such as animal studies, is even called into question. This disconnect illustrates the inherent tension between society's desire for a definitive answer and the nature of the scientific process itself, which is one of slow evolution, said Hattis. The legal system has increasingly chosen

to view the expression of scientific uncertainty, even in small amounts, as cause for alarm and deconstruction.

In order to preserve the scientific process, there is a need to communicate better the evolutionary and dynamic nature of evidence involved in the scientific process, so that it is well understood by the public and is less vulnerable to dissection in a legal setting, said Hattis. Explaining the scientific process may include applying different standards of proof in legal settings, so that the expression of uncertainty by a scientist does not mean the end of a case or does not become fodder for the opposing side. One possible solution to the growing question of scientific uncertainty and the disconnect between the scientific and legal processes is that of transparency and communication, noted McGinnis. A call to improve the way in which the evolutionary and dynamic nature of evidence is communicated to the public needs to take place, so that the data process and evidence are not so vulnerable in a courtroom setting.

Conflicts of Interest, Bias, and Ethics

Conflict of interest has been the subject of discussion and concern in many areas of science. With the increased reliance on funding from sources outside of government, there has been renewed interest in the debate. Avoiding conflict of interest in order to achieve sound, unbiased science is in the vested interest of the scientific community as well as the general public. However, creating a system in which scientific decisions are made in an ethical manner while free of conflict and individual bias is a challenge. The workshop therefore explored how to identify, manage, and, in some situations, eliminate the conflict.

GENERAL OBSERVATIONS REGARDING CONFLICTS OF INTEREST

Thomas H. Murray, Ph.D., President, The Hastings Center

Conflicts of interest are ubiquitous. In and of themselves, conflicts of interest are not necessarily a failing, but rather a description of a set of circumstances that can take many forms and be manifested in many settings. They are usually based on situations in which there is reliance on the judgment of an outside party with some very specific professional expertise. Exercise of that judgment should promote the interest of a party, who may be an individual (e.g., the patient in a doctor-patient relationship) or, on a broader level, an institution. The judgment that the professional owes the client, patient, or institution can include specific recommendations, but often it includes just interpretation of information for the receiver (the party to whom loyalty is owed), who does not have the necessary expertise to understand the information without assistance.

Often there are questions as to who is the primary party to whom loyalty is owed. For scientists on a panel of the Food and Drug Administration, for example, it isn't immediately clear to whom they owe their primary loyalty; this is more complex than the doctor-patient example. Even at the largest relationship

level—a scientist conducting research—the primary loyalty isn’t always clear. Is it to the scientific community, the public, or policy makers? While this is not an easy question to answer, there is a shared understanding that scientists have profound obligations and therefore need to avoid being improperly influenced by extraneous considerations—most visibly, financial ones.

Types of Conflict

A number of factors can make one type of conflict more significant than others:

- Intensity of the conflict
- Expectations and transparency
- Conflicts of commitment
- Power and status
- Financial aspects

The intensity of the conflict—the profound “push or pull” on a person providing the advice—is important. For example, a large sum of money can be a more worrisome source of conflict than a small token. However, there are certain types of conflict that people are known to have and society is willing to accept if these conflicts are both expected and transparent. One such example is the doctor-patient relationship, in which the patient knows a doctor is being paid to give advice and provide an opinion. Because this relationship is open and transparent, it causes less concern about the intensity of the conflict. In other situations, in which a conflict that is expected is not disclosed, this “hidden” nature may take on a greater level of importance and may be seen as an attempt to keep an issue from the public.

While society tends to focus on financial conflicts of interest because they are the most visible and measurable, other types of conflicts can be quite powerful. Conflicts of commitment—being employed by one organization yet having other interests competing for time and attention away from the primary point of employment—have been cited as a concern at the National Institutes of Health and other government agencies. The question was how committed an intramural investigator was to his government job when he was making \$150,000 a year above his salary from consulting and other commitments. Another form of conflict, at times overlooked, involves status and power as prime motivators.

Most of the time and effort put into creating rules and guidelines focuses on a larger set of concerns about the influence of power and money on public policy decisions. It is widely agreed that these decisions should be based on an unbiased evaluation of the weight of scientific evidence. Examples range from decisions about the regulation of drugs to the regulation of workplace or environmental toxins.

In conclusion, to say that someone has a conflict of interest is not a moral criticism, but rather a description of a set of circumstances. That person has a primary interest that he or she needs to fulfill, although other interests may push or pull the person in different directions. A moral failure would be if the person neglected their primary interest and allowed these other interests to rule.

Values of Science and Impact on Policy

The values that govern scientific inquiry are not necessarily in line with the values that govern policy making, because they have different purposes. There is an inherent conservatism in the way science is taught and practiced. Scientists are taught not to go beyond the data. This strict emphasis on the data can often be used to inform policy decisions. However, this conservatism can also be used by those with an interest in denying that a certain relationship exists. Policy should be informed by the best science possible, yet in some situations, consensus cannot be reached. The absence of consensus does not mean there is insufficient evidence to warrant caution and regulation.

For example, opponents of regulation called into question just how much data was needed to define the exact risks of asbestos exposure. In the rule-making process surrounding asbestos, both sides agreed that the science was not definitive in answering what exposure levels should be permissible, which led to differing views to solve the problem. Opponents of strict regulation, the asbestos industry and its allies, argued that in the absence of conclusive scientific evidence, exposures at the level in question were not harmful and the limit should be set significantly higher. Those concerned with the health of workers argued from the identical evidence that the value of protecting health, when the threat was plausible if not definitive, meant that permissible exposure levels should be set very low. This was an argument over what could be called “allocating the burden of uncertainty.” Such arguments are typical when public policy confronts scientific data over causal relationships, whether they involve environmental or occupational hazards or global warming.

The misuse of scientific information in making, interpreting, and enforcing public policy is illustrative of the concern regarding the overall issue of conflict of interest. For example, uncertainty about the data can become magnified and misrepresented. This is true even though the nature of the scientific endeavor may not lead to full agreement and acceptance by all parties. Another example of the broad concern is the impact of money and power on the generation of scientific information and, in some cases, the selective generation of scientific information. An example is the tobacco industry-sponsored research on the relationship between viruses and cancer, presumably undertaken to deflect attention away from cigarettes as a cause of cancer.

Managing Conflict to Create the Best System

Several aspects are key in detecting, managing, and addressing all types of conflict of interest, including those financial in nature:

- Clarity
- Simplicity
- Fairness
- Predictability

When there is clarity about what constitutes a conflict because criteria and definitions have been set around types of relationships, there is greater acceptance of and adherence to the policies set forth by an organization. Confusion begets indifference and inattention. Next, a well-working system simplifies the issues that must be considered. For example, when clinical investigators are working under two types of federal regulations, they may be confused about which regulations to follow. In order to avoid such situations, it is best to pare down differences and strive for one set of overarching rules and regulations. Otherwise, researchers will make judgments to follow one system and not the other. Furthermore, any system needs to apply principles fairly to all parties involved in order to promote faith in the system and lessen the chances of its being undermined. Finally, the system should be made predictable by constructing a framework to determine the positive and negative repercussions of certain actions. Essentially, someone who follows the criteria and guidelines set forth is ultimately provided with protection against accusations of conflict of interest. This course also reflects the understanding that if these guidelines are not followed, known consequences will ensue.

Most people in the scientific community consider disclosure to be the fundamental element in addressing conflict of interest. However, it is crucial for disclosure to be done correctly and set up in a way that allows for the right type of information to be disclosed. While not a panacea, a disclosure system should be created to ask relevant questions while incorporating insights into typical human behavior. Such a system would not rely on individual judgment or be built around reporting every single relationship, but rather designed to elicit significant relationships that may require further scrutiny. This would raise the signal to noise ratio and thus make it possible to identify potentially significant conflicts.

MANAGING CONFLICTS OF INTEREST: THE INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

*Vincent Cogliano, Ph.D., Head of the Monographs Programme,
International Agency for Research on Cancer*

The International Agency for Research on Cancer's (IARC's) mission "is the identification of causes of cancer, so that preventive measures may be adopted

against them” (<http://www.iarc.fr/en/About-IARC>). The agency’s work has four main objectives: monitoring global cancer occurrence, identifying the causes of cancer, elucidating mechanisms of carcinogenesis, and developing scientific strategies for cancer control. These objectives are achieved through a number of programs such as the **IARC Monographs**. The objective of the program “is to prepare, with the help of international Working Groups of experts, and to publish in the form of *Monographs*, critical reviews and evaluations of evidence on the carcinogenicity of a wide range of human exposures. The *Monographs* represent the first step in carcinogen risk assessment, which involves examination of all relevant information in order to assess the strength of the available evidence that an agent could alter the age-specific incidence of cancer in humans” (IARC, 2000). These monographs are used worldwide as scientific support in decision making. For this reason, IARC has created a system to restore confidence in the scientific process in the development of the monographs by identifying and avoiding relationships that introduce conflict of interest.

Identifying Conflict of Interest

The many challenges in identifying conflicting interests include variations in individual interpretations of what is considered to be conflict. These can include not recognizing the potential for conflict or assuming impartiality because the monetary outcome is the same no matter the decision. Having criteria to determine the nature of conflict is therefore necessary in any scientific organization. One such set of criteria used by IARC is the World Health Organization’s (WHO’s) Declaration of Interests, which outlines three main categories:

- Employment and consulting. A review of whether in the previous four years the expert was employed by an interested party or consulted on a matter before a court or government agency.
- Research support. An account of support for the expert’s own research and that of his or her unit, including supplies and equipment.
- Financial interests. Stock, other securities, business interests, and patents or other intellectual property.

To identify these interests, IARC asks specific, objective questions. A question such as “Have you served as an expert witness in a court case involving the interested party?” leaves no room for ambiguity. These questions were also designed to highlight activities that are suggestive of an ongoing relationship with an interested party and not just a one-time offering of scientific information on a particular issue. As an extra cautionary step, IARC has also instituted a policy to verify the absence of conflicting interest by conducting a review of recent papers for acknowledgment of research support as well as simple Internet searches. As a final step to ensure proper identification of conflict, there is a requirement for experts to update their declarations of interests at the start of each meeting. Not

only does this allow for clarification, but it also provides an opportunity to identify newly acquired or solicited conflicting interests.

Addressing Conflicts of Interest

Different organizations have different techniques for addressing conflicts of interest. Some organizations ignore the issue altogether. Other organizations are addressing conflict by opting for a simple disclosure policy. A final group of organizations has chosen to build on a disclosure policy by limiting the number of experts who have conflicts. In other words, the experts with conflicts are assumed to be diluted by the experts who have no conflicts. A better approach is to actively balance experts who have a conflicting interest with experts with an opposing interest. IARC, on the other hand, strives to avoid conflicts of interest altogether.

A 2003 *Lancet* editorial criticized the IARC conflict identification process by saying “it only needs the perception, let alone the reality, of financial conflict and commercial pressures to destroy the credibility of important organizations such as IARC and its parent, WHO” (Baines, 2003). This criticism was taken very seriously and led to changes in how IARC addresses conflict. Depending on the type of conflict identified, a threshold for concern was developed with an accompanying period of relevance (see Table 3-1). One such example would be employment by an interested party, where a higher threshold for avoiding conflict of interest was established. Such activities as sponsored travel and consulting on a particular process or new product would also have a corresponding threshold and period of relevance.

To further manage the conflicts of interest process, *IARC Monographs* for the past 2 years has provided for independent neutral-party verification of conflicting interests of its experts through *The Lancet Oncology*. For example, after IARC identifies its experts and screens them for their conflicting interests, the conflicts of interest form used by *The Lancet Oncology* is distributed to the experts at the start of their meetings. Six to eight weeks after a meeting, a summary is published in this journal, along with the editor’s account of any conflicts of interests of those at the meeting, which provides another layer in addressing conflicts and making them transparent.

The Question of Best Versus Impartial Experts

With the reduction in federal funding and the reality that researchers turn to private sources of funding, another conflict emerges: the controversy surrounding the issue of “best experts” or “impartial experts.” In other words, what does an agency do when an expert with relevant knowledge and experience also has a real or apparent conflict of interest? This issue raises a dilemma involving two valid, yet different, ideals. On one hand, the selection of experts with real or apparent

TABLE 3-1 IARC Guidelines for Addressing Conflict of Interest

Type of Conflicting Interest	Threshold for Concern	Period of Relevance
EMPLOYMENT by an interested party	All	1 year with no collaborations
CONSULTING on matters before a court or government agency	All	3 years
CONSULTING on new products or process changes	2% of professional time or compensation	1 year
SPONSORED TRAVEL or sponsored presentations at scientific meetings	2% of professional time or compensation	1 year
RESEARCH SUPPORT for the expert's own research	All	1 year after last publication
RESEARCH SUPPORT for the expert's research unit	5% of research budget	1 year after last publication
STOCK and other financial instruments	\$10,000	Current interests only
PATENTS and other intellectual property	All	Current interests only

SOURCE: Cogliano, unpublished.

conflicts of interest can erode confidence in the integrity and impartiality of the results. On the other hand, the omission of prominent experts can create the perception of reduced scientific quality. IARC has strived to achieve both ideals through a category of meeting participant known as the “invited specialist.”

Invited specialists are experts with critical knowledge and experience who are recused from certain activities because of a conflicting interest. They are available at IARC meetings to contribute their unique knowledge and experience but are not serving in key decision-making or influencing positions. This approach ensures that IARC meetings include the best qualified experts, but the meeting positions are developed by experts with no conflicting interest. The use of the invited specialist was also reviewed by an advisory group, which recommended continued use of these individuals in a limited capacity.

Freedom from Interference

Maintaining conflict-free and unbiased input throughout the scientific decision-making process is the ultimate goal. To do this requires keeping the

entire process, in this case the *IARC Monographs* process, free from interference. To maintain a transparent process, IARC, over the past few years, has made it a policy to publish the list of participants two months before each meeting. While this does foster a more open environment, many were concerned about interference with members prior to the meeting. Therefore, along with the names, a statement is published discouraging outside parties from lobbying and contacting meeting participants. Reminders are also provided for the panel members to not accept certain invitations in order to safeguard the integrity of the process. By taking effective measures to identify and avoid conflicts of interest, it is possible to do good science while promoting public confidence in the impartiality and integrity of the results.

SESSION DISCUSSION: CONFLICTS OF INTEREST IN THE CURRENT RESEARCH CLIMATE

During the discussion, participants noted that managing conflicts of interest should be embraced by all parties. Although easily achieved in theory, in practice there are many points that remain problematic and that can contribute to additional forms of conflict in the scientific process. These issues are not only financial in nature, such as public-private partnerships, but also can include cultural differences in science, asymmetry in the decision-making process, and individual scientific bias.

While creating a process in which the original meeting on a particular issue is free from conflict, balance is needed throughout the entire process, especially in regulatory aspects, asserted John Balbus. Equal scrutiny should be applied not only to the data reviewed at a public regulatory meeting, but also to the review of the public comments submitted in support of, or against, a particular regulatory issue. Cogliano agreed that the interests of any person or party submitting a public comment should be clearly disclosed, yet this should not weigh down the decision-making process. Drawing from his work at IARC, he mentioned that the agency has implemented a process in which the public can submit comments within a certain time period and of a certain length, thus allowing for review even if there are limited resources to do so.

Some participants noted that scientists have an intellectual bias and a personal financial interest in continuing funding of their research in an area. While there was not a definitive answer to how to balance this bias, Murray asserted that once a particular issue is no longer relevant from a research perspective, then research monies should not be going toward that area. The scientists remain employed by applying their skills to other scientific research.

There was recognition that as federal dollars for research become tighter, privatization of research might be necessary in the future. Some participants questioned how this potential bias could be managed as the scientific questions put forth for study are developed by an interested party. This led to the overall

question of whether science can have public-private partnerships and not have society dismiss the science because of bias. Murray responded that the same principles apply to this as to any other level of support: a transparent system in place and a firewall to separate the science from the funding. Murray and Cogliano stated that while the pioneers in this area may experience significant backlash, it is necessary to fund research. They favor a system with multiple levels to protect confidence in the scientific endeavor.

In closing, Portier raised the issue of cultural differences in science and how these differences may lead to a level of conflict because of the many different countries involved in research. Cogliano agreed it is difficult to understand the public-private structure in some countries and suggested that the best way to address the potential for conflicts is for researchers around the world to continually refine the definition of conflicting interest and disclose whatever is pertinent.

Stakeholder Perspectives on Environmental Health Sciences Decision Making

In all scientific endeavors, whether of an environmental nature or not, there is the need to balance conflict of interest, address issues of bias, and understand the ethical implications involved in research. Opinions differ as to how to strike such a balance and conduct science that is viewed as credible and sound. In this chapter, which covered the panel discussion of four stakeholders, the individuals considered issues of disclosure of conflicts, criteria to ensure equal weighting of research, and peer review of data. The overall discussion from this panel and the general workshop discussion are captured in the next chapter.

FULL DISCLOSURE OF CONFLICTS OF INTEREST

Several preliminary studies of Rofecoxib (Vioxx) had conflicting interpretation of the same sets of data. Some researchers argued that the data supported an increased rate of cardiovascular disease, while company scientists suggested that the results could be attributed to possible confounding factors, including the impact of another chemical product. Eventually, this product was removed from the market. David Michaels of The George Washington University suggested that neither of these interpretations was a result of intentional misleading; however, the public may have been served better if, following these conflicting interpretations, an independent review had been conducted.

He further noted that eliminating all conflict of interest also would mean barring individuals who are employed by product defense or litigation support firms from serving on federal scientific advisory panels. These individuals should be viewed more as advocates than as impartial scientists, since scientists who are hired to defend products in a regulatory or legal arena are not paid to provide unbiased opinions but rather to promote the interests of the party that hired them, said Michaels.

A central tenet of the process is full disclosure and publication of conflicts

in publicly and privately supported science, asserted Michaels. Full disclosure implies having this information available to the public and not just leaving the decision about managing conflicts of interest to the judgment of an agency or an editor. Disclosure needs to encompass the entire research enterprise and needs to be applied equally to the publishing of research and the regulatory setting.

THE CREDIBILITY OF SCIENCE

Protecting scientific integrity and credibility given human fallibility is an ongoing challenge. Ultimately, all scientific findings must be judged on their merits, whatever the source of funding, argued Myron Harrison of ExxonMobil Corporation. In an ideal world, the people who sit in judgment should not have conflicts and should have the best expertise to render a decision. However, they need to be guided by an established set of rigorous criteria that must be equally applicable to research from all sources.

It is a reality that the science used in public health is particularly unstable and uncertain, and therefore scientific disagreement and controversy should be expected. In the face of this uncertainty, other human factors, such as personal beliefs and values, often play a large role. Scientists are not usually trained in methods, such as argumentation, that try to establish particular and contingent “truths” in the realm of human affairs. Thus, there is often a misuse of empirical evidence to support decisions that are primarily value based, noted Harrison.

The challenge remains: How can an agency optimize the credibility of science used in rule making? Some characteristics of good research can strengthen its credibility:

- Using good lab practices and good epidemiological practices, which include such tools as research protocols, auditable data management practices, and publication of all results.¹
- Protecting human subjects in all settings, including private institutions (oversight by institutional review boards also addresses the value and quality of research).
- Applying rigorous peer review not only for the purposes of journals, but also separately in the rule-making process.
- Disclosing all potential conflicts of interest.
- Implementing strong management systems, including external reviews, to oversee the priorities and conduct of the research program.

¹There is a basic challenge to publishing all data, as studies reporting negative findings (lack of an effect) are more difficult to publish in peer-reviewed journals than those that show an effect.

ASYMMETRY IN DECISION MAKING

Due to the challenges of a very high burden of proof faced by many regulatory agencies, too few environmental health decisions are actually made, noted John Balbus of the Environmental Defense Fund. For example, under the Toxic Substances Control Act (TSCA), the current law governing industrial chemicals, the Environmental Protection Agency (EPA) must demonstrate that a chemical “presents or will present an unreasonable risk” before it can take any regulatory action. Yet there is no routine requirement for the maker of that chemical to generate data indicating safety, and the EPA must present evidence of potential harm even to require testing on a case-by-case basis. In practice, this presumption of innocence for industrial chemicals creates such a large evidentiary burden on the agency that it has essentially abandoned efforts to regulate them under the TSCA.

An additional hindrance to environmental health decision making is the growing mistrust of risk assessment. When risk assessments were first put in place, the goal in general was to determine a level of exposure that was presumed, in the face of uncertainty, to be well below the level expected to cause harm. Over time, government risk assessors have been challenged by the regulated industry to increase the precision of risk estimates. But because of such factors as the substantial variability in susceptibility in the population and the reality that individuals are exposed to many different environmental agents, determining actual risk—whether to the population as a whole or to any given individual—is an elusive and unrealistic goal. By pursuing precise estimates of actual risk, assessors are now more likely to end up with an inadequately protective outcome for an unknown percentage of the population.

Furthermore, asymmetry in the regulatory process impedes decision making based on sound science, asserted Balbus. On one hand, the work of agency scientists in the early phases of the rule-making process undergoes intense scrutiny and review by expert scientific advisory committees. On the other hand, in the latter phases, such as during the finalization of air pollution standards, the agency must respond to and may even incorporate comments or data from studies that have not had to undergo such rigorous scientific review. Balbus called for equally rigorous review of all data that may be incorporated into the rule-making process.

DATA DEVELOPMENT FOR RISK ASSESSMENT

In order to move the environmental health decision-making process forward, there is a need to think strategically about how data can inform risk, noted William Farland of Colorado State University. Focusing on basic instead of applied research and on disease-based instead of topic-based research creates an inability to generate the type of data necessary for rigorous assessment of chemicals. As noted often during the workshop, the absence of data does not equal the absence of risk. The United States needs to have a commitment to sound science while

participating as a global partner in trade and guidance to developing countries, asserted Farland.

Science is a moving target, and it is essential to think about what information is needed to inform decision making. One idea is the development of a systematic approach to working with data and weighing the evidence. In discussing scientific evidence, it is common to “take studies off the table” until the process reaches a point at which there isn’t enough information to make a decision. If a decision has been made, there is general reluctance in the United States to revisit the science and the decision, either because of antibacksliding regulations or the inability to change the regulation.

To move forward, a new decision paradigm is needed in which there is the flexibility to take into account new insights and scientific information, asserted Farland. This approach would not create an environment in which the discussion of risk based on the information is avoided. Currently, although most state and federal regulations are not designed to protect individuals, they protect the public without defining what the public is or how many individuals constitute the public. As part of a new paradigm, researchers and policy makers would carefully consider whether current federal regulations are in fact designed to adequately protect individuals, especially those in vulnerable subpopulations. Any procedural change, noted Farland, is an opportunity to engage stakeholders on how these regulations are structured to address these populations and under what context. Finally, the paradigm should incorporate evaluation into the decision-making process, as assessing the impact of a decision is vital to the success of future decision making.

General Workshop Discussion¹

TRANSPARENCY

Throughout the final discussion, the issue of transparency in the scientific processes was pervasive. This served as the underpinning for other discussion topics, which included the need for context when looking at conflicts of interest and the weight of the evidence, a possible scientific code, and the future direction of scientific decision making.

THE CONTEXT AROUND CONFLICT AND EVIDENCE

When discussing conflicts of interest, it is important to determine what it means, for example, whether it is financial or intellectual bias. Participants often noted that what individuals see as bias may in fact only be a perceived bias. Goldman pointed out the growing perception that government scientists, as well as industry scientists, will have a certain point of view or be advocates for a certain position, a perception that can make it very difficult to operate in an open and collaborative fashion. On that point, Hattis raised the issue of client-sponsor relationships and the overall need for an honest dialogue about the likely outcomes of the scientific endeavor, as well as the need for full disclosure and transparency for all outcomes, not just favorable ones.

Other participants suggested that conflict of interest needs to be put into the context of use. Some situations call for elimination of the conflict of interest, while others may necessitate managing it. Farland argued that what is problematic

¹The general workshop discussion encompasses the discussion of the panelists' comments in Chapter 4 and general themes of the workshop. These have been consolidated into this chapter.

for the scientific decision-making process is not the conflict itself but the impact it may have on the context of a situation. Michaels agreed that there may be certain situations for which context comes into play. For example, a government advisory committee meeting for which a vote is expected should not be composed of people with conflicts of interest, as the credibility of the process may be questioned. Some participants noted that conflict of interest can derail the scientific process and needs to be resolved.

CODE OF ETHICS

Further discussion focused on how to ensure openness and a systematic structure in the environmental health decision-making process. Goldman proposed that it may be time for the field to develop a code of ethics similar to that used in the legal profession, since there is no current agreed-on roadmap to ensure that biases and points of view are noted. In the legal profession's code of ethics, once a conflict is identified, lawyers recuse themselves from the situation; this is looked on favorably as a way to avoid conflict and bias. Hattis explained an effort to do this in the community of risk analysts that took the form of a set of "ideals" (Hattis, 2000). On this point, Michaels argued that while codes of ethical conduct can be beneficial in certain professions, when it comes to decision making, those with financial conflicts of interest should not be in a decision-making position, regardless of a code. Ultimately, one participant stated, the facts matter, and when looking at conflict, whether from a legal or scientific perspective, facts are what should drive the decision-making process.

FUTURE DIRECTIONS

The discussion concluded with input from the speakers and the audience as to the future direction of scientific decision making. Numerous suggestions were offered as a path to making overall improvements in the current decision-making process. The list below does not constitute recommendations of the group, but rather captures the range of ideas that people would like to see explored in future discussions. These include

- Not necessarily instituting a standard for how one actually weighs the evidence, but rather providing a rationale for the inclusion and exclusion of material studied in order to simply show why something should or should not be studied.
- Tailoring the approach to decision making to eliminate the "one size fits all" risk assessment and incorporate context.
- Discussing regulatory agency decisions to explain why agencies are regulating some substances and not others. This could eliminate the presumption of innocence in the current decision-making process.

- Developing more examples of successful risk assessment in which the science is complete and solid enough to actually perform a service to the risk assessment process.
- Realizing that risk assessment needs to be made from different perspectives (e.g., economics) and that these perspectives can change the outcome.
- Creating a term appointment for the heads of scientific agencies, which would stabilize the leadership of government agencies in order to make the process more scientifically focused.
- Engaging stakeholders, including the affected public, to a greater degree than currently exists and educating the public on the scientific decision-making process to provide opportunities to hear diverse viewpoints.
- Focusing on risk avoidance rather than acceptable risk, as this is the information that the American public wants.
- Recognizing that the risk assessment decision is not stagnant but dynamic and based on new science. As such, criteria should be put in place to review risk assessment decisions.
- Developing and using a metric to quantify how scientific information is understood and translated into public health.

Closing Comments¹

*David Eaton, Ph.D.,
Professor of Environmental Health and Occupational Health Sciences,
School of Public Health and Community Medicine,
University of Washington*

The workshop highlighted a number of challenges that scientists, public health officials, and policy makers face in protecting the public against harmful environments and promoting healthy ones (Figure 6-1). Central to the discussion was the inherent tension between science and public health in determining the burden of proof for a toxic chemical. Scientists, as a result of their training, do not exceed the limits of their data, which places chemicals in the “innocent until the data shows otherwise” category. However, those in public health, when faced with uncertainty, would prefer to err on the side of protecting health. While it is relatively easy to show that x can cause y or that there is a mechanism in which x might cause y , it is difficult to demonstrate and accumulate sufficient data to say that x cannot cause y . Thus, there is a conflict about how to establish the burden of proof for toxic substances and how to address this conflict in the regulatory setting.

The general belief is that more science will clarify research gaps. However, science itself may provide uncertainty. One place where this can occur is in the field of toxicology, which relies on the extrapolation of results between species. For example, rats fed aflatoxin at 15 parts per billion (the current tolerance level set by the Food and Drug Administration) develop liver cancer. However, mice fed aflatoxin 150,000 parts per billion do not develop liver cancer. The development of liver cancer is dependent on the expression of a single gene in the rats compared with the mice.

The choice of which species to use to predict human response could lead to vastly different conclusions and, depending on the “truth,” could lead to a false-positive or a false-negative result. In the example of aflatoxin just described, human epidemiological data suggest that the truth is somewhere in between. In

¹This chapter was prepared from the transcript of the summary presentation by Dr. Eaton. The views expressed within this chapter are attributed solely to him.

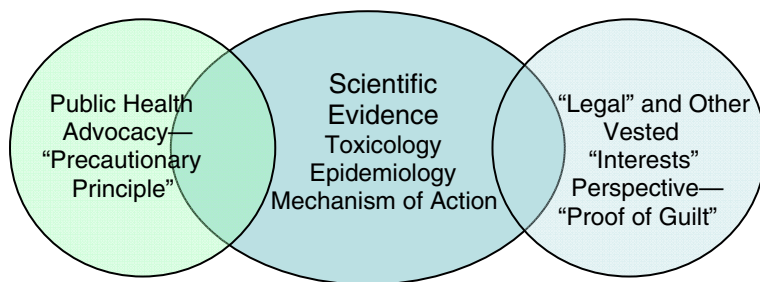


FIGURE 6-1 Scientific evidence has many uses that are not often apparent to the scientists. Scientific evidence can be used to define research, promote health, and inform the legal process. There is a tension in the use of science when there is uncertainty as to whether policy makers take a precautionary approach or a passive (i.e., “wait until the data shows harm”) approach.

SOURCE: Eaton, unpublished.

many instances, the benefit of human epidemiology is not available to resolve discrepant animal studies. In such circumstances, a false positive can lead to the limitation or ban of a particular useful chemical. However, public health scientists are perhaps more concerned about false negatives, such as the case with arsenic. In this example, animal bioassays for carcinogenicity generally have failed to identify the potent carcinogenic effects of arsenic that are known to occur in humans. Animal toxicology or human epidemiology alone does not address all of the challenges in regulating chemicals, and thus the science behind regulatory decisions requires a multidisciplinary approach.

In recent years, tremendous advances have been made in molecular biology to elucidate cellular pathways and mechanisms that contribute to the understanding of how chemicals might contribute to human disease, but these advances are not a panacea for regulatory policy. Many cellular and molecular pathways have been highly conserved throughout evolution, and thus fundamental biological knowledge learned from simple organisms may be quite relevant to human biology. However, the evolutionary processes that dictate how humans respond to their environment select against other pathways, giving rise to large species differences in how organisms respond to their immediate environment, including chemical exposures. This is a challenge in the “omics” technology, in which scientists can measure changes in the expression of 10,000–20,000 different genes in response to a chemical exposure, but they are not always able to interpret the significance of such changes in terms of human health. Similar to advances in science, advances in technology have resulted in the vanishing zero: Environmental health scientists are able to measure chemicals in the body at lower and lower concentrations. However, scientists are not yet at a point at which they can make biological sense of the low-level presence of these chemicals.

In addition to challenges of data interpretation, the workshop also highlighted many ethical issues. In the real world, perception is reality. It is often difficult for the public to differentiate between perceived bias, significant bias, and conflicts of interest. While many agencies that work at the science-policy interface, such as IARC and the National Academies, have begun to create a good model for conflicts of interest, it does not go far enough to consider conflicts of interest throughout the research enterprise. For example, in the past decade, the perception has been expressed by many people that if a study is funded by an industry, then the results must be biased, and the study is essentially discounted. However, most scientists feel strongly that science should be judged on its merits and not on who funded it. Once the funding source is noted, perception problems begin, as people have biases that will shape their attitudes in response to such knowledge. This is true for all sources of funding and not just for industry. Thus there is a need for the field to address the perception of bias in research and continued discussions as to how biases can be acknowledged and conflicts of interest can be managed.

In conclusion, environmental health sciences is sometimes caught between potential overuse of the precautionary principle, which can engender unwarranted fear on the part of the public, and lack of timely decisions of potential public health importance when data are insufficient to make science-based decisions. Continued efforts are needed to improve risk communication of environmental health hazards, as the public is often confused by mixed messages from the scientific community and thus may not understand risk or the scientific process that establishes the burden of proof for regulatory action. While there is clearly overlap, scientists need to address the credibility gap—or at least the public perception gap—by involving the public in these processes. There should be more discussions on how to address the needs of the environmental health decision-making process by establishing protocols to ensure that science is judged on its merits, while at the same time acknowledging biases and potential conflicts of interest.

References

- Armstrong, B., and R. Doll. 1975. Bladder cancer mortality in diabetics in relation to saccharin consumption and smoking habits. *British Journal of Preventive & Social Medicine* 29:73–81.
- Arnold, D., C. Moodie, H. Grice, S. Charbonneau, B. Stavric, B. Collins, P. McGuire, Z. Zawadzka, and I. Monro. 1980. Long term toxicity of ortho-toluenesulfonamide and sodium saccharin in the rat. *Toxicology and Applied Pharmacology* 52:113–152.
- Ashby, J. 1985. The genotoxicity of sodium saccharin and sodium chloride in relation to their cancer-promoting properties. *Food and Chemical Toxicology* 23:507–519.
- Baines, C. 2003. Transparency at the International Agency for Research on Cancer. *Lancet* 361(9359):781–782.
- EIA (Energy Information Administration). 2004. *International Energy Annual*. <http://eia.doe.gov/iea> (accessed May 5, 2008).
- EIA. 2007. *Projections: EIA, System for the Analysis of Global Energy Markets*. <http://eia.doe.gov/iea> (accessed May 5, 2008).
- EU (European Union). 2008. *Europa Glossary*. http://europa.eu/scadplus/glossary/precautionary_principle_en.htm (accessed April 10, 2008).
- FDA (Food and Drug Administration). 2006. *New Federal Health Initiative to Improve Cancer Therapy*. <http://www.fda.gov/bbs/topics/news/2006/NEW01316.html> (accessed March 20, 2008).
- Gohlke, J., and C. Portier. 2007. The forest for the trees: A systems approach to human health research. *Environmental Health Perspectives* 115(9):1261–1263.
- Hastein, T., B. Hjeltne, A. Lillehaug, J. Utne Skare, M. Berntssen, A. K. Lundebye. 2006. Food safety hazards that occur during the production stage: Challenges for fish farming and the fishing industry. *Revue Scientifique et Technique* 25(2):18.
- Hattis, D. 2000. Draft risk analysis ideals. *Human and Ecological Risk Assessment* 6(6):7.
- Hattis, D. 2004. The conception of variability in risk analyses: Developments since 1980. In *Risk Analysis and Society: An Interdisciplinary Characterization of the Field*, edited by T. McDaniels and M. J. Small. Cambridge, England: Cambridge University Press, pp. 15–45.
- Hattis, D.A., and E.L. Anderson. 1999. What should be the implications of uncertainty, variability, and inherent “biases”/“conservatism” for risk management decision-making? *Society for Risk Analysis* 19(1):13.
- HHS (U.S. Department of Health and Human Services) and NTP (National Toxicology Program). 2005. *Report on Carcinogens*. 11th ed. Washington, DC: HHS and NTP.
- IARC. 1987. IARC monographs on the evaluation of the carcinogenic risks to humans. In *Genetic and Related Effects: An Updating of Selected IARC Monographs from Volumes 1–42*. Suppl. 6:488–496.

- IARC. 2006. Preamble to the IARC Monographs. <http://monographs.iarc.fr/ENG/Preamble/currenta2objective0706.php> (accessed November 12, 2008).
- Majone, G. 2002. The precautionary principle and its policy implications. *Journal of Common Market Studies* 40:89–110.
- NTP (National Toxicology Program). 2005. *Questions and Answers About the Report on Carcinogens*. <http://ntp.niehs.nih.gov/index.cfm?objectid=03CA6383-97566-1F64-6637241FE0114FE9> (accessed May 5, 2008).
- NTP. 2008. *Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) Mission and Vision*. http://iccvam.niehs.nih.gov/about/ni_Mission.htm (accessed May 5, 2008).
- OMB (Office of Management and Budget). 2006. *Proposed Risk Assessment Bulletin*. http://www.whitehouse.gov/omb/inforeg/proposed_risk_assessment_bulletin_010906.pdf (accessed May 9, 2008).
- Palucka, T. 2004. Doing the impossible. *Invention & Technology Magazine* 19(3):22–31.
- Pearson, S.D., J. Sabin, and E.J. Emanuel. 2003. *No Margin, No Mission: Health-care Organizations and the Quest for Ethical Evidence*. New York: Oxford University Press.
- Steinzor, R., and M. Shudtz. 2007. Sequestering science: Secrets threatening public health. *CPR White Paper* 703(April).
- SUNY (State University of New York). 2004. Guide to research methods: The evidence pyramid. <http://library.downstate.edu/EBM2/2100.htm> (accessed November 11, 2008).
- Sweatman, T., and A. Renwick. 1979. Saccharin metabolism and tumorigenicity. *Science* 205:1019–1020.
- Taylor, J., M. Weinberger, and L. Friedman. 1980. Chronic toxicity and carcinogenicity to the urinary bladder of sodium saccharin in the in utero–exposed rat. *Toxicology and Applied Pharmacology* 54:57–75.
- Teutsch, S.M. 2008. The evidence for evidence-based public health. *Journal of Public Health Management and Practice* 14(2):92–93.
- Tisdell, M., P. Nees, D. Harris, and P. Derse. 1974. Long-term feeding of saccharin in rats. In *Symposium: Sweeteners* (pp. 145–158). Westport, CT: Avi Publishing Co.
- United Nations. 1992. The Rio Declaration on Environment and Development. United Nations Conference on Environment and Development, June 13–14, Rio de Janeiro.
- Wagner, W., and R. Steinzor. 2006. Rescuing science from politics: Regulating and the distortion of scientific research. *CPR White Paper* 604(August).
- Whysner, J., and G. Williams. 1996. Saccharin mechanistic data and risk assessment: Urine composition, enhanced cell proliferation, and tumor promotion. *Pharmacology and Therapeutics* 71:225–252.

Appendix A

Workshop Agenda

ENVIRONMENTAL HEALTH SCIENCES DECISION MAKING: RISK MANAGEMENT, EVIDENCE, AND ETHICS

Sponsored by the Roundtable on Environmental Health Sciences,
Research, and Medicine

January 15, 2008

- 8:30 a.m. **Welcome**
The Honorable Paul G. Rogers, J.D.
Chair, Roundtable on Environmental Health Sciences, Research,
and Medicine
Partner, Hogan & Hartson
- 8:35 a.m. **Overview of Environmental Health Science Decision Making
and Workshop Objectives**
Lynn Goldman, M.D., M.S., M.P.H.
Vice-Chair, Roundtable on Environmental Health Sciences,
Research, and Medicine
Professor of Environmental Health Sciences and
Chair, Interdepartmental Program in Applied Public Health
Johns Hopkins Bloomberg School of Public Health

SESSION I: OVERVIEW OF DECISION MAKING

- Moderator: **Lynn Goldman, M.D., M.S., M.P.H.**
Professor of Environmental Health Sciences and
Chair, Interdepartmental Program in Applied Public Health
Johns Hopkins Bloomberg School of Public Health
- 8:45 a.m. **Human–Environment Network: Challenges to Environmental Health**
Christopher J. Portier, Ph.D.
Associate Director
Office of Risk Assessment Research, NIEHS
- 9:05 a.m. **Alternatives Assessment as a Strategy for Decision Making**
Mary O’Brien, Ph.D.
Oregon Toxics Alliance
- 9:25 a.m. **Beyond Precaution**
Bernard D. Goldstein, M.D.
Professor
Department of Environmental and Occupational Health
University of Pittsburgh Graduate School of Public Health
- 9:45 a.m. **Discussion**
- 10:20 a.m. **Break**

SESSION II: WEIGHING EVIDENCE IN ENVIRONMENTAL HEALTH DECISION MAKING

- Moderator: **Myron Harrison, M.D., M.P.H.**
Senior Health Adviser, ExxonMobil Corporation
- 10:35 a.m. **Evaluating Weights of Evidence for Decision Making**
J. Michael McGinnis, M.D., M.P.P.
Senior Scholar
Roundtable on Evidence-Based Medicine
Institute of Medicine

- 10:55 a.m. **The Role of Uncertainty and Susceptible Populations in Environmental Health Decision Making**
Dale B. Hattis, Ph.D.
Research Professor
George Perkins Marsh Institute, Clark University
- 11:15 a.m. **The Use and Misuse of Science in Decision Making**
Rena Steinzor, J.D.
Jacob A. France Research Professor of Law
University of Maryland School of Law
- 11:35 a.m. **Rationale for Revisiting an Environmental Health Decision: NTP as a Case Study**
Kenneth Olden, Ph.D., Sc.D., L.H.D.
Principal Investigator
The Metastasis Group, Laboratory of Molecular Carcinogenesis, NIEHS
- 11:55 a.m. **Discussion**
- 12:30 p.m. **Lunch**

**SESSION III: ENVIRONMENTAL HEALTH RESEARCH:
CONFLICT OF INTEREST, BIAS, AND ETHICS**

- Moderator: **Richard J. Jackson, M.D., M.P.H.**
Adjunct Professor, Environmental Health Services Division,
University of California, Berkeley
- 1:15 p.m. **Ethics, Values, and Conflicts of Interest in Environmental Health Sciences Research**
Thomas H. Murray, Ph.D.
President
The Hastings Center
- 1:40 p.m. **Managing Conflict of Interest (Including Transparency)**
Vincent Coglianò, Ph.D.
Head of the Monographs Programme
International Agency for Research on Cancer

2:00 p.m. **Discussion**

3:00 p.m. **Break**

3:15 p.m. **Reactant Panel Discussion: Challenges of Environmental Health Science Research and Policy**

David Michaels, Ph.D., M.P.H.

Director

The Project on Scientific Knowledge and Public Policy

Associate Chairman, Department of Environmental and Occupational Health

The George Washington University School of Public Health and Health Services

Myron Harrison, M.D., M.P.H.

Senior Adviser

ExxonMobil Corporation

John Balbus, M.D., M.P.H.

Director, Environmental Health Program

Environmental Defense Fund

William H. Farland, Ph.D.

Vice President for Research

Colorado State University

4:15 p.m. **Discussion**

CLOSING

4:55 p.m. **Closing Comments**

David Eaton, Ph.D.

Professor of Environmental Health and Occupational Health Sciences

School of Public Health and Community Medicine

University of Washington

5:15 p.m. **Adjourn**

Appendix B

Speakers and Panelists

The Honorable Paul Grant Rogers, J.D., is a partner in the Washington, DC, office of Hogan & Hartson L.L.P. and a member of the firm's Health Group. His areas of practice include administrative and regulatory, antitrust, health, and environmental law; legislative strategy; and health policy. He served for 24 years as a member of the U.S. House of Representatives from the 11th District of Florida. Of those 24 years, he spent 8 as the chairman of the House Subcommittee on Health and the Environment and became nationally recognized as an innovative leader. In Congress he became known as "Mr. Health."

Some of the prominent pieces of legislation that he sponsored and played a major role in enacting are the National Cancer Act of 1971 and 1977; the Health Manpower Training Act; the Heart, Blood Vessel, Lung and Blood Act; the Research on Aging Act; the Comprehensive Drug Abuse Prevention and Control Act of 1970; the Medical Device Amendments of 1976; the Emergency Medical Services Act; the Health Maintenance Organization Act; the Clean Air Act; the Safe Drinking Water Act; the Radiation Health Safety Act; the Medicare-Medicaid Anti-Fraud and Abuse Amendments of 1977; and the Sea Grant College Act.

Mr. Rogers joined Hogan & Hartson, LLP, in January 1979. He has represented a wide range of providers, manufacturers, suppliers, and associations in the health care field in matters involving antitrust, federal and state legislation, reimbursement, litigation, food and drug regulation, international trade, government grant and contract, and corporate and tax matters. He is a member of the Food, Drug and Cosmetic Law Committee of the American Bar Association and was made an honorary member of the American Health Lawyers Association.

He is chairman of the National Osteoporosis Foundation, Research!America, the Trustees of the National Foundation for Infectious Diseases, and the Friends of the National Library of Medicine and co-chairman of the National Leadership Coalition on Health Care. He serves as a director or trustee on the following boards: the Scripps Research Institute, the Cleveland Clinic Foundation, the Foundation

for Biomedical Research, the American Cancer Society, and the CDC Foundation. He is a member of the Institute of Medicine (IOM) and served as a member of the Advisory Committee on Civil Rules of the Judicial Conference of the United States (1979–1984). He has received honorary degrees from 15 universities.

Mr. Rogers was awarded the Public Welfare Medal by the National Academy of Sciences in 1982; the Year 2000 Award from the National Cancer Institute in 1987; the 1991 Health Policy Award from the American Health Lawyers Association; the Founders Award from the National Coalition for Cancer Research in 1992; the 1993 Albert Lasker Award for Public Service; the 1994 APhA Hugo Schaefer Award; the 1994 AlliedSignal Achievement Award in Aging; the 1994 Distinguished Leadership Award from the University of Florida Health Sciences Center; the 1995 NOF Leadership Award; the 1996 Maxwell Finland Award; the 1997 American Cancer Society Distinguished Service Award; the National Community Pharmacists Association 1998 Distinguished American Award; and the 1999 IONA's Outstanding Citizen award. He was also the first recipient (1999) of the Association of Academic Health Centers' Paul G. Rogers Award. By an act of Congress, the main plaza at the National Institutes of Health (NIH) was designated as the Paul G. Rogers Plaza and dedicated on June 12, 2001.

Mr. Rogers is a member of the Harvard School of Public Health Dean's Council, the University of Chicago's Council for the Division of the Biological Sciences and the Pritzker School of Medicine, Washington University's National Council of the School of Medicine, and the University of Pennsylvania's Medical Center Trustee Board. A graduate of the University of Florida in 1948, he is a member of the bars of Florida and the District of Columbia and is admitted to practice before the federal courts in several districts, federal courts of appeal, and the United States Supreme Court.

Lynn R. Goldman, M.D., M.S., M.P.H., a pediatrician and an epidemiologist, is a professor at the Johns Hopkins Bloomberg School of Public Health, where her areas of focus are environmental health policy, public health practice, and children's environmental health. Her appointment is in the Department of Environmental Health Sciences, with a joint appointment in the Department of Health Policy and Management.

In 1993, she was appointed by the president and confirmed by the Senate to serve as assistant administrator for the EPA's Office of Prevention, Pesticides and Toxic Substances (OPPTS). Serving in that position for more than 5 years, she was responsible for the nation's pesticide, toxic substances, and pollution prevention laws. Under her watch, EPA expanded right-to-know under the Toxics Release Inventory and overhauled the nation's pesticide laws. She made significant progress on the issues of testing of high-volume industrial chemicals and identification of chemicals that disrupt endocrine systems. At EPA she was successful in promoting children's health issues and furthering the international agenda for global chemical safety.

Prior to joining EPA, Goldman served in several positions in the California Department of Health Services, most recently as head of the Division of Environmental and Occupational Disease Control. She has conducted public health investigations on pesticides, childhood lead poisoning, and other environmental hazards. She has a B.S. in conservation of natural resources from the University of California, Berkeley, an M.P.H. from the Johns Hopkins Bloomberg School of Public Health, and an M.D. from the University of California, San Francisco. She completed pediatric training at Children's Hospital in Oakland, California.

She has served on numerous boards and expert committees, including the Committee on Environmental Health of the American Academy of Pediatrics, the Lead Poisoning Prevention Advisory Committee of the Centers for Disease Control and Prevention, and numerous expert committees for the National Academies. She currently is vice chair of the Institute of Medicine's Roundtable on Environmental Health Sciences and served as the chair of the IOM Gulf War and Health Study.

John Balbus, M.D., M.P.H., is a senior scientist and director of the health program for the Environmental Defense Fund. He holds adjunct appointments at both the Johns Hopkins University Bloomberg School of Public Health and the George Washington University School of Public Health and Health Services. He received his A.B. degree in biochemistry from Harvard University, his M.D. from the University of Pennsylvania, and his M.P.H. from Johns Hopkins University.

Vincent Cogliano, Ph.D., serves as head of the *IARC Monographs Programme* at the International Agency for Research on Cancer (part of the World Health Organization) in Lyon, France. *IARC Monographs* is a series of scientific reviews identifying environmental factors that can increase the risk of human cancer. Cogliano received his Ph.D. from Cornell University, then worked for 20 years in quantitative risk assessment at the U.S. Environmental Protection Agency (EPA) in Washington. Professional interests include cancer hazard assessment, qualitative and quantitative health risk assessment in general, and identification of susceptible populations and life stages.

David Eaton, Ph.D., received his Ph.D. in pharmacology from the University of Kansas Medical Center in 1978. He joined the faculty of the University of Washington (UW) in 1979 and is professor and director of the Center for Ecogenetics and Environmental Health at UW, as well as professor of public health genetics, adjunct professor of medicinal chemistry, and affiliate member of the Fred Hutchinson Cancer Research Center. He currently also serves as associate vice provost for research at UW and was previously the associate dean for research in the School of Public Health. Nationally, he has served as secretary and president of the Society of Toxicology and serves on numerous scientific advisory boards for other centers and program grants. He served on the National

Academy of Sciences/National Research Council (NAS/NRC) Board of Environmental Studies and Toxicology from 1996 to 1999 and on the NAS/NRC Committee on Arsenic and Drinking Water (2001 update); he recently chaired the NAS/NRC/IOM Committee on Assessment of the Health Implications of Exposure to Dioxin. He maintains his own active research and teaching program focused on the area of the molecular basis for environmental causes of cancer, with an emphasis on how chemical carcinogens are metabolized in the liver. He has published over 150 scientific articles and book chapters in the field of toxicology and risk assessment, is an elected fellow of the American Association for the Advancement of Science and the Academy of Toxicological Sciences, and is a lifetime national associate of the National Academies.

William H. Farland, Ph.D., joined Colorado State University in 2006 as the vice president for research, bringing decades of interdisciplinary research leadership experience to the position. He serves as the chief institutional advocate and facilitator for faculty research activities and is responsible for programmatic excellence in research. Specific responsibilities of the position include oversight and promotion of external research funding and associated regulations, needs, and capabilities; serving as liaison with federal research officials and agencies; identification of research opportunities; and development and oversight of interdisciplinary programs and research centers.

Previously, he was the highest ranking career scientist at the Environmental Protection Agency, serving as chief scientist in the Science Advisor's Office as well as acting deputy assistant administrator for science in the Office of Research and Development (ORD). Prior to that appointment, he was director of ORD's National Center for Environmental Assessment, which has major responsibility for the conduct of chemical-specific risk assessments in support of EPA regulatory programs, the development of agency-wide guidance on risk assessment, and the conduct of research to improve risk assessment. His 27-year federal career has been characterized by a commitment to the development of national and international approaches to the testing and assessment of the fate and effects of environmental agents. He has led the EPA's extensive reassessment of the exposure and health effects of dioxin and related compounds.

Farland holds a Ph.D. (1976) from the University of California, Los Angeles, in cell biology and biochemistry and a master's in zoology. He obtained his bachelor's degree from Loyola University in Los Angeles. He serves on a number of executive-level committees and advisory boards in the federal government. He is also a member of the Scientific Advisory Council of the Risk Sciences and Public Policy Institute at the Johns Hopkins Bloomberg School of Hygiene and Public Health, a public member of the American Chemistry Council's Strategic Science Team for its Long-Term Research Program, and several other industry- and university-based science advisory panels. In 2002, he was recognized by the Society for Risk Analysis with the Outstanding Risk

Practitioner Award. He continues to teach and publish and has been a member of the editorial board *Risk Analysis* since 1987 and *Environmental Health Perspectives* since 1997.

Bernard D. Goldstein, M.D., is a professor in the University of Pittsburgh's Graduate School of Public Health, where he was previously dean. He served as the director of the Environmental and Occupational Health Sciences Institute, a joint program of Rutgers, the State University of New Jersey, and the University of Medicine and Dentistry of New Jersey (UMDNJ)—Robert Wood Johnson Medical School, from 1986 to 2001. He was the chair of the Department of Environmental and Community Medicine, UMDNJ—Robert Wood Johnson Medical School, from 1980 to 2001. He was the first principal investigator of the Consortium of Risk Evaluation with Stakeholder Participation. He served as acting dean of the UMDNJ—School of Public Health in 1998-1999, the first year of its formation. He earned his B.S. degree at the University of Wisconsin in 1958 and his M.D. degree at New York University School of Medicine in 1962. He is a physician, board certified both in internal medicine and hematology and in toxicology.

He was assistant administrator for research and development in the U.S. Environmental Protection Agency from 1983 to 1985. His past activities include member and chairman of the NIH Toxicology Study Section and the EPA's Clean Air Scientific Advisory Committee; chair of the Institute of Medicine's Committee on the Role of the Physician in Occupational and Environmental Medicine, the National Research Council's Committees on Biomarkers in Environmental Health Research and Risk Assessment Methodology, and the Industry Panel of the World Health Organization's Commission on Health and Environment. He is a member of the Institute of Medicine, where he has chaired the Section on Public Health, Biostatistics, and Epidemiology and served on the Committee on Environmental Justice: Research, Education, and Health Policy Needs. He is also president-elect of the Society for Risk Analysis, vice president of the Scientific Committee on Problems of the Environment, and a member of the National Advisory Environmental Health Sciences Council. He is the author of over 200 articles and book chapters related to environmental health sciences and to public policy.

Myron Harrison, M.D., M.P.H., is the senior health adviser for ExxonMobil Corporation and a member of its corporate Safety, Health and Environment staff. Previously, he served as the medical director of Exxon's U.S. Medicine and Occupational Health Department. Before specializing in the field of occupational medicine, he practiced emergency medicine for 10 years. He earned a master's of public health degree at Columbia University and is a past president of the Texas College of Occupational and Environmental Medicine.

Dale B. Hattis, Ph.D., is research professor with the George Perkins Marsh Institute at Clark University. For the past three decades, he has been engaged in

the development and application of methodology to assess the health, ecological, and economic impacts of regulatory actions.

His work has focused on approaches to incorporate interindividual variability data and quantitative mechanistic information into risk assessments for both cancer and noncancer endpoints. Recent research has explored age-related differences in sensitivity to carcinogenesis and other effects, a taxonomy of different nonmutagenic modes of action for carcinogenesis with likely differential implications for age-related sensitivity, PBPK modeling of acrylamide dose in rats and humans, and mechanism-based dose-response modeling of carcinogenic effects from ionizing radiation. He is a leader in efforts to replace the current system of uncertainty factors with distributions based on empirical observations. He is a member of the Environmental Health Committee of the EPA Science Advisory Board, and for several years he has served as a member of the Food Quality Protection Act Science Review Board. In 2007, he was chair of the Dose Response Specialty Group of the Society for Risk Analysis. He has also served as a member of the National Research Council's Committee on Estimating the Health-Risk-Reduction Benefits of Proposed Air Pollution Regulations. He has been a councillor and is a fellow of the Society for Risk Analysis and serves on the editorial board of its journal, *Risk Analysis*. He holds a Ph.D. in genetics from Stanford University and a B.A. in biochemistry from the University of California, Berkeley.

Richard J. Jackson, M.D., M.P.H., is professor of environmental health at the University of California, Berkeley, School of Public Health. In June 2005, he received the Presidential Distinguished Executive Award for his outstanding leadership and extraordinary achievement in service to the nation, and in particular to improving environmental public health. He has served in many leadership positions, including as the state health officer for the state of California. For nine years he was director of the Centers for Disease Control and Prevention's (CDC's) National Center for Environmental Health in Atlanta. A native of Newark, New Jersey, he is a graduate of the University of California School of Medicine at San Francisco, where he began his residency as a pediatrician. During his residency he took time off for a two-year stint with CDC as an officer in the Epidemic Intelligence Service (EIS). He then obtained a master's degree in public health from the University of California, Berkeley, and began work as a public health medical officer with the California Department of Health Services. His contributions include successfully pushing for passage of California's Birth Defects Prevention Act, assisting in the establishment of California's tough guidelines for reporting pesticide use, and major contributions to a National Academies report on *Pesticides in the Diets of Infants and Children*, which helped lead to passage of the Food Quality Protection Act in 1996.

Selected to be director of the CDC's National Center for Environmental Health in 1994, Jackson studied and addressed such issues as cancer, asthma,

radiation effects, pesticide exposure, and toxicology, especially lead poisoning in children. In recent years, he has taken on the critically important and underappreciated environmental health issue of the built environment, collaborating with other professionals to create a website called Designing and Building Healthy Places (<http://www.cdc.gov/healthypplaces>). His chief goal at present is to recruit and train new leaders in environmental health, drawing young people whose backgrounds might not make them aware of the opportunities for such a meaningful career. In August 2003, he became the CDC director's senior adviser and co-lead on CDC's strategic planning process areas related to health systems.

J. Michael McGinnis, M.D., M.P.P., joined the Institute of Medicine as senior scholar in 2005 to help develop the IOM leadership on evidence-based medicine and expansion of research on the comparative effectiveness of clinical interventions. From 1999 to 2005, he served as senior vice president and founding director of the Health Group, as well as counselor to the president, at the Robert Wood Johnson Foundation (RWJF). Much of his career has been spent as a participant and leader in national policy in disease prevention and health promotion, including continuous appointment, from 1977 to 1995, as assistant surgeon general and deputy assistant secretary for health (disease prevention and health promotion) through the Carter, Reagan, Bush, and Clinton administrations.

During this period, he led the development of *Healthy People*, the nation's prevention agenda, and the creation of the U.S. Preventive Services Task Force, a body that has for two decades evaluated the effectiveness of clinical preventive services and pioneered the advance of evidence-based medicine. Other programs and policies launched at his initiative include the first Health and Human Services–U.S. Department of Agriculture (HHS–USDA) *Dietary Guidelines for Americans*, now in its sixth edition (first edition co-produced with USDA in 1980) and the first *Surgeon General's Report on Nutrition and Health* (1988); the work of the Public Health Functions Steering Committee to develop the *10 Essential Services of Public Health*; the RWJF *Health & Society Scholars Program*; the RWJF *Young Epidemiology Scholars Program*; and the RWJF *Active Living* family of programs. His current and recent board memberships include the IOM Committee on Children's Food Marketing (chair), the NIH State-of-the-Science Conference on Multivitamins in Chronic Disease Prevention (chair), the Health Professionals Roundtable on Preventive Services (chair), the board of directors of the Nemours Foundation; the board of directors of the Partnership for Prevention, and the board of trustees of the United Way of the National Capital Area (chair, resource development).

His international service includes appointments as chair of the World Bank/European Commission Task Force on postwar reconstruction of the health sector in Bosnia in 1995–1996; state coordinator for the World Health Organization smallpox eradication program in Uttar Pradesh, India, in 1974–1975; and coordinator for U.S.–Eastern European health programs in 1972–1973. He is an

elected member of the IOM, a fellow of the American College of Epidemiology, and a fellow of the American College of Preventive Medicine. Other recognitions include the Wilbur Cohen Award, the Porter Prize, the National Health Leader of the Year Award, and the Distinguished Service Medal of the U.S. Public Health Service. He has earned degrees in political science, medicine, and public policy from the University of California, Berkeley; the University of California, Los Angeles; and Harvard University.

David Michaels, Ph.D., M.P.H., is a scientist and former government regulator. During the Clinton administration, he was assistant secretary of energy for environment, safety and health, responsible for protecting the health and safety of workers, neighboring communities, and the environment surrounding the nation's nuclear weapons facilities. He is research professor and associate chairman of the Department of Environmental and Occupational Health at The George Washington University School of Public Health and Health Services, where he directs The Project on Scientific Knowledge and Public Policy (www.DefendingScience.org). In 2006, he received the American Association for the Advancement of Science's Scientific Freedom and Responsibility Award for his work on behalf of nuclear weapons workers and for his advocacy for scientific integrity. He is the author of the forthcoming book *Doubt Is Their Product: How Industry's Assault on Science Threatens Your Health* (Oxford University Press, 2008).

Thomas H. Murray, Ph.D., is president of The Hastings Center. He was formerly the director of the Center for Biomedical Ethics in the School of Medicine at Case Western Reserve University, where he was also the Susan E. Watson professor of bioethics. He is a founding editor of the journal *Medical Humanities Review* and is on the editorial boards of *The Hastings Center Report*; *Human Gene Therapy*; *Politics and the Life Sciences*; *Cloning, Science, and Policy*; *Medscape General Medicine Teaching Ethics*; the *Journal of Bioethical Inquiry*; and the *Journal of Law, Medicine & Ethics*. He served as president of the Society for Health and Human Values and of the American Society for Bioethics and Humanities. He has testified before many congressional committees and is the author of more than 200 publications. His most recent books are *The Worth of a Child* (University of California Press); *Healthcare Ethics and Human Values: An Introductory Text with Readings and Case Studies* (Blackwell Publishers, edited with Bill Fulford and Donna Dickenson); *The Cultures of Caregiving: Conflict and Common Ground Among Families, Health Professionals and Policy Makers* (edited with Carol Levine); and *Genetic Ties and the Family: The Impact of Paternity Testing on Parents and Children* (edited with Mark A. Rothstein, Gregory E. Kaebnick, and Mary Anderlik Majumder). He is also editor, with Maxwell J. Mehlman, of the *Encyclopedia of Ethical, Legal and Policy Issues in Biotechnology* (John Wiley & Sons, 2000). In January 2004, he received an honorary doctor of medicine degree from Uppsala University.

Mary O'Brien, Ph.D., has worked as a staff scientist and organizer for the past 26 years with toxics and conservation organizations, including the Northwest Coalition for Alternatives to Pesticides, the Environmental Research Foundation, the Science and Environmental Health Network, and the Hells Canyon Preservation Council. From 1992 to 1994 she taught as assistant professor in the graduate Environmental Studies Program at the University of Montana. She currently works for Grand Canyon Trust on the conservation of wildlife habitat and native ecosystems in southern Utah's three national forests. Her book, *Making Better Environmental Decisions: An Alternative to Risk Assessment* (MIT Press, 2000), focuses on the power of alternatives assessments to leverage positive change.

Kenneth Olden, Ph.D., Sc.D., L.H.D., is the most recent past director of the National Institute of Environmental Health Sciences (NIEHS) and the National Toxicology Program (NTP) in the U.S. Department of Health and Human Services. He held these positions from 1991 to 2005. He was the first African American to become director of one of the NIH institutes. He has returned full time to his research position as chief of The Metastasis Group in the Laboratory of Molecular Carcinogenesis at the NIEHS, which he also held while director. He held the position of Yerby visiting professor at the Harvard School of Public Health for the academic year 2006–2007.

He received his Ph.D. in cell biology/biochemistry from Temple University. He is the recipient of several honorary degrees, namely, Sc.D. degrees from Metropolitan University, San Juan, Puerto Rico; the University of Medicine and Dentistry of New Jersey; and the University of Rochester and an honorary doctorate of science from Tulane University. He also holds an honorary L.H.D. from the College of Charleston. After completing his Ph.D. degree, he was a research fellow and instructor of physiology at Harvard University (1970–1974); a senior staff fellow and then a research biologist at the Laboratory of Molecular Biology in the Division of Cancer Biology and Diagnosis at the National Cancer Institute, NIH (1974–1979); associate director for research in the Howard University Cancer Center and associate professor of oncology at the Howard University Medical School (1979–1982); professor of oncology and deputy director at the Howard University Cancer Center (1982–1985); and director (1985–1991), professor, and chair of the Department of Oncology (1985–1991).

His honors and awards include the Toxicology Forum's Distinguished Fellow Award, the Presidential Distinguished Executive Rank Award; and the Presidential Meritorious Executive Rank Award for sustained extraordinary accomplishments; the HHS secretary's Distinguished Service Award; the American College of Toxicology's First Distinguished Service Award, the National Minority Health Leadership Award (2005); and an invitation to participate in the International Conference on Disaster Prevention and Mitigation sponsored by the Harvard School of Public Health (2006). Alone among institute directors, he was awarded three of the most prestigious awards in public health: the Calver Award (2002),

the Sedgwick Medal (2004), and the Julius B. Richmond Award (2005). He was elected to membership in the Institute of Medicine in 1994 and appointed member of the Visiting Committee, Board of Overseers, of Harvard College (2007–2010). He is on the editorial board of numerous journals, serving in most instances as associate editor. He has been cited in *Current Contents*, *Life Sciences* for having published two of the 100 most-cited papers in 1978–1979. Over 28 visiting or postdoctorate fellows have trained in his laboratory, and he has published over 125 manuscripts in peer-reviewed journals and more than 45 review articles and book chapters. He has chaired or cochaired numerous national and international meetings and has been an invited speaker or keynote speaker at over 150 symposia seminars.

Christopher J. Portier, Ph.D., is associate director of the National Institute of Environmental Health Sciences (NIEHS), director of its Office of Risk Assessment Research, and leader of the Environmental Systems Biology (ESB) Research Group in the Laboratory of Molecular Toxicology. As associate director, he organizes and coordinates all research activities related to risk assessment both inside and outside the NIEHS with grantees and institutional collaborators. As head of ESB, he conducts research on quantifying and modeling the interactions of mammalian systems with environmental agents. Previously, he was director of the Environmental Toxicology Program and associate director of the National Toxicology Program.

He received his Ph.D. in 1981 from the University of North Carolina in biostatistics. He is an internationally recognized expert in the design and analysis of toxicology data and in risk assessment methodology. He has published over 150 peer-reviewed scientific manuscripts and over 50 book chapters or reports covering such diverse topics as risk assessment, statistics, cancer biology, immunology, development, genetically modified foods, and genomics. He has received numerous awards, including the Spiegelman Award from the American Public Health Association and the Outstanding Practitioner of the Year Award from the Society for Risk Analysis. He has aided in the development of risk assessment guidelines for both national and international authorities and has either directed or contributed significantly to numerous risk assessments, most notably those for dioxins, aflatoxins, and electromagnetic fields. In cooperation with the U.S. Department of State, CDC, and EPA, he has led efforts by the U.S. government to begin research on the health effects of Agent Orange in Vietnam. He is currently an adviser to the Finnish Academy of Sciences on the Centers of Excellence Research Program and a member of a number of World Health Organization/International Agency for Research on Cancer scientific committees. In the past 2 years, he has been invited to speak at over 50 scientific conferences, including international meetings in Vietnam, Germany, China, Japan, France, Australia, Italy, Finland, Switzerland, and Canada.

Rena Steinzor, J.D., is a professor at the University of Maryland School of Law and teaches courses in risk assessment, critical issues in law and science, torts, and a survey of environmental law. During the course of her academic career, she has written extensively on efforts to reinvent environmental regulation in the United States, the use and misuse of science in environmental policy making, and the devolution of legal and administrative authority to the states.

Steinzor is a founder and member of the executive committee of the board of the Center for Progressive Regulation (CPR) (www.progressiveregulation.org), a virtual think tank composed of 34 member scholars from universities across the United States. CPR is committed to developing and sharing knowledge and information, with the ultimate aim of preserving the fundamental value of the life and health of human beings and the natural environment. One component of CPR's mission is to circulate academic papers, studies, and other analyses that promote public policy based on the multiple social values that motivated the enactment of the nation's health, safety, and environmental laws. CPR seeks to inform the public about scholarship that envisions government as an arena in which members of society choose and preserve their collective values. CPR rejects the idea that government's only function is to increase the economic efficiency of private markets.

Before joining the law school faculty, Steinzor was the partner in charge of the environmental practice at Spiegel & McDiarmid, a Washington DC, law firm specializing in the representation of state and local government entities in the energy and environmental areas. Prior to joining the firm, she was counsel to the Subcommittee on Commerce, Transportation and Tourism of the House Energy and Commerce Committee, which was then chaired by James J. Florio (D-NJ). She advised the subcommittee during its consideration of the Superfund Amendments and Reauthorization Act of 1986 and the Asbestos Hazard Emergency Response Act of 1986. She also served as an attorney adviser to Commissioner Patricia P. Bailey of the Federal Trade Commission (FTC) and worked as a consumer protection attorney at the FTC in various staff positions. She is a 1976 graduate of Columbia Law School and a 1971 graduate of the University of Wisconsin.

Appendix C

Workshop Participants

Eileen Abt

National Research Council

Arthur Allen

washingtonindependent.com

Michael Babich

U.S. Consumer Product Safety
Commission

Cal Baier-Anderson

Environmental Defense Fund

Mark Baldwin

U.S. Environmental Protection
Agency

Gary Bangs

U.S. Environmental Protection
Agency

Nancy Beck

Office of Management and Budget

Rick Becker

American Chemistry Council

Paul Billings

American Lung Association

Ann Bradley

Integral Consulting

David Butler

National Academy of Sciences

Clark Carrington

U.S. Food and Drug Administration

Margaret Chu

The National Center for
Environmental Assessment

George Corcoran

Society of Toxicology

William Couzens

Next Generation Choices Foundation

Betty Dabney

University of Maryland School of
Public Health

Darinka Djordjevic

International Life Sciences Institute
North America

Timothy Donaghy

Union of Concerned Scientists

Monique Falconer

University of Maryland, Baltimore

Colleen Flaherty

U.S. Environmental Protection
Agency

Mary Gant

National Institutes of Health

Barbara Greenberg

U.S. Department of Health and
Human Services

James Harvey

Analytic Services, Inc. (ANSER)

Dan Hochman

University of Texas Medical Branch

Michael Holsapple

ILSI Health and Environmental
Sciences Institute

Nancy Hughes

American Nurses Association

Mohammad Asif Ismail

Center for Public Integrity

Ken Jacobson

House Committee on Science and
Technology

Stephanie Johnson

American Psychological Association

Russell Keenan

AMEC Earth & Environmental, Inc.

Melissa Kramer

U.S. Environmental Protection
Agency

Yanna Lambrinidou

Parents for Nontoxic Alternatives

Stephen Lester

Center for Health, Environment &
Justice

Kim Li

Amgen, Inc.

Kathryn Mahaffey

U.S. Environmental Protection
Agency

Nikki Maples-Reynolds

ICF International

Catherine McMahon

American Cancer Society

Michele Monti

Division of Environmental
Epidemiology

Moiz Mumtaz

The Agency for Toxic Substances and
Disease Registry

Brian Myhr

Genotox Consulting

Lauren Park

The Weinberg Group, Inc.

Pasky Pascual

U.S. Environmental Protection
Agency

Gerain Perry

U.S. Environmental Protection
Agency

Preston Pittman

Weinberger Group

Ana Pomaes

U.S. Environmental Protection
Agency

Kathleen Quinn

University of Maryland

Kathleen Raffaele

U.S. Environmental Protection
Agency

Matthew Shudtz

Center for Progressive Reform

Dale Strother

ToxSolve, LLC

Kimberly Thigpen Tart

National Institutes of Health

Sally Tinkle

National Institutes of Health

Lorna Totman

Lorna Totman Consulting, LLC

Ram Tripathi

Virginia Department of Health

Jay Vodela

U.S. Department of Agriculture

Amy Wang**Darren Webb**

Health and Medicine Counsel of
Washington

Douglas Weed

The Weinberg Group

Philip Wexler

National Library of Medicine

Mary Wolfe

National Toxicology Program

Gerri Wolffe

National Institutes of Health

