EPA
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Agency

Framework for Assessing the Public Health Impacts of Risk Management Decisions

Office of Research and Development

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Disclaimer

This document has been reviewed by ORD's Science Council and their comments have been addressed. This report does not constitute an Agency position or policy concerning public health research. Any mention of trade names does not constitute Agency endorsement.

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Acronyms and Abbreviations

Agency	U.S. Environmental Protection Agency
CAIR	Clean Air Interstate Rule
CDC	Centers for Disease Control and Prevention
COSEPUP	Committee on Science, Engineering, and Public Policy
EPA	U.S. Environmental Protection Agency
GAO	Government Accountability Office
GEOSS	Global Earth Observation System of Systems
GPRA	Government Performance and Results Act
HEI	Health Effects Institute
HHS	Health and Human Services
MOU	Memorandum of Understanding
MSAT	mobile source air toxics
MYP	Multi-year Plan
NARSTO	North American Research Strategy for Tropospheric Ozone
NASA	National Aeronautical and Space Administration
NCER	National Center for Environmental Research
NCI	National Cancer Institute
NHANES	National Health and Nutrition Examination Survey
NHEXAS	National Human Exposure Assessment Survey
NHMES	National Human Exposure Monitoring Survey
NIEHS	National Institute of Environmental Health Sciences
NOAA	National Oceanic and Atmospheric Administration
NO_X	nitrogen oxide
OAR	Office of Air and Radiation
OMB	Office of Management and Budget
ORD	Office of Research and Development
PAHs	polycyclic aromatic hydrocarbons
PART	program Assessment and Rating Tool
PCBs	polychlorinated biphenyls
RFA	Request for Application
ROE	*Report on the Environment*
TRI	Toxic Release Inventory
USGS	U.S. Geological Survey

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Executive Summary

Over the last several years, there has been increased interest in assessing the effectiveness the Agency's regulatory and nonregulatory decisions. In 2001, the U.S. Environmental Protection Agency (EPA) Administrator noted that, for the Agency to measure the progress achieved in meeting its environmental goals and fulfill its public health mission, it must go beyond its historic reliance on process indicators to measurable changes in ecological and human health outcomes. The Government Performance and Results Act (GPRA) now requires the Agency to establish strategic goals, measure performance, and report on the degree to which those goals were met. Such goals and performance measures were included in the *2006-2011 EPA Strategic Plan*. The Office of Management and Budget (OMB) also has encouraged the Agency to develop a formalized process to measure how the Office of Research and Development (ORD) supports its risk assessment goals. OMB now requires the Agency to develop demonstrable performance measures that document improvement in some measure of public health or the environment.

The 2003 *Report on the Environment* (ROE) was the first attempt of EPA to provide a national assessment of environmental and human health at the national level. The ROE was updated in 2007 to focus on assessing trends in human disease and exposure that may be associated with environmental factors on a national scale. Both versions of the ROE noted several gaps in our knowledge that currently impair the ability to measure effectiveness of regulatory and nonregulatory decisions by the Agency. Of primary concern in the ROE was the lack of indicators linking source to exposure to effect that could be used to evaluate changes in health baselines that follow risk management decisions.

The purpose of this *Framework for Assessing the Public Health Impacts of Risk Management Decisions* is to provide an understanding of the research needed to develop and validate indicators of the source-to-exposure-to-effect paradigm. Such indicators are essential for developing subsequent approaches to assess the public health impacts of risk management decisions.

I. Introduction

A. Overall Objective

This document describes a strategic framework for research to aid the U.S. Environmental Protection Agency (EPA or the Agency) efforts to assess the effectiveness of its regulatory and nonregulatory environmental decisions with respect to improved human health or environmental conditions. ORD will use this strategic framework to develop an implementation plan for a research program that will identify and address knowledge gaps currently limiting this effort. It is envisioned that the research program will consist of an integrated, multidisciplinary approach utilizing ORD's many scientific disciplines and resources in concert with the extramural grants program managed by the National Center for Environmental Research (NCER). In developing this framework, it was recognized that the needed scientific disciplines (e.g., exposure science, development of biological indicators, risk management sciences, statistical approaches) are in varying stages of maturity. Thus, the rate of evolution in certain disciplines will determine the time required to develop principles that can be used by the Agency to assess effectiveness of its environmental decisions.

B. Risk Assessment and Risk Management

Protecting human health from the effects of environmental stressors such as chemical contaminants is an integral part of the Agency's mission. Sustaining or restoring the health of people and communities is also a central focus of various research and regulatory programs as the Agency moves toward a preemptive role in reducing the burden of environmental health effects. To determine how well the Agency is accomplishing its mission, the human health impacts of environmental stressors in air and water and on land are estimated routinely. Thorough study of adverse health effects associated with environmental exposures and the identification and evaluation of effective risk management technologies and approaches have enabled the Agency to manage harmful levels of exposure. As a result, guidelines exist for the safer production and handling of a number of environmental agents; however, this work is far from complete.

During the last few years, there has been increased interest in assessing the effectiveness of the public health impact of environmental decisions. As seen in Figure 1, assessing risk consists of evaluating exposure and dose-to-effects to develop a risk assessment, which informs development of risk management options. Assessing the effectiveness of these

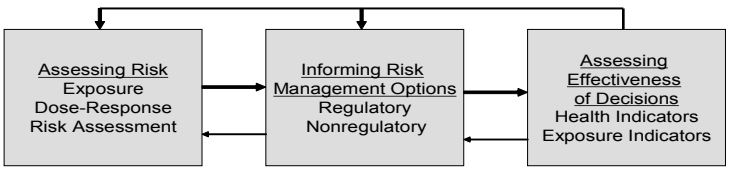

Figure 1. Process for Assessing Public Health Impacts of Environmental Decisions

decisions is now seen as an integral part of the risk assessment/risk management process. If environmental decisions are found to be ineffective, then this observation should lead to additional research to refine the first step of the process. Although the Agency has made significant strides in establishing metrics for

evaluating the risk assessment component of this process, it has less experience in establishing metrics to evaluate the effectiveness of its environmental decisions.

The Government Performance and Results Act (GPRA) requires the Agency to set strategic goals, measure performance, and report on the degree to which these goals are met. The Government Accountability Office (GAO) has also noted that the Agency's GPRA strategy could be improved by including more outcome goals (i.e., those that reflect actual environmental or health improvement) to complement process goals. These can inform the public about the validity of our performance measures. Although outcome measures have been proposed, GAO and the Agency agree that there is a lack of scientific tools and processes to measure environmental outcome.

In the 1999 report, "Evaluating Federal Research Programs: Research and the Government Performance and Results Act," the National Academy of Science's Committee on Science, Engineering and Public Policy (COSEPUP) evaluated the strategic and performance plans of 10 Federal agencies that engage in basic and applied research, including EPA. The committee concluded that meaningful outcomes of basic research cannot be measured directly on an annual basis because of their inherent unpredictability. Instead, different types of indicators should be used to measure the quality of the research, the relevance of the research to the Agency's mission, and research outputs compared to that of the international research community (i.e., Is the research cutting edge compared to the rest of the world?). The committee further asserted that these evaluations can be accomplished by expert review. COSEPUP had similar recommendations for applied research, concluding that milestones can be established so that progress can be evaluated annually.

Recent program reviews by the Office of Management and Budget (OMB) also have encouraged the Agency to develop a formalized process to measure how ORD supports its risk assessment goals. An integral component of this evaluation is to determine the extent to which ORD is meeting the needs of the Agency's Program and Regional Offices as they develop approaches to evaluate the benefits of their rules, regulations, and environmental management decisions. OMB now requires the Agency to develop performance measures that demonstrate improved public health and environment.

It is also noteworthy that the importance of assessing the effectiveness of regulatory decisions is now being recognized by media-specific regulatory programs. For example, in its 2004 report "*Air Quality Management in the United States,*" the National Academy of Sciences recommended the country's air quality management system ". . . strive to emphasize results over process, create accountability for the results, and dynamically adjust and correct the system as data on progress are assessed . . . ." The Agency's Clean Air Act Advisory Committee has called for an "overarching accountability framework" that includes a systematic effort to track air quality achievements and evaluate air program results. This effort will be focused on the progression and associations of air emissions as they interact and ultimately affect public health and the environment. To move beyond the current

approach of relying predominately on air quality measurements, the Agency needs to further develop and apply the capability and capacity to monitor, assess, and report on how changes in emissions impact air quality, atmospheric deposition, exposure, and effects on human health and ecosystems. Similarly, the Agency's National Drinking Water Advisory Council formed a subgroup in 2005 to identify drinking water performance indicators and measures.

C. Strategic Planning and Indicator Research

Establishing measures to evaluate progress of the Agency in meeting its mission now plays a prominent role in the *2006-2011 EPA Strategic Plan.* For example, the Agency developed strategic targets and related measures of progress. One measure focuses on mercury blood levels in women of childbearing age as a reflection of the health risk from consuming contaminated fish. Another strategic target involves human-body-burden of pesticides. The *2006-2011 EPA Strategic Plan* clearly articulates the need to develop and use a suite of scientifically sound indicators to track trends in environmental influences on human health. Clearly, the challenge will be to identify valid and predictive indicators. We need to establish the relationships between specific management actions and the related indicators that provide the Agency with the means to assess current health conditions and establish a baseline against which progress may be measured.

In response to emerging needs in this area, ORD initiated an exploratory program to develop principles that could be used to verify the protective benefit of environmental decisions. In 2005, ORD launched a pilot proof-of-concept program that engaged the Program and Regional Offices in identifying and submitting proposals on ongoing or anticipated decisions and actions that would be appropriate for assessing public health impact. Multidisciplinary teams from ORD and Regional and Program Offices helped develop and evaluate the research proposals for scientific and programmatic content. Two proof-of-concept environmental health and diseases projects were selected. Studies are underway, including one on cumulative air pollution reduction programs and environmental health indicators for children and the elderly and another on salivary antibody responses as an indicator of waterborne infections. In addition, NCER recently issued a Request for Application (RFA) that focuses on the use of existing databases of environmental (ambient), biological, and health-related data to develop indicators that reliably signal the impact of changes in environmental conditions, management approaches, or policies on human health.

Our nation's approach to environmental protection largely has been reactive. Environmental laws, institutions, and regulations have been created in response to existing environmental and public health threats. Policymakers and research planners rarely have the opportunity to contemplate long-term or emerging environmental challenges that lie ahead or how to adapt to transformative or disruptive changes.

Futures analysis helps position organizations to anticipate future environmental issues and encourages proactive planning to avoid problems, rather than responding after the

fact. An awareness of the environmental consequences of future social, economic, and technological changes can help public sector leaders make better informed, strategic decisions about environmental protection in a rapidly changing world.

A more anticipatory vision of research is required to gain a better understanding of underlying phenomenology of increasingly complex interrelated global issues (energy, climate, environment, water, demography, and health). Exploiting early warning signs from observable ecological phenomena that link to potential human health effects (e.g., climate change effects and spread of anthroponotic and zoonotic infectious diseases, Hurricane Katrina) could inform a systems approach to environmental and public health protection. ORD established a goal to anticipate future environmental issues, which has three objectives:

(1) develop an organizational capability for environmental foresight,
(2) stimulate dialogue both inside and outside the Agency on future environmental developments and their significance, and
(3) pilot futures analysis for a few key environmental issues.

Under this goal, we expect to identify and understand potential future risks to human health and the environment, recommend new directions for research and program management decisions, and identify innovative, cost-effective solutions and alternatives through an ongoing futures effort. We do not intend to predict the future, but rather " . . . to interpret the present in a new way—a way that makes more sense and seems more conventional the farther into the future one goes . . . . " In March 2007, ORD published the report "*Shaping Our Environmental Future: Foresight in the Office of Research and Development.*" This document examines how futures analysis can enhance ORD's research planning and development of science policy, describes approaches that ORD will take to implement its office-wide futures activities, provides examples of past applications, and represents a point of departure for a continuing course of action to inform planning and policy. Whereas this framework was written specifically for use and implementation by ORD, the content is of broader application and may offer helpful guidance in establishing futures efforts in other organizations.

II. Research Needs Identified in the *Report on the Environment*

A. *Report on the Environment*

The 2003 *Draft Report on the Environment* (ROE) was the first attempt by the Agency to provide an assessment of environmental and human health at the national level. The ROE was the first step in the Agency's Environmental Indicators Initiative, which was developed to provide better indicators for the Agency to use and track the state of the environment and support improved environmental decisionmaking. The ROE indicated that understanding the effectiveness of environmental programs and measuring actual progress require being able to track trends in valid and predictive indicators of public health and environmental condition. In that respect, the ROE described a hierarchy of indicators, including administrative metrics.

These include number of permits issued (Level 1), regulatory actions (Level 2), reductions in pollutant emissions (Level 3), changes in ambient concentrations of a chemical (Level 4), measures of exposure (Level 5), and changed ecological or human health status (Level 6).

The 2003 ROE had two main categories of indicators. Category 1 indicators were peer-reviewed and supported by national level data for more than one time point. Category 2 indicators were peer-reviewed, but supporting data were available only for part of the nation or did not have a measure for more than one time point.

The Human Health Chapter in the 2007 ROE emphasizes the continuing need to identify appropriate indicators to help identify the extent to which human exposures may be occurring and measures of health outcomes that possibly are influenced by environmental exposures. Table 1 summarizes the questions raised by the two versions of the ROE and the indicators that were discussed.

The 2007 ROE also focuses on assessing trends in human disease and exposure that may be associated with environmental factors on a national scale. Indicators selected are incidence or prevalence data for cancer and noncancer (e.g., cardiovascular disease, respiratory disease, birth outcomes) end points that affect multiple biological systems and are associated with a number of causal factors, including environmental factors. Although certain trends in the health data can be discerned over time for some end points, there are a number of limitations to this approach. Generally, these indicators track the incidence or prevalence of a given disease over time, but these trends cannot be linked directly to a contaminant source or specific contaminant. The ROE indicated that there is a need to track other diseases and conditions (i.e., neurodegenerative diseases, developmental behavioral disorders, reproductive disorders) for which there are potential environmental risk factors and a need to establish databases applicable to the regional and local levels.

The 2007 ROE concludes that there is a significant gap in outcome measures that could provide a clearer understanding of how environmental factors contribute to public health outcomes such as disease. The ROE notes a number of limitations in this regard associated with currently available indicators. For example, although there appeared to be a number of adequate measures of outdoor air quality and diseases for which air quality was a risk factor, there were no measures of such diseases that could be attributed specifically to exposure to air pollutants.

With regard to indoor air quality, trends in health effects, such as asthma, could not be definitively ascribed to trends in certain indoor air contaminants, such as molds. The same is true for indicators of health effects that could be definitively linked to exposure to contaminated waters or to consuming contaminated fish and shellfish. The ROE found that, despite a dramatic increase in the use of chemical products in the landscape over the last 50 years, it is impossible to correlate indicators of the existence of chemicals in the environment, either singly or in combination, with indicators of the corresponding health effects observed in any given population. Health effects from exposure to toxic chemicals can range from short-term acute effects, such as respiratory distress, to

long-term chronic effects, such as cancer. In addition, populations of people have differential vulnerabilities and may show different effects at comparable exposures. Thus, developing indicators that respond to the appropriate time and population scales remains problematic.

The 2007 ROE also discusses the application of biomonitoring data to assess trends in exposure of the population to environmental contaminants. Such approaches have been used to measure or estimate the levels of human exposure to environmental contaminants, including ambient pollution measures, models of exposure, personal monitoring data, and biomonitoring data. The ROE used a subset of data from the Center for Disease Control and Prevention's (CDC)'s National Health and Nutrition Examination Survey (NHANES) to demonstrate changes in the presence of specific environmental contaminants, such as lead, mercury, cadmium, persistent organic pollutants, cotinine, pesticides (carbamates, organophosphates, pyrethroids, and herbicides), and phthalates. These data can provide information at the national level on the general magnitude of exposures to a subset of contaminants. However, biomonitoring data usually do not identify and explain possible differences among some subpopulations or provide information on the geographic distribution of the populations of concern, nor do they reveal the source of exposure. Biomonitoring also does not provide information on conditions of exposure (for example, pathways and routes of exposure or the frequency, duration, and magnitude of exposure) or information on other contaminants of possible interest or consider multiple exposures or measure levels that are likely to cause harmful health effects.

There is a need for better information on the chemistry (including fate and transport), quantities, and longevity of various substances in the environment and in biological tissues. We also need to focus on the cumulative effects of various chemicals in humans, the pathways and effects, and the need for monitoring data to link exposures to health effects. For example, although there are databases that provide information concerning the presence of a chemical or its metabolite in biological tissues, these data are not necessarily valid measures of actual exposure, nor are they necessarily predictive measures of adverse public health outcomes.

The ROE identifies a number of key research challenges concerning the development of more effective indicators to assess public health impacts, including the needs to

- develop an integrated set of health indicators that could be used at all spatial scales and assessed over time,
- develop indicators that would provide risk assessors and risk managers with the capability to distinguish acceptable from unacceptable conditions (i.e., a threshold), and
- establish the link between an indicator of exposure and the change in risk of a public health measure.

B. Need To Develop Indicators To Assess Impact of Environmental Decisions

The 2003 ROE concludes that the United States has made significant strides in meeting environmental challenges over the last 30 years. However, to better understand the status of and

trends in public health, better indicators of human exposure and health are needed. Indicators mentioned in either the 2003 or 2007 Draft ROE are summarized in Table 1. There are several major challenges currently associated with the development of indicators. It is very important, for example, that indicators be applicable at the national, regional, and local levels. There also needs to be consensus on the inclusion of specific end points to develop an integrated core set of indicators. Indicators need to be able to help decisionmakers distinguish acceptable from unacceptable conditions and establish the linkage between risk management actions, exposure, and subsequent health effects. In moving forward, it is important to note that the current national-scale ROE indicators do not directly link exposure with outcomes and cannot be used to demonstrate causal relationships. However, when combined with other information, such as environmental monitoring data and data from toxicological, epidemiological, or clinical studies, these indicators can be an important key to improve the understanding of the relationship between environmental contamination and health outcomes.

It is also clear that new indicators need to be developed to address specific risk management and exposure scenarios and for conditions for different classes of chemicals of interest. For example, health effects from exposure to toxic chemicals may range from short-term acute effects following exposure to organophosphate pesticides to long-term chronic effects, such as cancer or asbestosis. Some chemicals are metabolized extensively and cleared by the body in a relatively short period of time, whereas others, such as persistent organic pollutants or toxic metals, do not break down and tend to accumulate in humans. Some health effects may appear shortly after exposure, whereas others may require a long leadtime before the disease occurs. There is also the possibility for epigenetic or multigenerational effects. Furthermore, some groups within the population may be predisposed to toxicity, such as children or older adults. These people may be more vulnerable to some chemicals because of life-stage-specific pharmacodynamic or pharmacokinetic factors. There is the possibility there may be combined, synergistic, and cumulative effects following exposure to multiple pollutants in the environment. Finally, risk management activities may involve site specific risk-risk tradeoffs, for example, switching from chlorine to chloramine drinking water disinfection, which trades off the potential security risk of chlorine tanks, with increased leaching of lead and copper from water distribution systems.

The 2007 ROE clearly articulates several criteria that should be used in the development and validation of indicators to be used in assessing the impact of environmental decisions on public health; some follow below.

- The indicator must be useful—it answers or makes an important contribution to answering a question in the ROE.
- The indicator is objective—it is developed and presented in an accurate, clear, complete, and unbiased manner.
- The underlying data are characterized by sound collection methodologies, data management systems to protect its integrity, and quality assurance procedures.

Table 1. Questions and Indicators Mentioned in the Draft 2003 and 2007 ROE

Indicator Name	2003	2007	Section in Draft ROE 2003	Question in 2007 ROE
General Mortality	X	X	*Health Status of the U.S. Compared to the Rest of the World*	***What are the trends in health status in the United States?***
Life Expectancy at Birth	X	X	*Health Status of the U.S. Compared to the Rest of the World* *Health Status of the U.S.: Indicators and Trends of Health and Disease*	***What are the trends in health status in the United States?***
Infant Mortality	X	X	*Health Status of the U.S. Compared to the Rest of the World* *Health Status of the U.S.: Indicators and Trends of Health and Disease*	***What are the trends in health status in the United States?***
Cancer Incidence	X	X	*Health Status of the U.S.: Indicators and Trends of Health and Disease*	***What are the trends in human disease and conditions for which environmental contaminants may be a risk factor, including across population subgroups and geographic regions?***
Cancer Mortality	X		*Health Status of the U.S.: Indicators and Trends of Health and Disease*	
Childhood Cancer Incidence	X	X	*Health Status of the U.S.: Indicators and Trends of Health and Disease*	***What are the trends in human disease and conditions for which environmental contaminants may be a risk factor, including across population subgroups and geographic regions?***
Childhood Cancer Mortality	X		*Health Status of the U.S.: Indicators and Trends of Health and Disease*	
Cardiovascular Disease Prevalence and Mortality	X	X	*Health Status of the U.S.: Indicators and Trends of Health and Disease*	***What are the trends in human disease and conditions for which environmental contaminants may be a risk factor, including across population subgroups and geographic regions?***
Chronic Obstructive Pulmonary Disease Prevalence		X		***What are the trends in human disease and conditions for which environmental contaminants may be a risk factor, including across population subgroups and geographic regions?***
Chronic Obstructive Pulmonary Disease Mortality	X	X	*Health Status of the U.S.: Indicators and Trends of Health and Disease*	***What are the trends in human disease and conditions for which environmental contaminants may be a risk factor, including across population subgroups and geographic regions?***
Asthma Prevalence	X	X	*Health Status of the U.S.: Indicators and Trends of Health and Disease*	***What are the trends in human disease and conditions for which environmental contaminants may be a risk factor, including across population subgroups and geographic regions?***

Table 1 (cont'd). Questions and Indicators Mentioned in the Draft 2003 and 2007 ROE

Indicator Name	2003	2007	Section in Draft ROE 2003	Question in 2007 ROE
Asthma Mortality	X		*Health Status of the U.S.: Indicators and Trends of Health and Disease*	
Infectious Diseases Associated with Environmental Exposures or Conditions	X	X	*Health Status of the U.S.: Indicators and Trends of Health and Disease*	***What are the trends in human disease and conditions for which environmental contaminants may be a risk factor, including across population subgroups and geographic regions?***
Birth Defects Rates and Mortality	X	X	*Health Status of the U.S.: Indicators and Trends of Health and Disease*	***What are the trends in human disease and conditions for which environmental contaminants may be a risk factor, including across population subgroups and geographic regions?***
Low Birthweight	X	X	*Health Status of the U.S.: Indicators and Trends of Health and Disease*	***What are the trends in human disease and conditions for which environmental contaminants may be a risk factor, including across population subgroups and geographic regions?***
Preterm Delivery		X		***What are the trends in human disease and conditions for which environmental contaminants may be a risk factor, including across population subgroups and geographic regions?***
Blood Lead Level	X	X	Measuring Exposure to Environmental Pollution: Indicators and Trends	***What are the trends in human exposure to environmental contaminants, including across population subgroups and geographic regions?***
Blood Mercury Level	X	X	Measuring Exposure to Environmental Pollution: Indicators and Trends	***What are the trends in human exposure to environmental contaminants, including across population subgroups and geographic regions?***
Blood Cadmium Level	X	X	Measuring Exposure to Environmental Pollution: Indicators and Trends	***What are the trends in human exposure to environmental contaminants, including across population subgroups and geographic regions?***
Urinary Arsenic	X		Measuring Exposure to Environmental Pollution: Indicators and Trends	
Blood Persistent Organic Pollutants Level	X	X	Measuring Exposure to Environmental Pollution: Indicators and Trends	***What are the trends in human exposure to environmental contaminants, including across population subgroups and geographic regions?***
Blood Cotinine	X	X	Measuring Exposure to Environmental Pollution: Indicators and Trends	***What are the trends in human exposure to environmental contaminants, including across population subgroups and geographic regions?***
Urinary Pesticide Level	X	X	Measuring Exposure to Environmental Pollution: Indicators and Trends	***What are the trends in human exposure to environmental contaminants, including across population subgroups and geographic regions?***
Urinary Phthalate Level		X		***What are the trends in human exposure to environmental contaminants, including across population subgroups and geographic regions?***
Blood VOC Levels	X		Measuring Exposure to Environmental Pollution: Indicators and Trends	

- Data are available to describe changes or trends, and the latest available data are timely.
- The data are comparable across time and space and representative of the target population—trends depicted in this indicator accurately represent the underlying trends in the target population.
- The indicator is transparent and reproducible—the specific data used and the specific assumptions, analytic methods, and statistical procedures employed are stated clearly.

Additional improvements to indicator development are characterized in the emerging issues section of the Goal 4 chapter in the *2006-2011 EPA Strategic Plan*. "Through distributed sensor networks, we could collect and transmit environmental indicator data faster and more frequently, improve data quality, enhance data integration, and improve data sharing. . . . This technology could support our Report on the Environment, advance our foresight capabilities, and provide data that accurately portrays [*sic*] environmental conditions on a real-time basis." Distributed sensor networks and other advanced sensor systems can make possible dramatic improvements in many areas of performance measurement, program management and environmental monitoring. Although these technologies are not yet applicable to existing public health indicators, they offer the potential for tracking upstream indicators. These technologies also offer the potential to monitor across wide areas, detect a broad range of pollutants that could harm human health or the environment, provide information in real time, and make more accurate assessments of environmental loadings and trends and the results of our remedial actions. They can be applied in all areas of the Agency's responsibility, from water and air quality to land contamination. Sensor networks can help close the gap between our actions and the outcomes we hope to achieve.

III. Linking Source to Outcome in Developing Indicators

A. The Source-to-Outcome Paradigm

For the Agency to develop indicators to assess the public health impact of its environmental decisions, it must develop a better understanding of the linkages between various components of the risk management-source-environment-exposure-dose-health effects continuum. The environmental public health paradigm shown in Figure 2 illustrates the broad continuum of factors or events that may be involved in the potential development of human disease following exposure to an environmental contaminant. This series of events serves as the conceptual basis for understanding and evaluating environmental health. The figure illustrates that, for adverse health effects to occur (clinical disease or death) from exposure to an environmental contaminant, many things have to happen. A contaminant must be released from its source, transverse through the environment (air, water, and soil), reach human receptors (ingestion, inhalation, or dermal contact), enter the human body and be present within the body at sufficient doses to cause biological changes that ultimately may result in an observed adverse health effect.

Each block in Figure 2 can have indicators associated with it. Risk management

actions also may be associated with any of the boxes. For example, some risk management activities create stressors (disinfection by-products), some affect pollutant transport or transformation (scrubbers); some risk communication programs target exposure (ozone

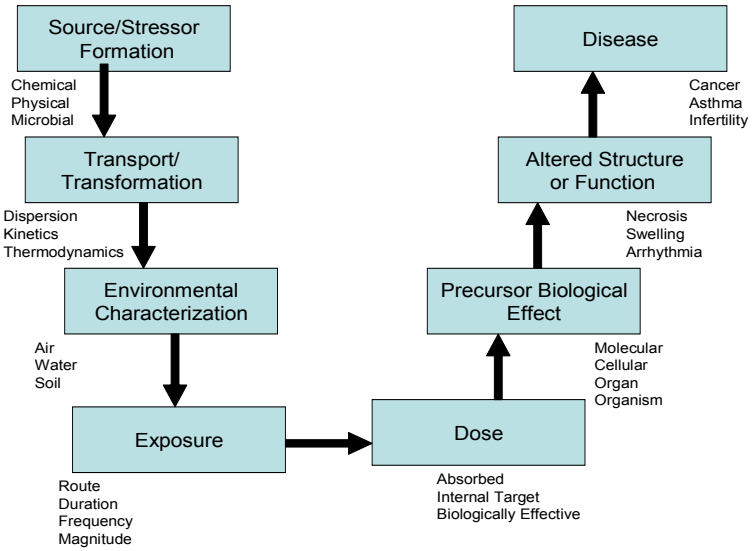

Figure 2. The Source-Exposure-Dose-Effects Continuum

watches, and fish advisories) or dose (sunscreens), or early biological effects (antioxidant supplements) or disease (drugs and surgery). The first three components represent the physical processes common to many pollutants, their formation, release, transport, and transformation in the environment. These indicators track the presence of contaminants or other stressors affecting air, water, and land and may be applicable to multiple pollutants and occur outside the body. The exposure component represents the interface between a human and the pollutant, and exposure science characterizes the processes by which humans are exposed to a pollutant (or other stressor). Measurements of exposures are different from the measurements of dose. The last four components of the paradigm, (1) dose, (2) precursor biological effect, (3) altered structure or function, and (4) disease, all represent the response of the body to environmental exposure. However, national-scale data do not exist for indicators of each component of the paradigm at this time. A major uncertainty in the interpretation of indicator information is the relationship between exposure to ambient contaminants and a subsequent linkage to some biological effect. Epidemiological data can provide statistical associations and may suggest causal relationships between environmental exposures and various diseases. Sound science mandates that accurate exposure estimates be used with public health data to make the relationships as reliable as possible. Extensive and collaborative data collection and research efforts across the scientific community continue to strengthen our understanding of the relationships between environmental exposures, risk management measures, and disease.

The 2003 ROE provided a few examples of successful linkages between exposure to environmental contaminants and disease, including water treatment and diarrheal deaths, air pollution levels and sudden deaths, and lead in gasoline and blood lead levels (as an indicator of neurological deficits). In developing and using indicators, the linkages between exposure and disease must be well established. The Agency relies on the possible linkages established through the types of studies highlighted above to

identify environmental contaminants and health outcomes of potential Agency interest. The current focus for the ROE is on national-scale indicators. Because data and effects may be regional or community based, and environmental management decisions are made at these scales, there needs to be careful consideration of the spatial relationship of outcome indicators and the data systems needed to collect such data.

A primary objective of a research program to develop indicators to assess public health impact of environmental decisions should be to provide the methods, models, and data that will represent the full spatial spectrum of linkage between exposure to environmental contaminants and health effects.

B. Using the Source-to-Outcome Paradigm To Assess Critical Data Needs

The source-outcome continuum describes the physical processes by which an environmental exposure occurs and leads to an adverse outcome. It is clear that health-outcome-oriented indicators—those representing risk management-exposure-dose effects—can provide the most direct evidence that the Agency's actions have had an effect in protecting human health.

Figure 3 arrays the availability of current environmental indicators against the quality of those indicators using the Hierarchy of Indicators that was mentioned earlier. The higher the level of the indicator, the more power and less uncertainty it has in documenting improvement in health resulting from an Agency action or regulation. Levels 1 and 2 are considered "Administrative," whereas Levels 3 through 6 are "Environmental." The levels in the hierarchy parallel the components of the source-exposure-effects continuum described in Figure 2. Source emissions are Level 3, ambient characterization is Level 4, exposure and dose are Level 5, and disease outcomes are Level 6. Clearly, environmental measures in the higher levels, such as improved ambient conditions, reduced exposure or body burden, and improved health condition, would be more optimal indicators to demonstrate progress in fulfilling the Agency's mission. The types of indicators described in the 2003 ROE are largely Levels 1 through 3. Currently, all indicators in the ROE are derived using national-scale data.

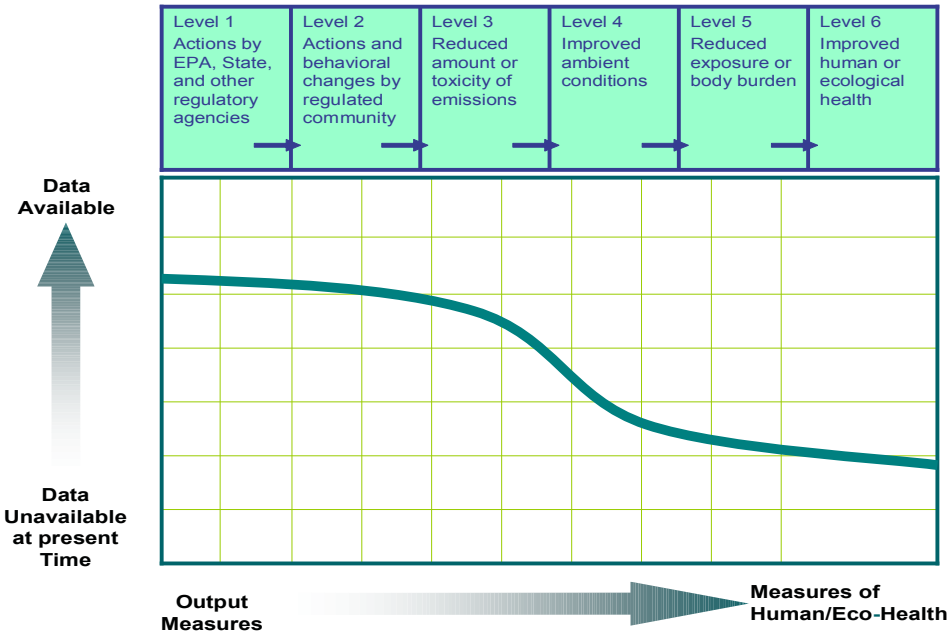

Figure 3. Comparing Data Availability Across the Source-to-Effects Continuum

The optimal circumstance would be to develop valid and predictive indicators at Levels 5 and 6. Level 5 indicators involve improved estimates of exposure or dose, and, although they are challenging enough, Level 6 indicators—measures of human health impacts from environmental conditions—require a comprehensive understanding of linkages between sources and human health effects and the understanding of the relationship between risk management actions and the impaired condition.

It is not sufficient, however, from a public health outcomes perspective, to measure simply biomarkers in the population. Without information about the determinants of exposures leading to those biomarkers, no objective evaluation of the effectiveness of Agency risk management decisions can be made. A program of biomarker measurements must be augmented with a program of exposure measurements to evaluate the effectiveness of regulatory programs. Examples of such a program would be the recently completed pilot program of the National Human Exposure Assessment Survey (NHEXAS) and the National Human Exposure Monitoring Survey (NHEMS). If done on a longitudinal basis in a sufficiently large population, this approach has the advantage of evaluating the impact of environmental management interventions on human exposure. This approach does not measure changes in public health directly but depends on an understanding of the exposure-dose-response relationship to extrapolate the changes in exposure to changes in public health.

IV. Developing a Framework for a Research Program

A. Essential Framework for Indicators

The framework guiding research in ORD's program to develop indicators to assess the public health impact of environmental protection decisions is illustrated in Figure 4. This figure represents a merger of the process for assessing the public health impacts of environmental decisions in Figure 1 with the source-outcome paradigm in Figure 2 and the hierarchy of indicators from Figure 3. Figure 4 suggests that indicators at all levels may be required to improve environmental regulations or other actions. Because the paradigm presumes that emissions of toxicants into the environment, whether anthropogenic or not, may lead to exposures that can produce or contribute to health effects in various human populations, public health outcomes or effects could be forecast by understanding the geographic and temporal trends associated with emission, ambient pollution concentrations, or exposure/dose. Given the scientific uncertainties involved in linking sources to outcomes, the closer the indicators are to the exposure/dose or human health response part of the paradigm, the less uncertainty there is in the predictions of outcomes or effects. Most of the data traditionally captured by the Agency has been from Levels 1 through 3, including emissions and toxicant production and use data, toxicant release or disposal data, and toxicant fate and transport data. Examples of these kinds of metrics include the widely used Toxic Release Inventory (TRI). Although useful on many fronts, information

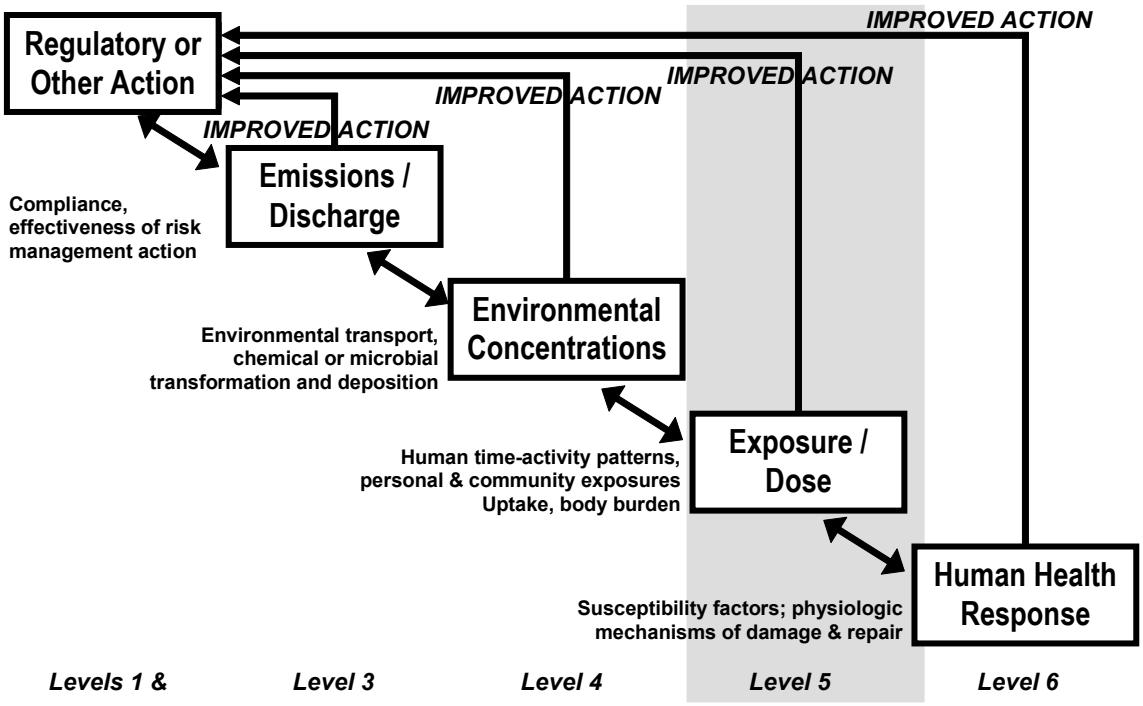

Figure 4. Essential Framework Guiding Research on Indicator Development

such as TRI has limited use in predicting outcomes because these data provide no information on potential receptors, potential routes of exposure, and inherent toxicity of compounds, thus, making exposure assessments extremely difficult.

Level 5 exposure/dose indicators, including body burden data captured by NHANES, can be useful in predicting outcomes when datasets are robust. The example with declining blood-lead levels is compelling because they, for example, are linked closely to neurotoxicity, and levels of blood-lead in children are tightly correlated with neurobehavioral outcomes. To be a valid and predictive indicator for the Agency's use, an exposure or dose (Level 5) indicator must be linked in both directions along the paradigm. The indicator of exposure or dose must represent and predict the environmental contribution to an adverse human outcome, even though many diseases or outcomes may be caused by several factors, only one of which is environmental exposure. If the indicator is to be useful in improving Agency actions and gauging effectiveness—which is the goal of ORD's indicator development research—then the Agency must be able to identify the sources and pathways that give rise to human exposures to develop effective risk management options (Figure 1).

Effects data (Level 6 indicators) would include measures of human health response (indicators will range from measures of early molecular changes to frank effects), including incipient measures of damage, such as DNA adducts and changes in gene expression, cytokine, or other cellular mediators or tissue hypertrophy. Various indicators or biomarkers of disease, including such measures as polyp

progression, coronary artery blockage, airway resistance, and others, lie close to the right in the paradigm. These early indicators of disease will be essential for diseases of long latency, where the time interval between exposures and health effects can be decades long, as in many cancers. Finally, changes in morbidity or mortality rates in populations can be counted by epidemiological investigations or estimated, in some cases, via the surveillance of surrogate data, such as estimating asthma through the use of sales data for asthma drugs or estimating diarrheal disease through antidiarrheal medicines. To be useful to the Agency, a Level 6 indicator must be valid and predictive. The indicator must reliably predict the probability of an adverse outcome, even if the final disease state may take years to develop. The indicator also must be an accurate representation of the environmental toxicant contribution to the response if the effectiveness of the Agency's regulatory actions is to be assessed. Indicators that can be apportioned to their environmental sources will be most effective in improving Agency actions. It will require a suite of Level 5 and 6 indicators to link back to exposures and sources to make the necessary connections and evaluate the effectiveness of regulatory actions.

ORD's proposed research program would take the emission-exposure-effect paradigm beyond the traditional risk assessment and risk management options to include an assessment of the effectiveness of Agency actions (considered broadly to include actions by States or tribes). Private-sector entities often have clearly defined missions and readily observable metrics, such as profits, to measure performance and observable metrics, such as costs, that allow managers to maximize profits while minimizing costs. This allows effectiveness to be calculated as a profit/cost or cost/benefit ratio. In contrast, many public-sector organizations exist outside the realm of the marketplace, where goods and services have less concrete benefits and costs, and there are no dollars-and-cents outcomes to measure the effectiveness of those programs. The challenge of effectiveness analysis is to create meaningful measures that provide indicators of how well various regulatory (and some voluntary programs) perform. The measures must focus on the public health outcomes, but, at the same time, they must be able to be observed and metrics developed for their assessment. The measurements must be transparent, feasible, and unambiguous.

B. Paradigm Guiding a Research Program on Indicators

Figure 5 expands the basic paradigm that will be used for indicator development by ORD. In evaluating the effectiveness of any particular Agency action, ORD should be able to identify potential indicators in each component along the action-source-exposure-effects paradigm. ORD's indicator research program will concentrate on the identification and development of indicators, the linkages between indicators, and the spatial and temporal requirements for indicator measurement. The five areas of focus in the development of indicators and linkages are indicated below.

(1) Indicator development (indicators)
(2) Methods (measurements)
(3) Networks and databases (monitoring systems)
(4) Linkages of indicators (analysis, synthesis, and models)

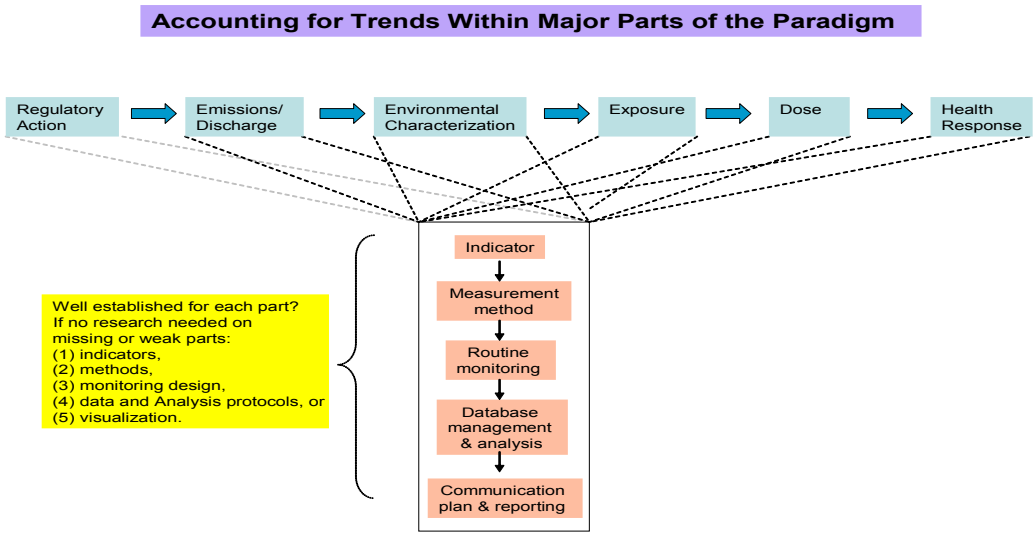

Figure 5. Paradigm Guiding a Research Program on Indicators

(5) Communication of results (visualization, technology transfer, and knowledge translation)

The first area, indicator development (tools), will involve the identification and development of valid and predictive indicators. Ideally, indicators will represent components on the right side of the emissions-to-effects paradigm, with linkages back to the left side. Indicator development prioritization will always require a plausible cause-and-effect relationship between two indicators in the action-to-outcome hypothesis. The second area, methods, will cover the measurement methods, models, and techniques to assess indicator trends in the environment or receptors. The third area, systems, will include the data systems and networks for collection, storage, and retrieval of indicator data for trend analysis. Figure 5 illustrates how these efforts work together to characterize the components (the boxes) in the guiding framework. The fourth area of focus, linkages, is critically important to the success of this research effort. Only through providing the scientific understanding and data necessary to move along the paradigm from one component to the next can the Agency evaluate the effectiveness of its regulatory actions. (See also Figure 6.). This is an area where the Agency's role will be unique. No other organization will be able to accomplish this. The fifth area, synthesis, will bring together the measurements and the models needed to evaluate the effectiveness of programmatic risk management strategies along the action-to-outcome paradigm. The primary research question for the overall program is " . . . how does one translate decreasing emission trends resulting from a quantifiable known risk management action tied to an agency decision separate and apart from, or in concert with, previous actions into decreasing morbidity, or case studies on specific emission units where trends don't yet exist?" The sixth area is that of communication. Much of this is knowledge translation and technology transfer. Additional components to the communication area include uncertainty descriptions. The overall goal of the research program is to ultimately develop valid measures of effectiveness to enable the Agency to quantify that its regulatory and nonregulatory decisions are having an effect on public health.

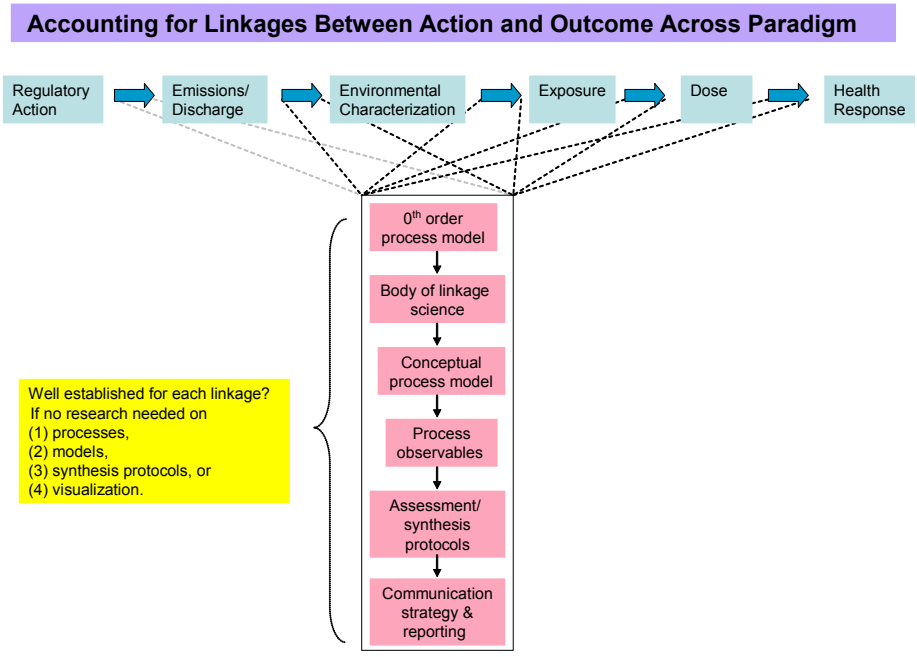

Figure 6. Elements Needed To Provide Linkages Between Components in the Guiding Framework

C. Linkages Between Indicators in the Emissions-to-Effects Paradigm

An important component of a research program to develop valid and predictive indicators is to establish linkages among the various components of the emissions-to-effects paradigm. As illustrated in Figure 6, linkages will be documented through a series of steps including those below.

- A zero-order process model
- Process research to establish the science to describe the linkages among components
- Measurement of process observables
- Development and use of a process model
- Assessment and synthesis protocols
- Communication and reporting of the linkage relationships

Scientific research has helped identify linkages between exposure to environmental contaminants and certain diseases, conditions, or other health outcomes. Examples include radon and lung cancer, arsenic and cancer in several organs, lead and nervous system disorders, disease-causing bacteria such as E. coli O157:h7 and gastrointestinal illness and death, and particulate matter and aggravation of cardiovascular and respiratory diseases. Such relationships between exposure and disease have been established through well-designed epidemiological and toxicological studies with a defined or specified population and known environmental concentrations.

The causes of many complex diseases and other health conditions are not well established. In some cases, environmental contaminants are considered important risk factors; in others, available data suggest that environmental exposures may be important, but definitive proof is lacking. Developing conclusive evidence that environmental contaminants cause or contribute to the onset, incidence, or severity of adverse health effects can be difficult, particularly for those effects occurring in a relatively small proportion of the population or for effects with multiple causes. In cases where exposure to an environmental contaminant results in a relatively modest increase in the incidence of a disease or disorder, a large sample size for the study would be needed to detect a true relationship. In addition, there may be factors that are related to both the exposure and the health effect

(confounding factors) that can make it difficult to detect a relationship between exposure to environmental contaminants and disease. In many cases, findings from studies in humans or laboratory animals may provide suggestive (rather than conclusive) evidence that exposures to environmental contaminants contribute to the incidence of a disease or disorder.

The Agency relies on the possible linkages established through the types of research highlighted above, including clinical, laboratory, and epidemiologic studies, to identify environmental contaminants and health outcomes of potential Agency interest. To reiterate, however, the national-scale ROE indicators do not directly link exposure with outcome and cannot be used to demonstrate causal relationships. However, when combined with other information, such as environmental monitoring data and data from toxicological, epidemiological, or clinical studies, these indicators can be important keys to improve the understanding of the relationship between environmental contamination and health outcomes.

The optimal approach for linkage analysis is that of epidemiologic study, which has the advantage of being able to evaluate whether exposure to a pollutant can actually be related to a public health outcome in a specific population. Several types of epidemiologic studies are possible, including cohort, case-control, time series, and molecular (biomarker) studies. An epidemiologic study could utilize several assessment measures of disease or use the continuum of disease (e.g., morbidity, mortality, clinical examination, biomarkers of exposure or effect) and classify the exposure of individuals in the study population to multiple pollutants through different exposure pathways.
A disadvantage of this approach is that there may be limitations related to the sensitivity of methods available to measure the effect or classify the exposure. In particular, short-term health effects, such as asthma, will be much easier to measure than long-term health effects like cancer.

An additional avenue is utilizing ecological and ecotoxicological studies that may help to illuminate the factors just discussed. Observations of organisms in natural environments and under controlled laboratory conditions may elucidate exposure levels and pathways and identify effects that are sentinels or early warnings of potential human health effects that merit further investigation. Ecological and ecotoxicological studies represent an additional resource that can inform public health research.

Three general approaches should be considered. The first is the use of available data for risk management actions, exposure, and effects. Examples of such databases include (as approximate surrogates for exposure) air monitoring networks, proximity to hazardous waste sites, and drinking water quality, and (for effects) cancer registries, birth defects registries, and infectious disease surveillance. (Note: The "effects" databases actually do measure effects (Level 6), but the "exposure" data sets are actually data on environmental concentrations (Level 4), rather than on exposure (Level 5). This illustrates one limitation with this approach, because such data sets may or may not be good surrogates for exposure or for linking exposure to dose and effects. Using environmental concentration data, instead of exposure data,

would be comparable to using data on hypertension in a community instead of actually counting heart attacks or strokes as an effect. A second approach is to consider the development of a database or surveillance program to monitor changes and fluctuations in the exposure and disease of interest over time. The first two options have strength when the data cover several years prior to the environmental management action and several years after that and where they can be teased from other interventions. They also have strength if they are implemented over several geographic regions or are national in scope. A disadvantage is that there may be incompleteness in the data, relatively insensitive methods may be used to assess the effect, and the surveillance systems may be costly to implement and maintain. In addition, because of the lack of scientific linkages between environmental quality measurements and actual exposure, exposure misclassification often makes it difficult to precisely and accurately detect changes in exposures or outcomes. A third approach is the conduct of an epidemiologic study or series of studies specifically designed to examine the effect of the environmental management action. Choosing an appropriate study design is based on the size of the population to be studied, the accuracy with which exposure can be classified, the magnitude of the effect associated with the exposures of interest, and the prevalence of the disease to be studied. Epidemiologic studies can be retrospective, prospective, or bi-directional. Whether to use existing data to establish de novo a new surveillance database, develop partnerships with agencies collecting similar data, or conduct an epidemiologic study or series of studies will be driven by issues of data availability, the methods available to measure exposure and effect, and resources. In addition, the feasibility of measuring reductions in illness incidence will depend on the degree to which such incidence is affected by risk factors other than environmental pollution and the biological mechanisms and time courses involved in the pathogenesis of the illnesses in question. The research needs for these linkages studies are large and include

- how to define and measure adverse effect,
- how to classify exposure (What are the significant determinants of exposure?)
- how to computationally evaluate multifactorial data to identify relationships among source-exposure-outcome for multiple environmental factors and complex disease outcomes, and
- how to manage accountability data to facilitate analysis, visualization, and communication.

Because of the statistical difficulty of detecting small changes in population effects, developing more sensitive health and exposure indicators would be quite useful for measuring exposure and effects and for statistically analyzing the exposure-to-effects relationship. As illustrated in Figure 7, a complete pathway from emission to exposure to effect can be captured in a series of indicators and linkages. The orange boxes require indicator research, and the pink boxes require linkage research. The pathway for describing regulatory effectiveness is analogous, and measuring the reductions in flux through the emission-to-effects paradigm is the key to assessing regulatory impacts on health. Combining the indicator and linkage blocks allows the formulation of a cross-regulatory action to the health effects paradigm model. As illustrated in Figure 8, the cross-paradigm

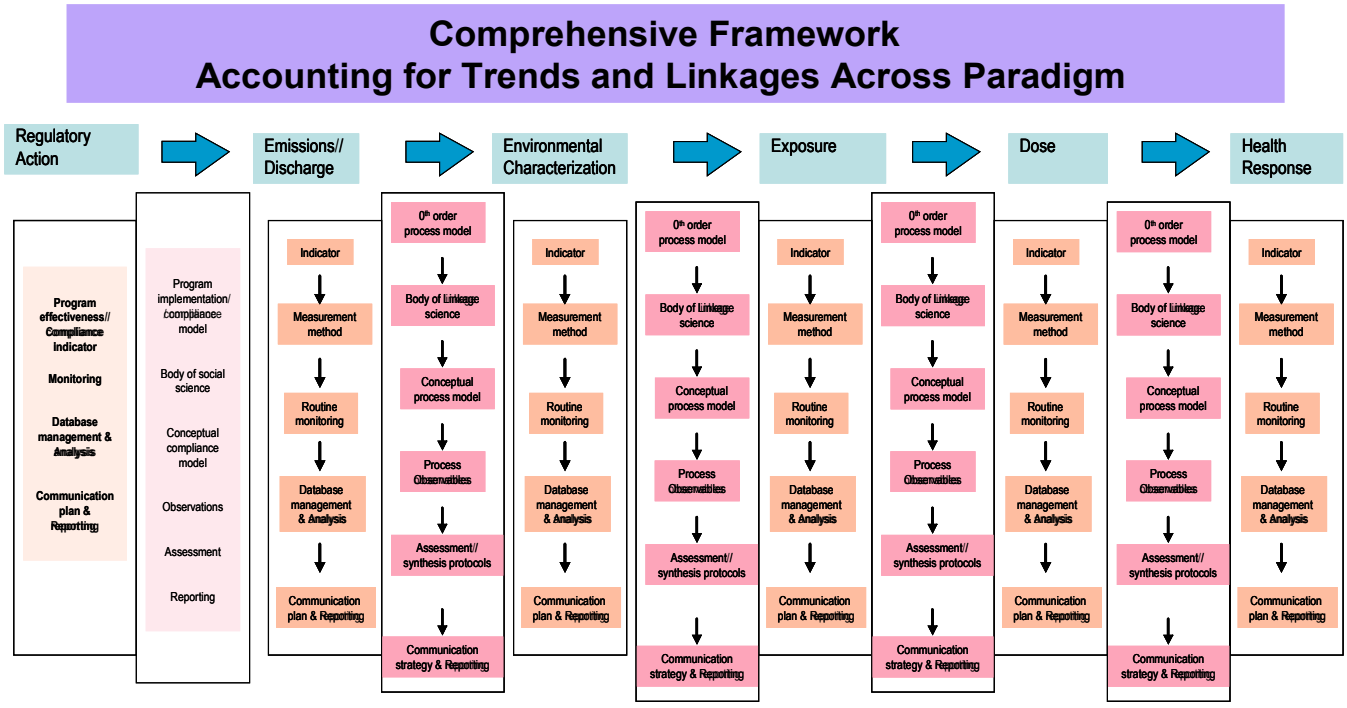

Figure 7. Comprehensive Framework Illustrating Indicators and Linkages

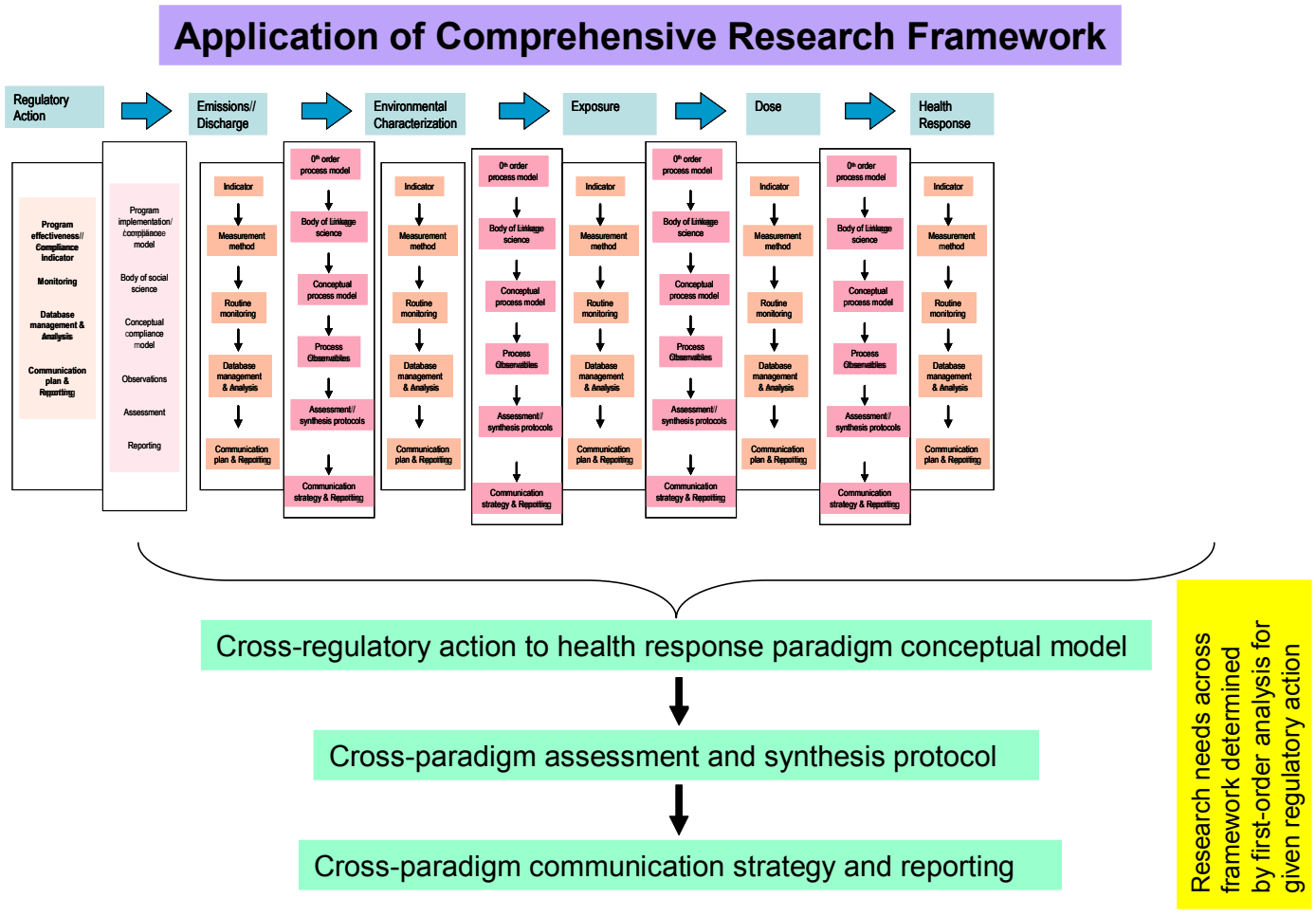

Figure 8. Application of the Framework as a Driver for Research

influences can be assessed and combined as appropriate to allow for cross-paradigm communication and responding to such documents as the ROE.

D. Strategic Approaches to a Research Program on Indicators

A decision tree could be used to decide between some of the strategic options for a specific chemical or regulatory program (Figure 9).

There are five potential strategic approaches to cross-paradigm accountability assessment that we describe here. The first is a holistic or "whole-system" approach in which all the pink and orange indicator and linkage boxes (from Figures 7 and 8) are filled in to describe all the indicators and all the linkage chains between them. This approach might be illustrated by the red circle around the accountability framework as shown in Figure 10. Obviously, although such a system might be ideal from some perspectives, it would be resource intensive.

Alternatively, a key indicator and its linkages may describe the system, and research could be prioritized toward identification of the key indicator and its linkage with the ultimate health effect. This approach is more of a surveillance approach, as illustrated as the blue ellipses in Figure 10. In the surveillance approach, one would need to

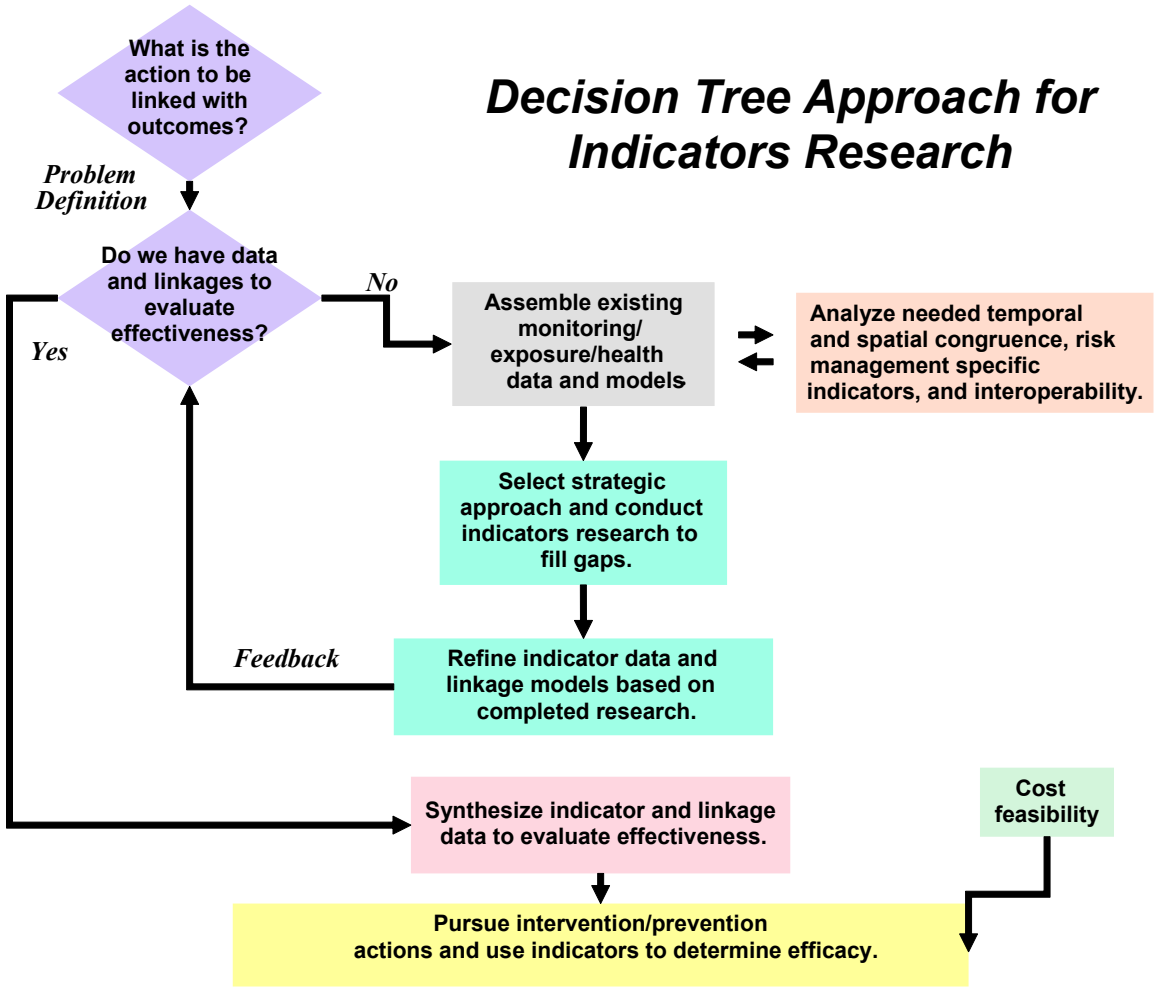

Figure 9. Decision Tree for Indicator Research Needs

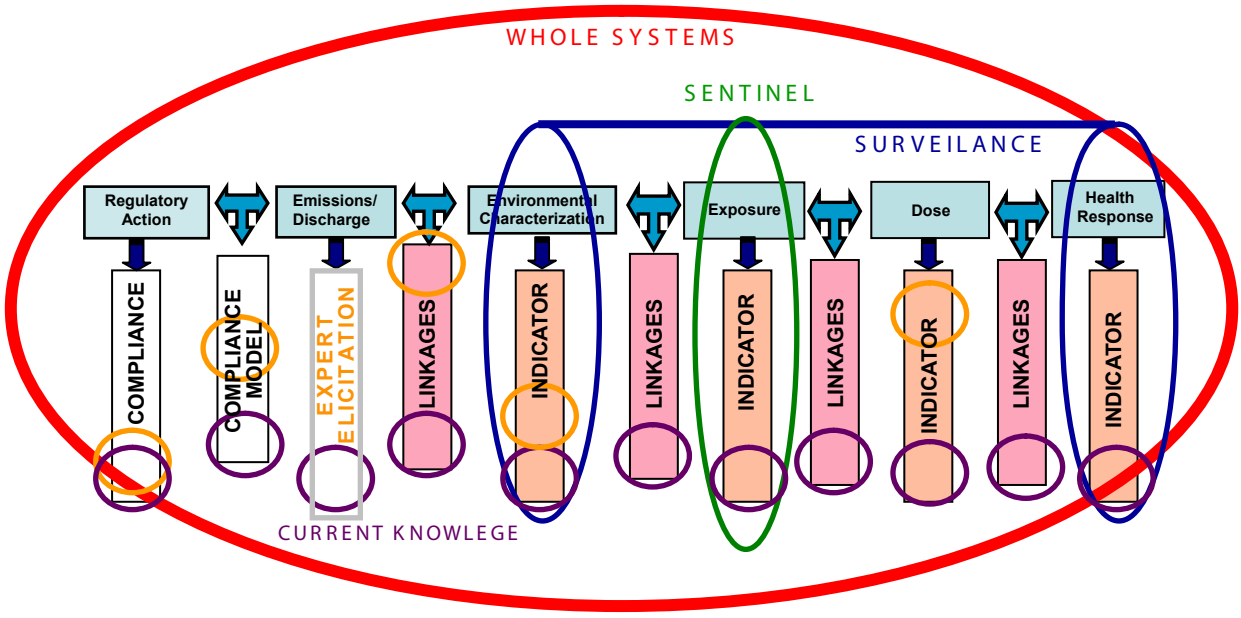

Figure 10. A Holistic Approach to the Indicator Framework

- identify key intermediates and endpoints with established linkages;
- review and evaluate indicators, measurements, monitoring, database management and analysis techniques and visualization, and communications;
- perform relative uncertainty/gaps analysis, with missing data patches;
- complete the research to fill the gaps; and
- continue looping.

Another alternative illustrated in Figure 10 is a current knowledge approach, which is indicated by the purple circles at the ends of the indicator chains. This approach would include synthesis of existing science to identify "leap-frogging" opportunities to completing a pathway. A current knowledge approach would require

- identifying issue and gathering current best available cross-program/policy data set,
- developing current best available cross-program/policy conceptual model,
- identifying critical uncertainties and corresponding research and development plan,
- completing research to fill gap, and
- continue looping.

A sentinel approach is illustrated in Figure 10 as the green ellipse, where a single well-understood indicator is used to describe the entire paradigm. A sentinel approach would involve the following steps.

- Identifying immediate exposure indicator bridging burden and effect
- Reviewing, evaluating, and documenting burden and effect linkages
- Reviewing and evaluating indicators, measurements, monitoring, database management and analysis techniques and visualization, and communication
- Performing relative uncertainty/gaps analysis, with missing data patches
- Identifying critical uncertainties and corresponding research and development plan
- Completing research to fill gap
- Continue looping

Finally, an expert elicitation alternative could be used to identify key gaps and key

uncertainties from the whole-system approach and direct research to filling those needs first. This approach is illustrated as the orange circles in Figure 10. The expert elicitation process would involve

- convening experts on the program/policy issue and identifying
  - critical uncertainties leading to the whole system approach, and
  - key gaps for a sentinel, benchmark, or best available control technology approach;
- identifying critical corresponding research and delevopment plan;
- completing research to fill uncertainties and gaps; and
- continue looping.

These five strategic alternatives are not intended to be mutually exclusive. Some programs or biological/chemical toxicants may fit better into one alternative or another, and some projects may evolve from one strategic alternative to another as data and resources accumulate.

Finally, the overall flow of information guiding human health research is reiterated here as Figure 11. As indicated in the figure, there are several drivers and feedback loops directing research in accountability. The ROE and its indicators are primary drivers for human health research. The ROE informs the goals and objectives of the Strategic Plan, the multiyear research plans and annual planning. The analysis of health outcomes established by the Program Assessment and Rating Tool (PART) process serves as a feedback loop to refine the Strategic Plan and MYPs.

E. Methods To Prioritize Chemicals or Programs

A series of ranking factors will be used to screen potential chemicals or regulatory programs for initial analysis. For chemicals, examples of priority-setting criteria could include measures of inherent toxicity of the chemical (such as 50% lethal dose, reference concentration, reference doce, slope environmental persistence, bioaccumulation potential, factor, etc.). Measures or surrogates for exposure would include items like production volumes, human exposure

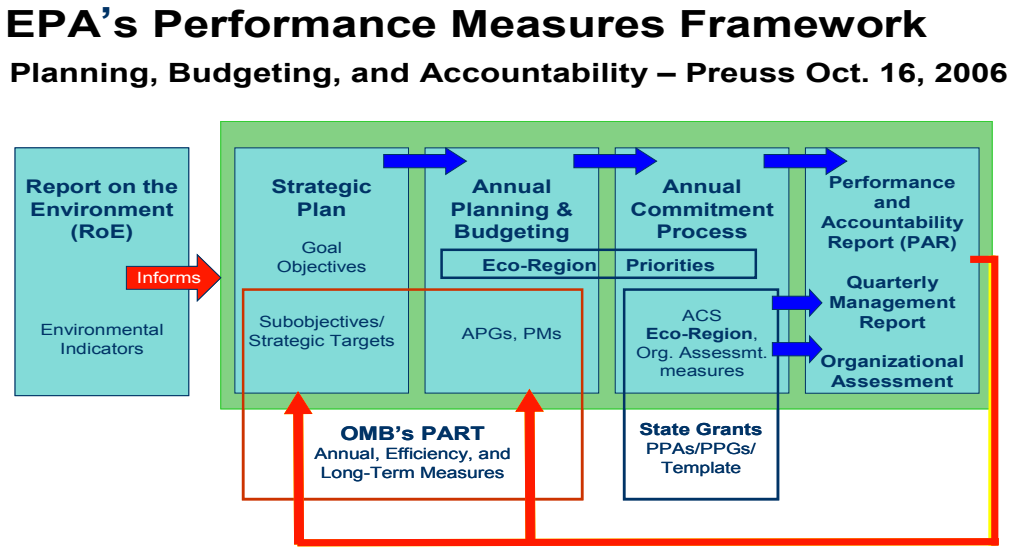

Figure 11. Closing the Loop on Research Planning

measures (including exposure panel studies, the National Children's Study, or body-burden data from NHANES and other surveillance programs), or ambient levels in the environment, including organisms there. Finally, measures of potential health impact, such as burden of environmental disease, morbidity, and mortality data, would be priority factors. For regulatory programs, a different set of ranking factors would be used that could include resource allocations and program age (likely surrogates for data availability), the degree to which the program is national in scope, and the magnitude of potential human or ecological health effects. Key gaps from resources such as the ROE are also important ranking factors.

F. Application of Methods and Data to Risk Assessment and Risk Management

Many of the new indicators and linkages immediately will benefit risk assessment directly and help reduce the uncertainty in existing risk assessments. However, the function of these research projects is to allow the evaluation of the effectiveness of real-world application of risk management tools and techniques in the field. Much of this work would reduce the reliance on default assumptions in risk assessments to estimate the public health significance of risk management actions; that is, more direct measurements would be used instead of estimates.

A significant investment in demonstration projects also would enable the "leap-frog" approach, whereby installation of a risk management option would be coupled with the assessment of appropriate health indicators. This new approach to the assessment of treatment technology or other risk management approach would, in some cases, reduce the need for additional proximal or intermediate indicators. Thus, if one understood the ultimate outcomes of the technology application, it would not be necessary or cost-effective to fill in all the data gaps in the early years of this program.

Many risk management activities, however, must be considered with all their subtleties. For example, outcome analysis of risk management options for drinking water treatment cannot simply include whether a control strategy was installed in a community because the details matter. In this example, one would have to develop indicators specific to the various risk management strategies, such as indicators specific to what fraction of the exposures come from alternative water sources (or other dietary sources), indicators reflecting potential multiple water sources (wells versus surface water), indicators keying whether the distribution system changes the nature of the exposure, and indicators relative to co-contaminants from the source that influence the efficiency of the treatment option to allow meaningful comparisons and to generalize across multiple sites. Voluntary risk management actions by individuals acting on fish advisories, for example, will differ by demographic variables (ethnicity, gender), and indicators could be developed to allow portability of such actions.

The Office of Air and Radiation (OAR) is putting a number of new risk management programs in place, programs on national scales such as the Mobile Source Air Toxics (MSAT) rule, on regional scales such as the Clean Air Interstate Rule (CAIR), and on local scales such

as the Diesel Bus Retrofit and the Woodstove Replacement program. The Agency's national and regional air offices and their State and local counterparts all are looking for outcome measures that will demonstrate their impacts. Projects already are being planned for local-scale programs to develop and apply methodologies that might be applied elsewhere (see discussion on the Air Accountability Framework in Section V). As the scale of program and impact increases, the difficulty in separating their impacts from other factors increases. Being able to separate the change in environmental signal of sulfate and nitrate reductions from CAIR from those of other mobile source and fine particulate reductions will be difficult enough, but separating their respective health signals may be extremely difficult. Similarly, as the temporal scale increases, such as in the case of cancer risks associated with MSATs, the difficulty in finding a short-term health outcome indicator increases. Finding leap-frog approaches for this area is a path worth pursuing and will be a focal point of this strategy.

V. Related Activities

A. Internal Activities

National Center for Environmental Research Grants

In 2004, NCER published an RFA on Early Indicators of Environmentally Related Disease. Grantees funded through this RFA are working to develop tools that can be used as early indicators or predictors of environmentally induced disease. These grantees met with the Agency in January 2007, to discuss potential interactions between extramural and intramural scientists. One outcome of this meeting was to commit grantees and intramural scientists to a future dialogue about indicator development following the publication of this framework document. NCER recently published an RFA on the Development of Environmental Health Outcome Indicators. The purpose of this announcement was to solicit research on the development of outcome-based environmental health indicators that reliably signal trends in source to exposure; exposure to outcome; and, ultimately, source-to-exposure-to-outcome relationships using existing databases of environmental (ambient), biological and health related data. The RFA also noted that development of such indicators will require a clear understanding of the sequence of events that link changes in the environment to human exposure and adverse health outcomes. The anticipated outcome of this RFA will be the development of new indicators that can be used to assess the impact of environmental risk management decisions.

Using the following criteria, two proof-of-concept projects were funded by ORD to develop principles for the use of indicators to evaluate effectiveness of environmental decisions. They were ranked based on the criteria outlined below.

- Clarity of the objectives of the proposed research. As noted in the RFA, each of these projects derived from a preproposal to study an Agency action. Do the objectives appear to be consistent and responsive to the solicitation?
- Scientific merit of the proposed approach in addressing the objectives

- Qualifications and competency of the staff identified for the project in light of their demonstrated prior performance in the proposed or related research areas
- Strengths and weaknesses of the project as related to the probability of the project accomplishing the stated objectives

One proposal focuses on evaluating the potential use of direct health measures for assessing the impact of drinking water regulations targeting microbial pathogens. This research is designed to assess the health impact of drinking water regulations and target health effects measurement in communities where water treatment changes have been made to comply with the Safe Drinking Water Act regulations that minimize endemic waterborne infectious disease. The second project focuses on understanding the relationships among air pollutant concentrations, human exposures and adverse health effects. Using available emissions and environmental and health indicators obtained at the local and regional levels, along with questionnaire information on both activity patterns and confounders/effect modifiers for air pollution health effects analysis, this project will focus on assessing the cumulative impact of a suite of air pollution reduction programs on environmental health indicators for children and the elderly.

ORD utilizes MYPs to develop the strategic direction of the Agency and how its intramural and extramural research can evolve to best contribute to the Agency's mission to protect human health and the environment. These MYPs serve three purposes: (1) a description of the overall objectives of the research program, (2) documentation of significant projected outputs of the research over a 5- to 10-year period, and (3) communication of research plans within ORD and with stakeholders and clients. The need to develop approaches to evaluate public health changes following risk management decisions has been articulated in Long-Term Goal 4 of the 2006 Human Health Research Program MYP. In addition, in Long-Term Goal 2 of the Clean Air Research Program MYP, research to reduce uncertainties in linking health and environmental outcomes to air pollution sources to support effective air quality strategies, termed "air accountability," is described.

Air Accountability Framework

ORD, under its Clean Air Research Program MYP Long-Term Goal 2, plans over the next 5 years to strengthen the means to assess the effectiveness of air quality programs in reducing human exposure and consequent health impacts. By the end of 2009, ORD, in cooperation with OAR, will produce an Air Accountability Framework with program and technical designs. The program design will identify roles and responsibilities of offices inside and outside the Agency that will gather, analyze, and report accountability information. The technical design will describe well-established, best available developmental indicators and linkage techniques, the latter partially addressing factors that may confound the relationships among changes in emissions, air quality, exposure, and public health. By the end of 2009, ORD and other members of the North American atmospheric research consortium under the North American Research Strategy for Tropospheric Ozone (NARSTO) will complete an assessment of the

technical capacity of the atmospheric science community to meet air accountability needs. They will examine how well impacts of major pollution reduction programs can be related to emissions changes and air quality, and how well they can provide the information needed by exposure and health scientists to jointly identify resulting exposure, environmental, and health improvements. By 2009, ORD also will conduct a regional-scale pilot of approaches to identify and track regulatory outcomes. The pilot will investigate air quality and related health impacts over the New York region due to the nitrogen oxide (NO_X) State Implementation Plan Call of 1998 that required reductions of summertime NO_X emissions by May 1, 2004, in 21 Eastern states. Recently established relationships between high ozone, a product of NO_X emissions, and human health end points present a unique opportunity to establish indicators of exposure and effects suitable for program accountability. The potential for generating indicators through the Global Earth Observation System of Systems (GEOSS) Remote Sensing Information Gateway (see next topic) also will be examined. ORD will incorporate the results of other accountability research into its 2009 Air Accountability Framework, such as that sponsored by the Health Effects Institute (HEI) on methodologies to assess the changes in air quality and health status in several European areas. In 2012, the Air Framework will be reviewed and refined with improved indicators and linkage techniques coming out of multiple test-bed activities and intervention studies planned to further demonstrate the air accountability proof of concept. The updated framework also will incorporate the results of a second set of HEI initiated air accountability studies within and outside the United States.

This framework and the Air Accountability efforts will be coordinated in four ways:

(1) through the use and integration of comparable frameworks,
(2) through the exchange of data and information coming out of research that is beneficial to the accountability efforts of the other,
(3) through joint collaborations with external partners, and
(4) through the Air Framework serving as the means of applying new indicators developed under this research program.

Both the Air Accountability and this framework's programs will use the same overarching framework (see Figure 7) relating regulatory programs to emissions changes and these to environmental concentration, exposure, dose, and health response. They will both use a common set of indicator measurements and linkage process models to help OAR and the Agency meet administrative and technical needs for demonstrating program results and making mid-course adjustments in air quality management policies and programs.

The Air Framework will contribute information coming out of source emissions to environmental change to exposure research. The air program will contribute results of its research on biomarkers of exposure, dose, and health response. Program interdependence will help cement their integration. The Air Framework needs health-outcome indicators and process information to tie to changes in the environment. The Health Framework will use source emissions and environmental concentration information to

put exposure and health end points into meaningful and actionable context. The two programs rely on both their intramural efforts and the external efforts of others. Key external examples include the CDC Environmental Public Health Tracking program and the National Institute of Environmental Sciences (NIEHS) Exposure Biology program described in the next section. ORD staff who work on air and health issues will collaborate closely on interactions with these and other external efforts to see that their full benefits are realized in assessing the results of Agency actions on air pollution exposure and consequent health impacts.

Global Earth Observation System of Systems

GEOSS is an interagency and international effort representing a set of observational data, models, and decision-support tools that could be used to derive indicators at higher levels. For example, the National Aeronautics and Space Administration (NASA) may obtain satellite data that can have great usefulness to develop indicators of predicted ambient concentrations based on the ability to see total columnar atmospheric levels of pollutants such as nitrogen dioxide, sulfur dioxide, and formaldehyde. Similar opportunities exist with particulate matter $\leq 2.5\mu m$. The Agency and partners (Health and Human Services [HHS], NASA, National Oceanic and Atmospheric Administration [NOAA], U.S. Geological Survey [USGS]) already are involved in this research and exploring its associations with health end points.

B. External Activities

The Agency will utilize many resources and partnerships with other Federal, State, and local agencies for the health data and statistical reports that underlie the health outcome and biomonitoring indicators used in this research program. This includes vital statistics data primarily from CDC, data on human exposures derived from CDC, and data from surveillance activities from the National Cancer Institute (NCI) and CDC.

The CDC's NHANES began in the 1970s with the survey of approximately 32,000 persons in the United States (NHANES I). Additional measures were initiated in subsequent iterations of NHANES II and NHANES III. NHANES now is gathering data continuously. Although initially concentrating on health and nutrition, NHANES began measuring body burden of some environmental contaminants.

The National Human Exposure report, which follows on to NHANES for environmental contaminants, provides critical biomonitoring data (i.e., dose determinations), which are a critical nexus for the business of the Agency by supporting

- quantitative risk assessment (i.e., understanding actual human exposures and associated health risks) and
- effective risk management/pollution prevention efforts if we are able to reconstruct links back to sources.

CDC is expanding the number of chemicals included in the NHANES population exposure analysis. The *National Report on Human Exposure to Environmental Chemicals* provides an ongoing assessment of the U.S.

population's exposure to environmental chemicals using biomonitoring. The first *National Report on Human Exposure to Environmental Chemicals* was issued in March 2001 and included 27 chemicals such as lead, mercury, cadmium, and other metals; dialkyl phosphate metabolites of organophosphate pesticides; cotinine; and phthalates. The second report, released in January 2003, presents biomonitoring exposure data for 116 environmental chemicals for the noninstitutionalized, civilian U.S. population over the 2-year period 1999 to 2000. Polycyclic aromatic hydrocarbons (PAHs), dioxins, furans, and coplanar polychlorinated biphenyls (PCBs), noncoplanar PCBs, phytoestrogens, selected organophosphate pesticides, organochlorine pesticides, carbamate pesticides, herbicides, pest repellents and disinfectants were reported. Unfortunately, these data are not available in a suitable geographic format, and, hence, exposures cannot be linked to emissions or other Agency data. The exposure report does allow the assessments of the impact of national regulatory decisions and actions that rely on "outcome" indicators to complement traditional process ones. It also provides biomonitoring data that may be more easily obtained than health data. The report may be the earliest reflection of success of national-level policies, help refine and redirect policy, and set priorities. The report's ability to serve as a surrogate for actual improvements in health outcomes remains to be proven.

CDC began a new program in 2002 that initiated pilot studies in many states to link health outcomes to various environmental measures. The goal of the program would be achieved " . . . by linking environmental and health data on a national level." This will allow us to be better equipped to identify problems and effective solutions, thereby reducing the burden of environment-related diseases on the public. The network is well funded, with appropriations of $17.5 million in fiscal year 2002, CDC has funded 17 States, 3 local health departments, and 3 schools of public health to begin development of this national environmental public health tracking network and to develop capacity in environmental public health at the State and local levels.

There is also a MOU between the Agency and CDC, which was signed in September 2004. The MOU was designed to

- advance efforts to achieve mutual environmental public health goals;
- strengthen bridges between environmental and public health communities;
- achieve better understanding among environmental hazards, ensuing exposures, and health effects; and
- cornerstone cross-institutional initiatives to link environmental and health information sources.

Two of these cross-institutional programs are (1) the Agency's National Environmental Information Exchange Network and (2) CDC's National Environmental Public Health Tracking Network.

The Agency's National Environmental Information Exchange Network commits the Agency and States to a partnership to build locally and nationally accessible, cohesive and coherent environmental information systems. It also ensures that both the public and regulators have access to the information to document environmental performance, understand

environmental conditions, and make sound decisions that ensure environmental protection.

The mission of CDC's National Environmental Public Health Tracking Network is to be better prepared to develop and evaluate effective public health actions to prevent or control chronic and acute diseases that can be linked to hazards in the environment. CDC's goal is to develop a national network that will be standards based; allow direct electronic data reporting and linkage within and across health effect, exposure, and hazard data; and interoperate with other public health systems.

As part of the new Exposure Biology Program, NIEHS awarded $74 million in grant opportunities in October 2006 for the development of new technologies that will improve the measurement of environmental exposures that contribute to human disease. These grant opportunities will support research to develop portable, easy-to-use sensing devices that will accurately measure personal exposure to a wide variety of chemical and biological agents. The grants also will support the development of sensitive biomarkers or indicators, based on subtle changes in DNA structure, proteins, metabolites, and other molecules that will enable scientists to study how the body responds to environmental stress.

The Exposure Biology Program at NIEHS is one of two complementary research programs outlined in the Genes and Environment Initiative, a 5-year, NIH-wide effort to identify the genetic and environmental underpinnings of asthma, diabetes, cancer, and other common illnesses. The program will focus on the development of innovative technologies for assessing exposures to chemical and biological agents, dietary intake, physical activity, psychosocial stress, and addictive substances, as well as of new methods for quantifying the biological responses to these environmental stressors.

NIEHS also supports a program on environmental sensors for personal exposure assessment that focuses on developing field-deployable or wearable sensing devices that provide direct measurements of exposure to ozone, fine particles, diesel exhaust, heavy metals, volatile organic compounds, pesticides, microbial toxins, and other environmental agents that have been linked with respiratory disease, cancer, and other common illnesses.

NIEHS supports several Biological Response Indicators of Environmental Stress Centers that will focus on the development of sensitive biomarkers that reflect subtle changes in inflammation, oxidative damage, and other pathways that can lead to disease, and the incorporation of these markers into field- and laboratory-based sensing devices. Through its extramural grants program, NIEHS supports research to evaluate the various epidemiological effects of environmental contaminants, such as fine particulate matter, lead, and pesticides. Several of these projects involve the use of biomarkers or indicators of exposure that may be useful for further development and refinement by the outcomes research program.

NCI maintains data from cancer surveillance that will assist in this effort. Data will be from active surveillance activities such as from NCI, which collects and publishes cancer incidence and survival data from population-based cancer registries.

VI. Next Steps

This *Framework for Assessing the Public Health Impacts of Risk Management Decisions* is intended to provide the strategic direction for future human health research in ORD. It also may be used to provide a focus for the development of an ORD-wide initiative to develop science necessary to evaluate effectiveness of ecological, and human health regulatory decisions.

This *Framework* was reviewed by ORD's Science Council in June 2007. Recommendations from this review were incorporated in the final draft. The strategic directions outlined in the *Framework* will be used to develop an ORD research implementation plan. A workshop consisting of intramural and other scientists is planned for January 2008 to help prioritize various approaches for a research program in this area.

VII. References

Centers for Disease Control and Prevention. National Report on Human Exposure to Environmental Chemicals. www.cdc.gov/exposurereport/

Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey. www.cdc/gov/nchs/nhanes.htm

Centers for Disease Control and Prevention. National Environmental Public Health Tracking Program. www.cdc.gov/nceh/tracking/

Government Performance and Results Act of 1993. www.whitehouse.gov/omb/mgmt-gpra/gplaw2m.html

National Academy of Sciences. Evaluating Federal Research Program: Research on the Government Performance and Results Act. The National Academies Press, Washington, DC, 1999. www.nap.edu/catalog/6416.html

National Academy of Sciences. Air Quality Management in the United States. The National Academies Press, Washington, DC, 2004. www.nap.edu/catalog/10728.html

National Cancer Institute. Surveillance Epidemiology and End Results Program. www.seer.cancer.gov/

U.S. Environmental Protection Agency. Draft Report on the Environment, 2003. www.epa.gov/indicators/roe/

U.S. Environmental Protection Agency. Draft Report on the Environment, 2007. www.epa.gov/indicators/

U.S. Environmental Protection Agency. National Environmental Information Exchange Network. www.exchangenetwork.net/

U.S. Environmental Protection Agency. 2006 Human Health Research Program Multi-Year Plan. www.epa.gov/ord/npd/hhrp/hhmyp.html

U.S. Environmental Protection Agency. 2006-2011 EPA Strategic Plan. www.epa.gov/ocfo/plan/plan.htm

U.S. Environmental Protection Agency. Shaping Our Environmental Future: Foresight in the Office of Research and Development, 2007. www.epa.gov/osp/efuture.htm

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