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A Conceptual Framework for U.S. EPA's National Exposure Research Laboratory

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1.0 Introduction

The challenges of environmental protection range from understanding the potential risk associated with exposure of humans and ecosystems to a newly manufactured chemical, to minimizing human exposure to pathogens at public beaches, to linking human activities on the landscape to physical alterations of ecosystems. In the United States, there are more than 75,000 industrial chemicals that are currently tracked by the U.S. EPA, with an estimated 2,200 new chemicals manufactured or imported each year. Since 2001, the list of environmental chemicals reported in the Centers for Disease Control and Prevention's First, Second, and Third *National Report on Human Exposure to Environmental Chemicals* has grown from 27 to 148 (NRC 2006), evidence of both the need and ability to monitor the public for exposure to contaminants of concern. The popular media routinely reports concerns about contaminants in drinking water supplies, at public beaches, and in the Nation's surface waters. A June 2007 Newsweek article highlighted a growing public awareness of potential risks associated with "emerging contaminants," including pharmaceuticals, cosmetics, and antibacterial soaps. Cited in the article was a 2002 survey by the U.S. Geological Survey which detected a number of these compounds in 80 percent of the 139 streams it examined. While each of the compounds was generally present in small quantities, the overarching question remains, "What happens when a person is exposed to a whole cocktail of them?" (Underwood 2007).

For ecosystems, environmental protection goes beyond minimizing exposures to chemical contaminants and includes the restoration and maintenance of the physical and biological integrity of ecosystems. Understanding the relationships between land use, such as urban development and agricultural activities, and how these activities can physically alter ecosystems is a critical component of environmental protection. In the U.S. EPA 's 2006 report on the condition of wadeable streams of the US, stream bed sediments and riparian disturbance were identified as two of the most widespread stressors which are degrading stream condition for fish and other aquatic life. Both of these stressors represent physical alteration of stream systems and are typically associated with human activity alongside streams.

Fulfilling the U.S. EPA mission to protect human health and the environment carries with it the challenge of understanding exposures for tens of thousands of chemical contaminants, a wide range of biological stressors, and many physical stressors. The U.S. EPA's National Exposure Research Laboratory (NERL) is uniquely positioned to address the Nation's most challenging environmental exposure questions. Exposure science provides the Agency with the fundamental research necessary to assess potential exposures and risks to emerging environmental threats and to mitigate exposures to known contaminants and stressors. NERL's combined expertise in modeling, chemistry, microbiology, ecology, molecular biology, geographic information systems, and remote sensing enables the Laboratory to bring cutting edge research and technology to the field of exposure science.

NERL's mission is to conduct human health and ecological exposure research that provides the tools necessary for the U.S. EPA to carry out its mission. NERL produces research to reduce critical exposure uncertainties associated with the U.S. EPA's policy decisions and

DRAFT

provides international leadership in exposure science. tgThis document provides a framework for both addressing NERL's research mission and for achieving its goal of scientific leadership. In the following sections, the document will:

- define the domain of exposure research (Section 2.0);
- describe the uses for exposure research within the U.S. EPA (Section 3.0); and
- provide the principles for developing and implementing NERL research within the context of the framework (Section 4.0).

DRAFT

2.0 Exposure Research

In simple terms, ***exposure*** occurs due to the contact of a stressor with a receptor. A stressor is any biological, physical, or chemical agent that leads to an adverse impact. A receptor is a living organism or group of organisms. In human health research, the individual or population of individuals is the receptor. In ecological research, the receptor can be individual plants or animals, communities of plants or animals, or entire ecosystems.

For exposure to occur, the stressor and the receptor must intersect in both space and time, as illustrated in Figure 2-1; exposure science characterizes, and predicts, this intersection. This fundamental definition is consistent with U.S. EPA's Guidelines for Risk Assessment (USEPA 1992) and its Guidelines for Ecological Risk Assessment (USEPA 1998).

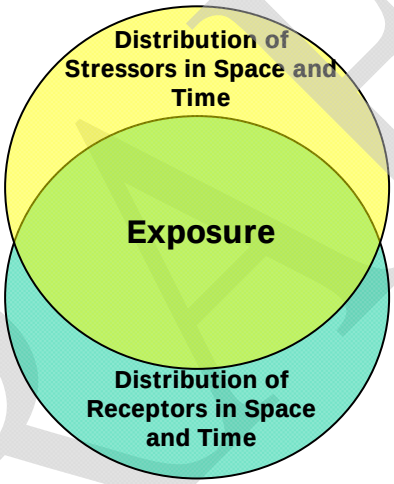


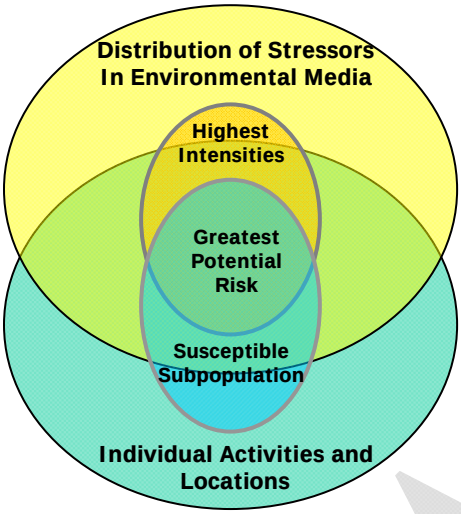
Figure 2-1. Illustration of exposure.

Exposure is described in terms of the magnitude or intensity, frequency, and duration of contact. For most stressors, the intensity of exposure is a critical element in defining adverse effects. Likewise, both the frequency and the timing of exposures can have an important impact. For many stressors, there are very specific time periods where exposure will lead to an adverse outcome. For other pollutants, exposure accumulated over time is important. Many chemicals, such as lead, dioxins, polychlorinated biphenyls (PCBs), and organochlorine pesticides, are persistent in the environment; thus, exposures will continue to occur over time as long as there is contact with the contaminated medium. Exposures to non-persistent chemicals may also accumulate if releases of these chemicals into the environment reoccur.

Exposure assessment seeks to identify potentially exposed populations and pathways of exposure, as well as to quantify the intensity, frequency, duration, and time-pattern of exposure. The adverse impact of exposure depends upon the characteristics of the exposure, the potency of

DRAFT

the stressor, and the susceptibility of the receptor. The greatest adverse impact of any given stressor will be to those individuals, populations, communities, or ecosystems that are most exposed and/or are most susceptible to the exposure. This concept is illustrated graphically in Figure 2-2, which expands upon the simplified illustration in Figure 2-1.



Vulnerability Factors (Exposure/Activity)

- Age or life stage
- Culture and lifestyle
- Activities and occupation
- Geographic locations/ distributions
- Socioeconomic status

Susceptibility Factors (Biological)

- Age or life stage
- Gender
- Genetic differences
- Prior status
- Previous exposures

Figure 2-2. The highest concentrations and the most susceptible populations create the greatest potential risk (assuming constant duration).

Within the exposure research framework, vulnerability refers to characteristics of a receptor (e.g., an individual, population or ecosystem) that may lead to greater exposure, while susceptibility refers to characteristics that lead to a greater response for the same exposure (see text box above). The concepts of vulnerability and susceptibility are crucial given the U.S. EPA's mandate to protect not only the general population, but also those populations at greatest risk. Exposure assessments, therefore, should identify and understand those conditions that lead to the highest stressor intensities and resulting exposures, as well as those situations that lead to exposure for the most susceptible receptors.

Figure 2-2 suggests that both stressors and receptors will vary in time and space; however, there is an important distinction between human and ecological exposure research in this regard. The human receptor is essentially the same in all locations; only stressor intensity, population characteristics (e.g., density), and susceptibility will vary in space. For ecological exposures, location determines not only the stressors present and their intensities, but also which receptors might be present, and the circumstances under which they encounter the stressor. That is, the organisms present vary as a function of location, as well.

There are many commonalities between human and ecological exposure research and these commonalities serve as the basis for this framework document. There are also differences that

DRAFT

must be recognized in order to have a complete understanding of the science. For example, our understanding of the concepts of human and ecological exposure research is influenced by the U.S. EPA's responsibilities in the two areas. The U.S. EPA is only responsible for human health outcomes related to environmental stressors (primarily chemical or microbial agents). In contrast, the Agency is also responsible for protecting the condition or state of entire ecosystems from multiple stressors, including physical, chemical, and microbial agents. Important differences between the human health and ecological disciplines are shown in the text box below.

Differences Between Human Health and Ecological Research Disciplines

Human Health Research	***Ecological Research***
• Agency is only responsible for human health outcomes related to environmental stressors	• Agency is responsible for health of the entire ecosystem
• Chemical and microbial agents are primary stressors of concern	• Physical conditions are often primary stressor of concern
• Single Receptor - human at individual or population,	• Multiple Receptors – individual plant or animal species, communities of plants and animals, or entire ecosystems
• Receptor is the same at all locations – population density, vulnerability, and susceptibility may change across location	• Receptors will vary across locations – location will determine what receptors are present and the circumstances for contact with the stressor
• Traditionally, risks have been evaluated for a single stressor at a time	• Risks are evaluated for multiple stressors, using a systems approach
• Exposures and outcomes stop with consideration of the human receptor	• Exposures and outcomes can cascade when the outcome in one receptor serves as the stressor for another

The goal of ***exposure research*** in NERL is to improve the ability to characterize, forecast, hindcast, and manage exposures. In addition to identifying and characterizing stressors and receptors, exposure research also characterizes and links the processes that impact the propagation and fate of stressors from their sources through the environment, and the intersection of stressors with receptors. Exposure research can be framed within a source-to-outcome continuum, in both forward and reverse directions, providing the critical link between sources of environmental stressors and associated impacts.

For illustration, Figure 2-3 shows the source-to-outcome continuum, as it has been developed for the human health research program. The processes that are important for characterizing exposure are primarily on the left-hand side of the figure. Starting in the upper

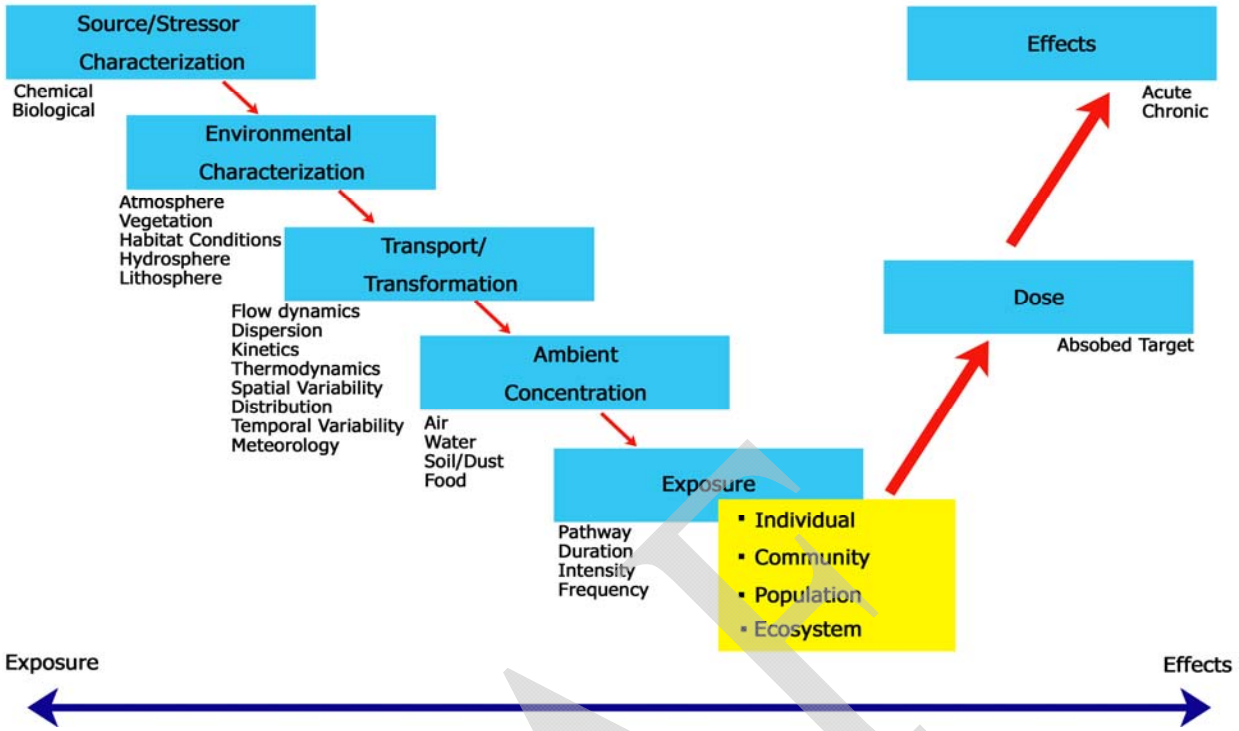


Figure 2-3. Source-to-outcome continuum for human health exposure research.

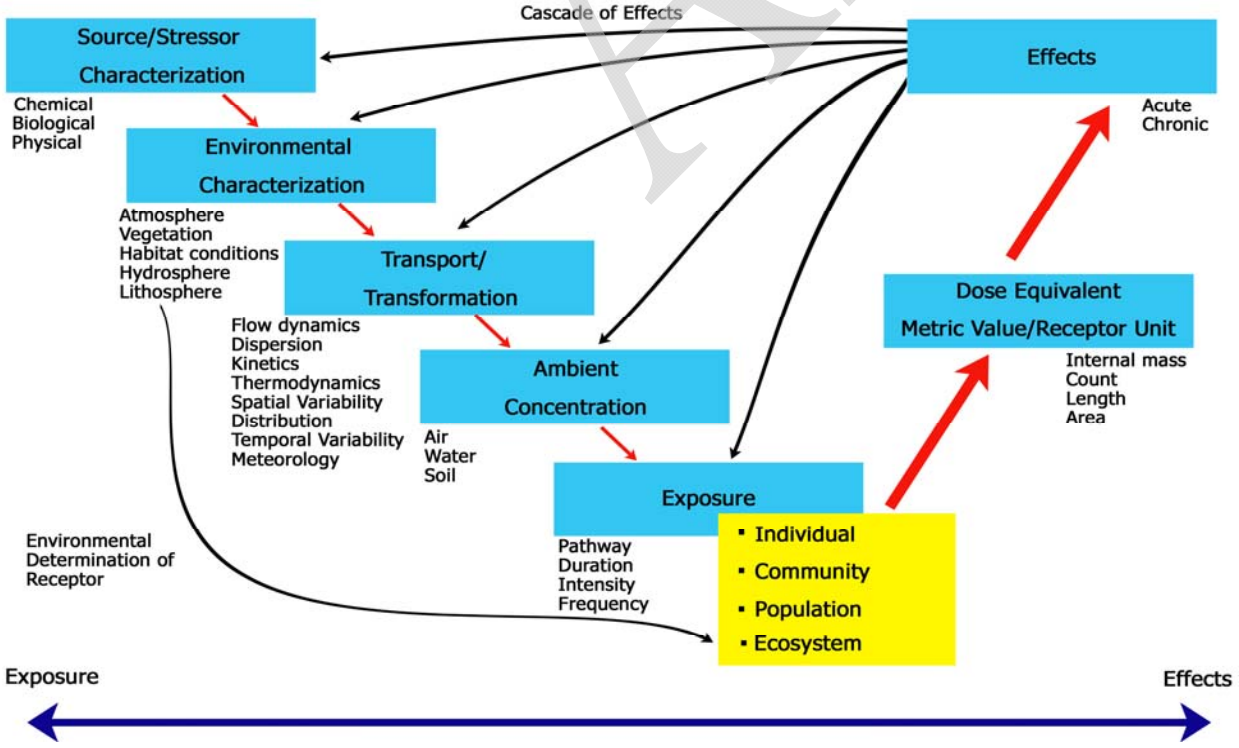


Figure 2-4. Source-to-outcome continuum for ecological exposure research.

left-hand corner, stressors (primarily chemical or microbial) are released into the environment from a source. Many stressors can be transformed through a number of processes, including chemical reactions and biological degradation. Stressors or their transformation products are transported through the environment and will be found in environmental media including air, water, soil, dust, and food. The intensity of exposure depends upon the stressor concentration in the media, as well as the duration of the contact with the receptor. Exposure becomes dose when the stressor moves across the body barrier. The text under each box in Figure 2-3 shows the information that is used to characterize the various processes represented in the boxes. The arrows between the boxes represent models that are used to link the processes.

Figure 2-4 shows that with several modifications, the same continuum can be used to describe the interaction of environmental factors that contribute to ecological exposures. For example, source may also refer to activities that give rise to non-chemical stressors, such as changes to habitat from expanding human populations. Environmental characterization includes the full suite of ecological conditions, as well as those that affect pollutant/stressor concentrations. In this continuum, dose is replaced by an equivalent measure of the stressor's impact on the receptor, that is, stressor intensity within the domain of the receptor. An example of a quantity equivalent to dose, where the receptor is a stream's fish community, might be the turbidity in a stream, caused by excessive sediments, that prevents a fish from finding its food. The multiple arrows from the effects box illustrate a sequence of cascading impacts where outcome in one receptor becomes the stressor for another receptor. Finally, the arrow at the bottom of the figure illustrates the concept that the receptor is determined by the location and environmental characteristics.

Exposure to environmental stressors is a complex process that can occur as a result of releases from many sources through a number of different pathways. Aggregate exposure is the sum of exposures to a single stressor from all sources and pathway(s) over a given time period. Cumulative risks are those that result from aggregate exposures to a single stressor over multiple time periods, or from concurrent and/or synergistic exposures to multiple stressors. Although the concepts of aggregate exposures and cumulative risk are relatively new for human health exposure research, understanding impacts from multiple stressors has been a fundamental aspect of ecological exposure research that should be extended to both disciplines.

Models are the underpinnings of this basic framework for conducting exposure research and using it in the context of regulatory decision making. Exposure research characterizes the movement, distribution, and interaction of stressors and receptors in time and space, at different locations and on multiple scales. With such a broad scope, we must go beyond the simple measurement of conditions for each component of the source-to-outcome continuum and focus on the processes that control movement along the continuum. Models provide the ability to summarize and link our knowledge of exposure processes and to mathematically quantify and predict concentrations of chemicals, biological and physical conditions, exposures, and dose. Process research and models enable us to be both prospective and retrospective in describing exposures and outcomes. The use of models is central to the Agency decision making processes (NAS 2007). The U.S. EPA uses models to inform the exposure assessment process (distributions, uncertainty, and variability), assess compliance, and evaluation alternate

regulations. As shown in the text box, there are many uses for exposure models. In addition to these uses, both conceptual and computational models also allow our state of knowledge to be systematically evaluated and data gaps and research needs to be identified. The importance of these models will continue to increase as computational methods advance.

Uses of Exposure Models

- Assess exposure to stressors
- Project future conditions or trends
- Extrapolate to situations where observations are not available
- Assess the contribution of individual sources
- Evaluate impacts of different policies or future scenarios
- Evaluate post-implementation impact of regulations
- Evaluate alternate policies

A complete exposure research program must include methods development and observational measurement research, along with modeling. Methods research provides the tools that allow observational measurements to be made and interpreted. These measurement tools have direct application for regulatory monitoring. Observational measurement studies provide a fundamental understanding of model processes , along with inputs for models, and data for model evaluation.

Although this document explicitly describes exposure research, all of the elements of research apply equally to the assessment and management of environmental risks. Linking all aspects of an environmental issue across the continuum from source to outcome can only be achieved through integrated, cross-disciplinary, and focused science and policy. This can be achieved by exposure researchers working in full coordination with health scientists, engineers, risk assessors, and decision makers.

DRAFT

3.0 Exposure Science at U.S. EPA

3.1 Role of Exposure Research in the Risk Assessment / Risk Management Context

The mission of the U.S. EPA is to safeguard public health and the environment from environmental stressors. The mechanism for environmental protection is minimization of human and ecosystem exposures to stressors of concern, either as part of a risk-based or cost-benefit assessment. The U.S. EPA sets its priorities, targets its actions, and measures its outcomes based on the assessment and management of risk. Regardless of the Agency program or regional office that raises the issue, there are three broad questions related to environmental decisions (see text box).

Broad Questions Related to Agency Problems

- Is mitigation necessary? (impact on the receptor)
- How best to mitigate? (impact on the stressor)
- Was the mitigation successful? accountability)

Figure 3.1 overlays the concepts of stressor and receptor on the source-to-outcome continuum. The figure then incorporates the processes associated with environmental management practices, including risk assessment, development of environmental policies and regulations, compliance monitoring, and risk management. Finally, the three questions that face the U.S. EPA are overlaid in the figure. As highlighted in the figure and discussed below, exposure is uniquely positioned at the intersection of the stressor and the receptor, and plays a pivotal role in addressing each of the broad agency questions.

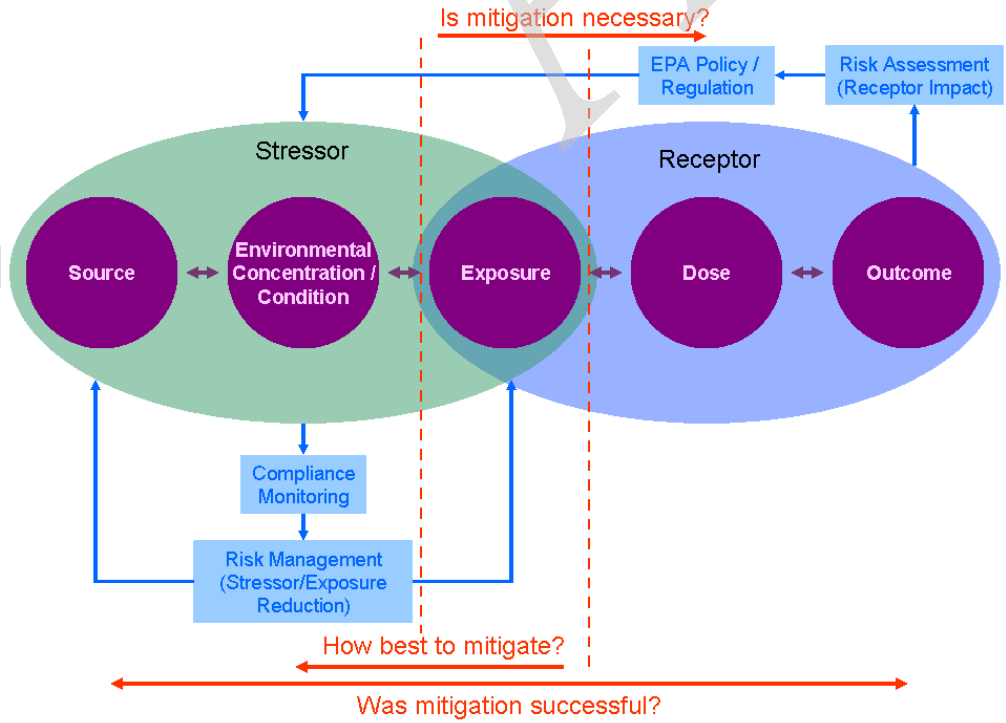


Figure 3-1. Framework for protecting human health and the environment.

Is mitigation necessary? Risk assessments are used to determine whether mitigation is necessary and focuses on impacts to the receptor. All risk assessments are based on the concept that:

Risk = Exposure x Hazard

Thus, exposure ***must*** be used implicitly or explicitly to determine risk. Very simply, risk assessment is a four step process (see text box; NAS,1983). Hazard identification determines, qualitatively, whether a stressor will cause an adverse outcome. Dose-response assessments establish the quantitative relationship between dose and incidence of effects. This information is used, in turn, to develop a "safe" exposure level, often referred to as a reference dose (RfD). Exposure assessment determines the route, magnitude, frequency, and distribution of exposure. Risk of an adverse outcome is characterized by comparing the "safe" exposure level to the distributions of exposure. Mitigation is required for exposures at or above the "safe" level. Although other information along the continuum (i.e., sources, environmental concentrations, etc.) may provide inputs to the exposure assessment, exposure is the metric that is used to evaluate risk.

Steps in Risk Assessment Process

- Hazard Identification
- Dose-Response Assessment
- Exposure Assessment
- Risk Characterization

How best to mitigate? Risk to a receptor can only be reduced by reducing exposure. The "safe" exposure level is determined by the dose response assessment described above. Activities designed to bring exposures down to that level are developed using information on the sources, pathways, and routes that lead to the exposures. These activities can be directed toward various processes along the source-to-outcome continuum. Standards most often target source controls or environmental concentrations, while some actions, such as fish advisories or ozone alerts, target individual actions in order to reduce exposure. For those standards that target environmental concentrations, environmental monitoring is used to assess compliance. When monitoring results exceed the standard, risk mitigation activities are then directed at the sources of the environmental stressors.

Mitigation activities can be developed without the use of exposure tools and information, but ensuring the development of activities that are the most protective, with the least burden, requires an understanding of exposure. Exposure science is used to provide information on the levels and processes that control fate and transport, environmental conditions and concentrations, and exposure pathways. Techniques, such a source apportionment and exposure reconstruction, are used to relate exposures or environmental concentrations back to sources. Monitoring methods are developed to evaluate exposures and to assess compliance to standards. Models across the continuum are used to summarize available knowledge needed for regulatory

DRAFT

decisions and provide the ability to evaluate alternative regulations, while also offering a framework in which to assess compliance (NRC 2007).

Was the mitigation successful? Over the last several years, there has been an increased interest in assessing the effectiveness of U.S. EPA's regulatory and non-regulatory decisions. Research and data across the entirety of Figure 3-1 can be used to address this area. This is a new area of research for the Office of Research and Development (ORD), with the initial emphasis placed on developing and validating indicators along the source-to-outcome continuum (USEPA 2007). Exposure science is expected to play a very important role in this research area, because it is critical to linking stressor based metrics to receptor based metrics.

3.2 Role of Exposure in U.S. EPA Regulations

The U.S. EPA's regulations and policies have been formulated to use exposure information according to the general principles outlined above. However, depending on the nature of the contaminant, the environmental medium, and the appropriate treatment of risk, regulations may outline different activities and address exposure in either an explicit or implicit manner. There are four primary areas where the U.S. EPA can increase the effectiveness of environmental protection programs by enhancing its emphasis on exposure assessment, and investing in exposure research:

1. **Development of current standards/policies** (e.g., developing and evaluating exposure metrics and models that can be used in the risk assessment process, understanding the mitigation or enhancement of exposure by human activity or natural processes);
2. **Achieving current standards/policies** (e.g., development of analytical methods for determining compliance, models to predict the impact of migitgation strategies, and information to implement mitigation);
3. **Evaluation of the impact of standards/policies** (e.g., ability to reconstruct exposures to determine environmental concentrations of contaminants relative to exposed populations; development of indicators along the source to outcome continuum, simulate alternative scenarios and policies); and
4. **Development of the science for the next generation of standards/policies** (e.g., cumulative risks, regulating sources of air pollution with the greatest risk; determination of the potential extent of exposure to emerging contaminants).

The following text box identifies the major exposure elements of the U.S. EPA's enabling legislation; identifying and understanding those elements is critical to strengthening and expanding the Agency's use of exposure science. In the past, exposure did not often play a large role in the risk assessment and risk mitigation processes. Environmental regulations would often be developed to address contamination that was so severe and immediate to its source that ambient monitoring data or source emissions were adequate surrogates for exposure. The National Ambient Air Quality Standards, developed under the Clean Air Act, and the U.S. EPA's drinking water standards, developed under the Safe Drinking Water Act, are but a few examples of this approach.

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Environmental Regulations and Statutes with Exposure Components

Clean Water Act – Establishes the structure for regulating the discharge of pollutants into U.S. waters. Exposure information is used to set standards to achieve uses, determine achievability of uses via technology and total maximum daily load (TMDL) controls (point, nonpoint sources), and establish watershed planning and best management practices.

Safe Drinking Water Act – Establishes safe standards of purity and require all public water systems to meet primary standards. Exposure research is used to develop methods to improve exposure assessments, improve microbial detection techniques, detect and classify unregulated contaminants

Clean Air Act – Established National Ambient Air Quality Standards for the protection of public health and the environment; sets limits on how much of a pollutant can be released in the air. Exposure research is used to develop exposure metrics for epidemiological research that evaluates health impacts of criteria pollutants, develop exposure assessments for air toxics, determine impact of atmospheric processes on air quality, provide models for air quality and exposure analysis and prediction.

Toxic Substances Control Act – Require reporting and/or testing of industrial chemicals produced or imported into the U.S. that may pose an environmental or human-health hazard. Exposure information is used to develop methods to measure exposures to industrial chemicals, analyze and report exposure levels based on real world data, conduct exposure assessments on a wide array of chemicals

Federal Insecticide, Fungicide & Rodenticide Act – Establishes federal control of pesticide distribution, sale and use. Exposure research is used to develop methods and models to characterize exposures to pesticides, model the fate and transport of pesticides through ground water

Endangered Species Act – Prohibits any action that results in a "taking" of a listed species, or adversely affects habitat of a listed species. Exposure information is used to determine (cumulative) risks to individuals of endangered species (including habitat), and register pesticides based on exposure risk to endangered species.

Food Quality Protection Act – Requires U.S. EPA to set limits on the amount of pesticides that may remain in or on foods based on risks to infants and children from exposure from all sources. Exposure research is used to develop important exposure scenarios, identify and quantify factors for children's exposure, develop high quantity, high quality exposure data, develop models for estimating exposure and dose to pesticides

Federal Food, Drug & Cosmetic Act – Requires U.S. EPA to address risks to infants and children from exposure to pesticides in diets; requires the development and implementation of a screening program for endocrine effects, including estrogenicity. Exposure information is used to study exposures to susceptible population, analyze exposures to endocrine disrupting compounds, develop generic techniques to model consumer exposure

This process has worked well for the U.S. EPA in the past and will continue to work well for situations, as long as certain conditions are met:

- The standard is not a risk-based standard (e.g., best available technology); therefore, the risk assessment process is not used.
- The surrogate exposure estimate is either much greater or lower than the risk level, thus better, more realistic exposure information will not change the action.
- There is only one source and pathway of exposure, and the relationship between source, environmental concentration, and exposure is well defined.
- There is only one pathway for exposure, and the pollutant concentration is relatively homogenous, so that a single measure of environmental concentration can be used to estimate exposure.

The need for good exposure information is highlighted when we consider the potential risks and adverse outcomes associated with underestimating exposures, along with the potential costs to society of overestimating exposures. This is especially true for those situations where a simple approach to exposure assessment is not adequate (see text box). In these situations, the overall quality of the risk assessment will be limited, to a great extent, by the quality of the exposure assessment. As an example, in risk assessments of waterborne pathogens which have a very large temporal and spatial variability, the uncertainty surrounding the various components of the exposure assessment can easily be up to several orders of magnitude. This level of uncertainty can have a profound impact on the regulatory action that is taken, as well as the confidence in that action.

Assessments Requiring Refined Exposure Estimates

- Aggregate exposures from multiple pathways and routes
- Cumulative risks from exposures to multiple stressors
- Exposures to stressors with significant spatial and temporal variability (e.g., fine particulate sulfate vs. coarse particulate matter in air, chemical contaminants vs. microbes in drinking water, etc.)
- Exposures and risks from sources rather than to single pollutants from a source
- Total risk associated with regulatory options

The U.S. EPA is facing a number of new challenges for which a one pollutant, one medium, one exposure approach for assessing and managing risk is no longer adequate. There is a growing awareness of potential exposures to new types of contaminants (e.g., nanomaterials), pressures of population growth on natural ecosystems, complex systems that involve multiple stressors, and pollutants with significant spatial and temporal variability (leading to different exposure scenarios for different populations). In addition, there is a need to consider how the consequences of a particular risk management action may lead to unintended consequences. For example, a regulation established to reduce exposure to one contaminant may increase exposure to another contaminant (e.g., decreases in nitrogen loading in streams may increase the bioavailability of mercury). Understanding exposures and approaches for reducing exposures

will be critical in meeting these challenges and in making informed decisions that protect public health and the environment while preserving human well-being and sustainability.

DRAFT

4.0 Exposure Research at NERL

As a research organization, NERL has two interrelated goals: to provide leadership in exposure science and to conduct high quality research to support the U.S. EPA's regulatory mission. Achieving these goals requires a strategic approach to research planning and implementation. The development of this NERL exposure framework is the first crucial step in this strategic approach, providing a common understanding of exposure science and its role in supporting the U.S. EPA's environmental protection agenda. The final section of this framework document will discuss how the concepts of exposure science, presented in Sections 2.0 and 3.0 and Figure 3-1, provide the foundation to a process that NERL can utilize to: (1) develop a portfolio of relevant exposure research programs that is responsive to the U.S. EPA's high priority research needs; (2) ensure that a process is in place to implement its research in a collaborative, creative, and efficient way; and (3) communicate the results of its research in a manner that will have the highest impact on advancing environmental protection and the state of exposure science.

4.1 Defining NERL's Research

4.1.1 Developing a Research Portfolio

To achieve the goals of science leadership and high quality responsive research, NERL's portfolio should contain a set of programs that address critical exposure science needs directly related to the Agency goals for air, water, and land protection, as well as the health of humans and ecosystems. NERL's research portfolio has been developed and strongly aligns with ORD's planning process and the Multiyear Plans (MYPs) in each of these areas. Development of NERL's range of research programs is a dynamic process that entails periodically assessing the current programs and identifying future areas of research both within and outside the MYPs. As new areas emerge, a number of factors are used to evaluate potential programs for inclusion in our research portfolio (Figure 4-1).

Evaluation factors range from questions about Agency priorities to NERL's ability to advance the state of the science. First and foremost, the area of research must be important to the U.S. EPA's and ORD's environmental protection mission. Next, and of great importance to NERL, it must be exposure research as articulated within this document. Areas that pass though these initial filters are then considered in light of several other factors. One overarching aspect is the extent to which NERL can significantly contribute to a research area. Does NERL bring a unique capability to the issue, either through the Laboratory's expertise or unique facilities that is unavailable elsewhere? Does it require an integrated program that only NERL can provide? Some research areas are well engaged by other organizations and NERL's incremental contribution may not justify the added effort. Alternatively, the problems within the area may be too broad in scope or generally intractable and would require a disproportionate amount of resources for little return in results.

Additional aspects to consider regarding whether to invest in a research program include the overall importance or priority of the problem to ORD or the Agency, the relative significance

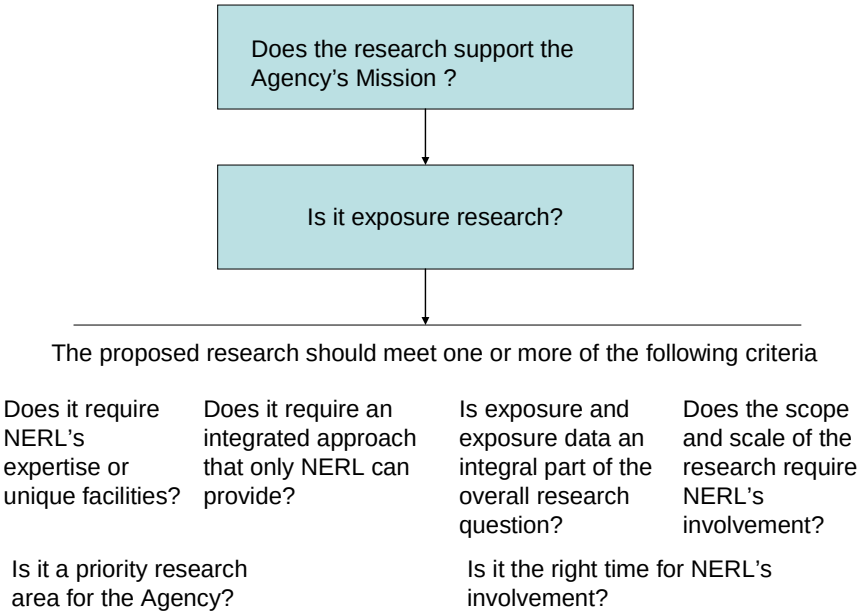

Figure 4-1. Evaluation factors for assessing potential research areas.

of exposure data to resolution of the overall problem, and the scope and scale of the problem (i.e., it requires the capability and capacity of a national laboratory). Timing issues should also be considered. For example, a problem with an exposure component may be of significant importance to the Agency, but the efficiency of the exposure research may depend on the availability of other research data. Additionally, the timeframe required for the research may be too short to effectively implement a program. Decisions to engage in a research area must also be considered in light of NERL's existing expertise and resources to do the work. This necessitates a consideration of issues, such as workforce size, skill mix, funding levels and existing commitments to other activities.

4.1.2 Designing a Research Program

Research at NERL is founded on the principles of exposure assessment/exposure mitigation, and is designed to be results-oriented and customer-focused. The types of research conducted by NERL scientists generally fall within two complementary and interactive categories – core and problem-driven. Core research seeks to understand the key biological, chemical, and physical processes that underlie environmental systems, and leads to products that may address issues common to many U.S. EPA programs. Examples of core research in NERL include efforts to understand exposure and factors responsible for exposure, as well as research to develop models and tools for describing exposure pathways of stressors in human and

ecological systems. Problem-driven research is directed at specific Agency needs that arise due to regulatory requirements or court-ordered deadlines. NERL research on the fate and transport of airborne particulates and on analytical methods for unregulated drinking water contaminants is being conducted in response to specific regulatory requirements under the Clean Air Act and the Safe Drinking Water Act, respectively. By maintaining a balanced portfolio of more fundamental core research, and problem-driven research that addresses specific regulatory requirements, NERL is able to better address the exposure science research needs of the Agency.

An integrated, multidisciplinary, exposure research program should be developed for each area identified as appropriate for NERL's portfolio. Each research investment is intended to provide critical scientific knowledge for U.S. EPA actions. Programs should be part of an ORD multiyear plan, have clear priorities, critical paths for meeting each priority, and a set of products and outcomes that demonstrate the research effectiveness. Figure 4-2 demonstrates the steps that ORD and its laboratories and centers use to develop and implement research programs within a Multiyear Plan.

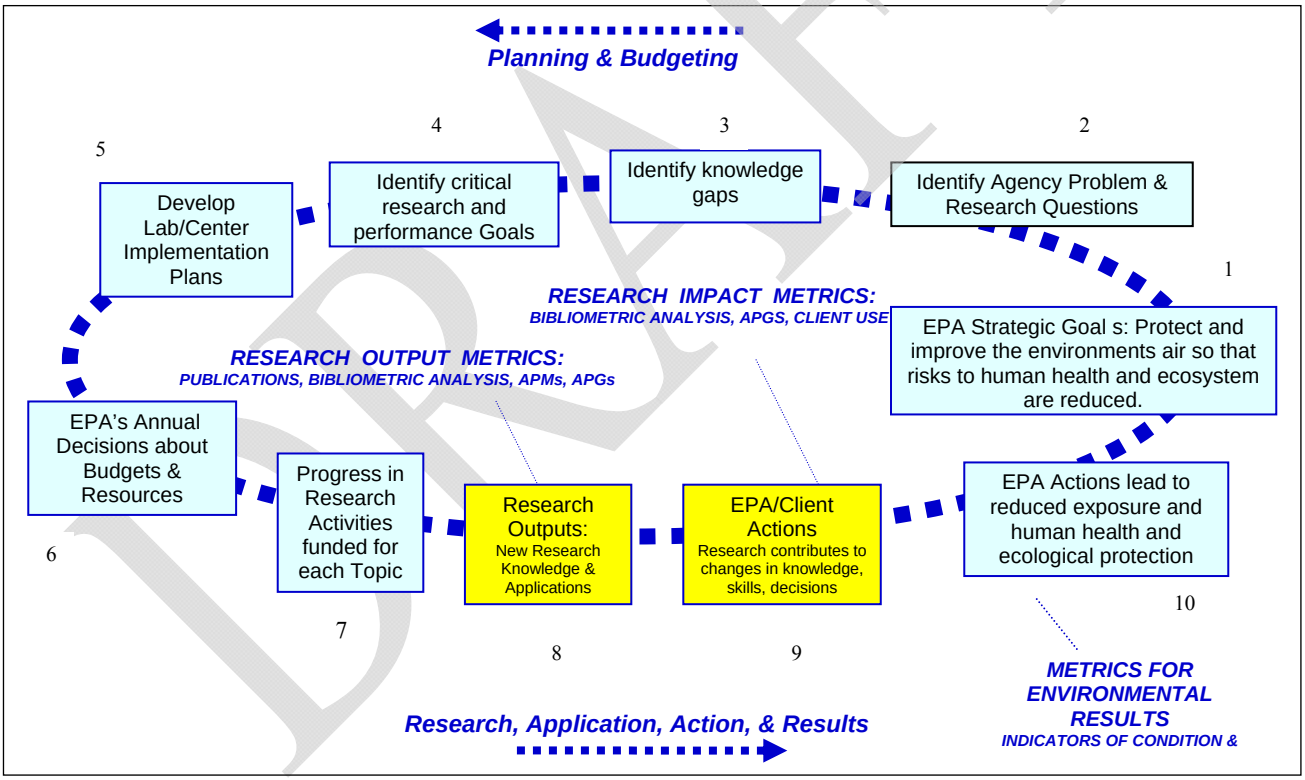

Figure 4-2. ORD's Research Planning and Implementation Process

Steps 1 to 4 represent the planning process used to develop a MYP. The EPA strategic goal (step1) is set by the Agency. ORD structures it research agenda around strategic goal by identifying key agency problems and the research questions identified by the scientific community (step 2). Critical research and performance goals (step 4) are developed to address the knowledge gaps (step 3) associated with the Agency problems. Researchers work with their

Lab/Center representatives in this process. Lab/Center specific implementation plans are then developed that address specific critical research. Although these steps are shown as sequential, the planning steps (2-5) are actually iterative in nature where planning at the Laboratory level also feeds into developing/identifying research questions, knowledge gaps, research areas and performance goals.

In all circumstances, research programs are initiated with the Agency's environmental protection goals and issues related to achieving these goals. Examples of recent problems facing the Agency include:

- Does exposure to particulate matter 2.5 µm or smaller (PM2.5) in ambient air cause death and hospitalizations?;
- How is the introduction of invasive species through ballast water discharge regulated?; and
- Has the recent mercury rule resulted in a measurable decrease in the levels of mercury in the environment, leading to reduced exposures of humans and ecosystems?

Regardless of the Agency goal or the office that is responsible for achieving the goal, there are three broad questions related to Agency problems that must be addressed: (1) Is mitigation necessary?; (2) How best to mitigate?; and (3) Was the mitigation successful?

A general approach for developing an exposure research program uses these broad Agency questions, combined with an understanding of the management practices for environmental and public health protection. As highlighted in Figure 3-1 and Section 3, exposure and exposure science play a pivotal role in addressing each of the three broad questions. A research program within NERL may focus on only one of these questions, or it may involve any combination of the three questions, depending on program and regional office priorities. The main driver of the development of the research program must be the ***key exposure science questions*** underlying the Agency problem. In every case, regardless of which of the three broad questions initiated the research program, NERL should always consider the wider potential use of the research in the areas of risk assessment, mitigation, and determination of effectiveness of the regulatory action.

For each broad area there are a number of key exposure questions to consider. In some cases, these questions are unique to the problem area, while in others there is a degree of overlap. For example, exposure methods developed for the risk assessment may also be applicable for compliance monitoring. A discussion of each of thee broad Agency questions, along with examples of the types of exposure information applicable to each question, provides a starting point for designing a research program.

Does EPA need to take action? The U.S. EPA uses the risk assessment framework to determine if a regulatory action should be taken. This process is shown on the right-hand side of Figure 3-1 and involves combining exposure risk assessment with hazard assessment. The specific question that the Agency is trying to answer is: "Does exposure to a stressor (e.g., PM2.5, arsenic,

PFOS/PFOA, etc.) lead to a human health or ecosystem risk?" Client offices typically provide information regarding the stressors and receptors of concern. NERL's potential role in answering this question is grounded in the exposure assessment. As a start, it is important to understand how the U.S. EPA performs the exposure assessment and whether the assessment is adequate. Generally, exposure assessments are considered adequate if the estimated exposure levels estimated are significantly lower than the risk level. In these cases, more information will not change the outcome of the assessments. It is also important to understand the limitations of the exposure assessment process. Possible questions to consider when evaluating the need for research to support the exposure assessment include:

- What are the levels of the stressor in the environment?;
- What is the extent of exposure to the stressor for humans and ecosystems?;
- Are the exposure concentrations higher or lower than the risk level for the contaminant?;
- Is the level of uncertainty of the exposure estimates acceptable?; and
- Is the risk of exposure to the contaminant of concern enhanced or mitigated by the presence of other stressors or physical parameters (i.e., is there a need for cumulative risk assessment)?

What action should EPA take? This becomes a question for the U.S. EPA once it has been demonstrated that an action is needed. The Agency must determine for a specific stressor, the most effective way to reduce exposures and to demonstrate compliance. The left-hand side of Figure 3-1 shows the U.S. EPA's risk management activities. Again, exposure research is necessary to make informed risk management decisions and NERL must ascertain, for the stressor of concern, what exposure questions remain to be answered. Examples of exposure questions in this area would include:

- What are the major route, pathways and sources of exposure?;
- What is the relationship between source, environmental concentration, and exposure?;
- What are the factors that impact the relationship between source, environmental concentration, and exposure?;
- How is the exposure to a stressor reduced, thereby reducing the risk?;
- What are the tools (models and methods) and data needed to identify effective risk management procedures? What are the critical limitations to these tools?;
- How should compliance be determined?;
- Where, what, and how does one measure for compliance monitoring?; and
- Are there non-regulatory policies and/or public information that could be used to mitigate exposures?

Was the EPA action successful? The final piece from U.S. EPA's perspective is to ascertain if the Agency's policies to reduce exposures to a stressor of concern have been effective. The entire Figure 3-1 addresses this issue. Exposure questions related to this issue include:

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- How can the impact of environmental policies on the health of humans and ecosystems be measured?;
- What are the exposure data and indicators that can be used to address effectiveness?;
- Are exposure indicators available that are sensitive and specific for the stressor of concern?; and
- How are these indicators related to sources, environmental concentrations, and to health effects?

In each case, the goal is to identify limitations with current exposure science and to determine the critical exposure data, methods, and models that are needed to improve it. A systematic approach, such as that described above, will allow NERL to go from a list of research possibilities to identifying the *critical* exposure research needed by the Agency. A simple conceptual model based on the source-to-outcome continuum provides an overall framework for developing a set of detailed research questions to address the area of interest. Each question is evaluated to determine what is already known, what research is currently underway, what information still needs to be developed, and how this information will contribute to the overall understanding of exposure. As a fundamental principle, NERL should direct its research towards those questions that either have the greatest uncertainty or provide the greatest opportunity for advancing science to support exposure and risk assessment. To illustrate this approach, an example is provided in Appendix A that shows the model and research questions used to develop a human exposure research program in response to exposure uncertainties associated with the 1997 National Ambient Air Quality Standards (NAAQS) for PM2.5.

Identifying the problem and articulating the science questions are the first two steps in developing an overall research program. Figure 4-2 presents a total of five steps that are involved in the design of a research program. When implemented, this combined top-down and bottom-up approach results in a fully articulated research agenda, initiated by a problem facing the Agency, and ends with science-based products and decisions that support Agency actions.

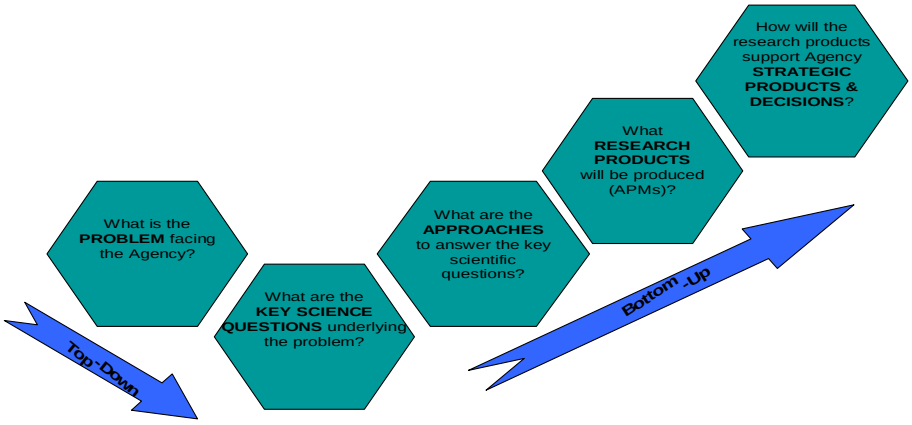

Figure 4-3. Steps to research program design

4.3 Implementing NERL's Research

NERL is a large research organization with six divisions at four different geographical locations. Across these divisions, is a diverse set of skills and expertise that can be used to address complex exposure research questions (Figure 4-4). In order to have the highest impact with these resources, NERL must conduct its research in a collaborative, creative, and efficient way. The challenge for NERL is to create a culture that operates at the laboratory level, where the motivation for managing research is to bring the best science to bear on the Agency problems as a laboratory. This requires integrating the research across divisions, scientific disciplines, and Multi-Year Plans (MYPs).

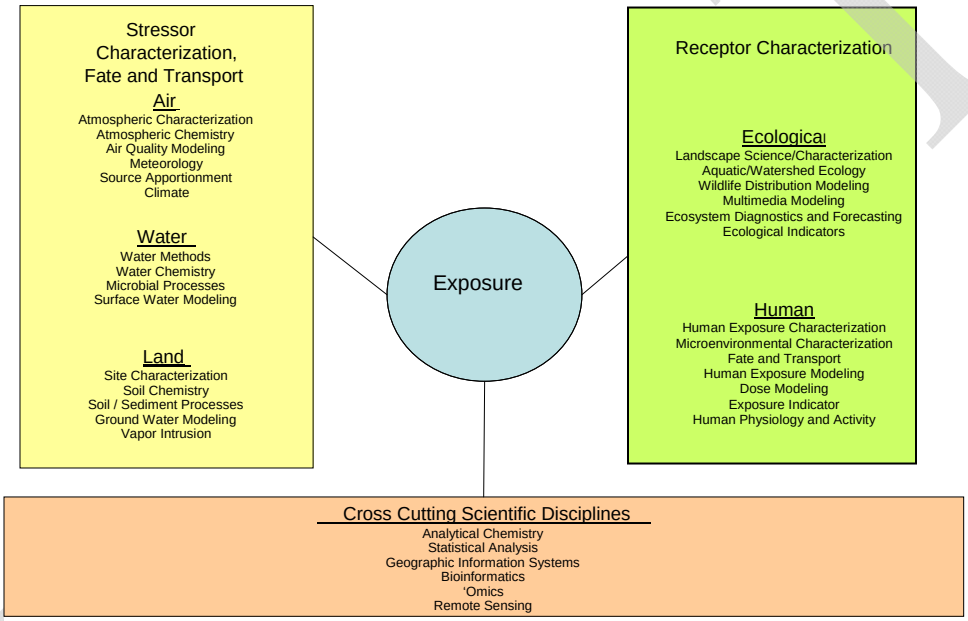

Figure 4-4 Scientific disciplines for exposure research.

Planning and implementing at the laboratory level will enable NERL to:

- Achieve the mission of conducting high quality exposure research that provides scientific knowledge to support U.S. EPA's regulatory mission;
- Create better solutions through linkages, integration, and synergy;
- Ensure efficiency of research and resources;
- Leverage resources and expertise; and
- Provide a stable environment for conducting and completing research.

Discussions within this section focus on the fundamental principles that should drive the management processes, the barriers to achieving NERL goals, and finally, the management processes for implementing research.

4.3.1 Management Principles

Management systems can be driven by many goals. It is important that those organizational principles that are important to NERL are articulated prior to developing structures and processes for conducting research. The following core principles will provide the framework for NERL management processes:

- We are the National Exposure Research Laboratory. The title NERL embraces several important principles. We think and act as a single laboratory. We provide leadership at the national/international level in exposure science. Finally, the U.S. EPA is the client base, thus NERL must plan and conduct its research based on direct consultation and communication with the clients within the Agency.

- Science comes first. We need to understand where we are going with our science, and then manage ourselves and our resources to get there. As a corollary, NERL will develop and use only those processes that are required to manage its science. NERL will not use processes that are more complex than needed to achieve its science goals.

- Apply multidisciplinary approaches where applicable. The U.S. EPA is faced with many large, complex problems and many of these are best addressed with multidisciplinary research programs that use cutting edge research tools (see text box). Developing an environment that fosters such collaborative, multidisciplinary research will set NERL above other organizations. Collaborative research allows the scientific processes that impact stressors as they move from sources to human and ecosystem health impacts to be understood and managed. This brings multiple perspectives to a problem for better solutions, and provides opportunities to leverage NERL's state-of-the-science knowledge and skills in multiple areas.

A Solution to a Complex Problem

NERL completed two very large surveys concerning the assessment of pesticide levels in stream waters. No one NERL division could have successfully completed such a large complex survey. The Ecological Exposure Research Division (EERD) and the Environmental Sciences Division (ESD) teamed up to cover the field sample collection, chemistry analysis, landscape metric calculation, biological sample identification, data management and data analysis.

- Seek functional solutions first. "Organizations use structural fixes to deal with functional problems," and this usually does not work. NERL should be able to work

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within the current structure and optimize its implementation processes to achieve the established goals.

- Optimize use of existing resources. NERL has an impressive array of resources to accomplish its mission. In addition, the Agency has many different high priority problems to address. NERL will strive to optimally align its existing resources, including staffing, with the highest priority Agency problems that require exposure science.

4.3.2 Moving Forward

Several processes must be in place for NERL to implement an optimized cross laboratory research program. These processes should allow NERL to fully integrate planning across the laboratory; optimize use of staff, research dollars, and facilities; and efficiently manage resources. If successfully executed, they should serve as a starting point for changing the laboratory culture and moving forward. Importantly, they will allow NERL to work together as a laboratory to produce relevant, high-quality research results.

As a basic requirement, NERL must first plan its research to be fully integrated across the laboratory. Currently, Implementation Plans serve as the basis for planning and should provide the mechanism for integration. Separate plans are developed for each of ORD's Multi-Year Plans (MYPs) and are intended to develop focused, integrated research programs specific to that plan. The process is designed to consider the clients' highest priority needs and all of NERL's resources in addressing key Agency needs. A discussion of how NERL planning fits into the ORD planning process is found in Appendix B.

Basis for Prioritizing Research

- Client needs
- Ability to demonstrate an impact
- Ability to make a novel contribution
- Appropriate balance between core and problem driven research

Developing and conducting an integrated research program at the laboratory level is an optimization challenge. Research Implementation Plans will be developed to describe research programs specific to a single MYP. Once they are developed, NERL must then look across plans to prioritize the research and identify leveraging opportunities (see text box). It is understood that the highest priority research should be resourced first. However, as a part of this process, resources (staff and FTEs) must also be balanced across both divisions and MYPs. The overall goal is to ensure that sufficient resources are available for successfully conducting the most relevant research in those areas where NERL plans to make a commitment. Understanding the priorities and the distribution of resources will also allow NERL to make informed decisions about redirecting resources, when needing to respond to new initiatives or when faced with reduced resources. Finally, NERL should use the information on science priorities and proposed research to direct workforce planning. Currently, NERL is in a transition period in the development and utilization of Implementation Plans. It is anticipated

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that it will take approximately three years to develop these plans and to integrate the research across the laboratory.

A number of non-traditional approaches will be needed to staff and implement multidisciplinary research across NERL. The primary goal is to ensure that critical expertise is provided to all programs across the laboratory. Other goals include greater efficiency, increased collaboration, development of new skills and capabilities, advancement of new technologies, and increased scientific leadership. Centers of Excellence (COE) are envisioned as one approach for efficiently using critical technical expertise in integrated laboratory research programs. The bottom box in Figure 4-3 shows those technical disciplines that could appropriately be used to develop COEs. The general concept for a COE would be to group facilities and experienced staff to optimize performance in supporting program needs across the laboratory. Staff in a COE would function in areas, such as development of new methods and technologies, regulatory support, direct project support, and data interpretation. Virtual research teams might be another approach to bringing multidisciplinary expertise from different divisions together to implement a research program. These teams would be responsible for developing, conducting, and communicating the results of research designed to address a specific Agency need.

NERL has traditionally managed much of its research at the level of the individual researcher or the branch. Resource management (staff, facilities, and research dollars) can be relatively simple at this level. However, moving to larger multidisciplinary projects, virtual research teams, COEs, and other nontraditional approaches will require new management approaches. As a laboratory, NERL must recognize that more complex systems are needed simply to get the research done. As NERL moves forward it is important that it identify and implement proven and time-tested best management and organizational practices, that it seek the counsel of organizational leaders and consultants to guide the process, and that it commit to adopting management systems that simplify rather than complicate laboratory operations.

4.3.3 Barriers

The ability of NERL to successfully accomplish its goals will require management and staff to work together to overcome the barriers that invariably exist in a large, multidisciplinary, geographically-dispersed, and resource-constrained organization with a wide range of clients. Several of the most critical barriers are identified below:

- Planning research at several levels (i.e., branch, division, NERL, and ORD) may require the development of multiple research plans and strategies, and involve different planning leads and team members. These efforts have the potential to become overly burdensome and time-intensive if the planning goals are not clear, the value of the efforts is not clearly articulated, and the time is not efficiently managed.

- Collaborating across organizational boundaries has implications for how teams are led, managed, rewarded, resourced, and held accountable. Special challenges exist when team members, facilities, and equipment are geographically separated.

- Research priorities of the client and research organizations may differ, even with frequent consultation and communication. Disagreements may arise, for example, if a Program Office places a higher priority on research to address a near-term regulatory priority, rather than on a longer-term research effort favored by NERL.

- Efforts to make organizational improvements are often met by a natural resistance to change. This is particularly a problem when decisions are made in a non-transparent manner, staff involvement in identifying barriers and solutions is limited, or the value of enacted or proposed changes is not fully appreciated by those who are impacted.

Overcoming these barriers requires strong and effective leadership, effective resource management, and the active participation by both management and staff in identifying and implementing solutions to problems that arise. Communication within and between all levels of the organization must be clear, frequent and open. Creating an environment of trust and a joint sense of purpose are fundamental to overcoming barriers in the changing ORD research environment.

4.3 Communicating NERL's Research

To be recognized as leaders in exposure science, NERL must communicate effectively with its customers and the scientific community. NERL's communication strategy for research will focus on having a high impact in advancing environmental protection and the state of exposure science.

NERL scientists are recognized as leaders in the research community and communicate via publications in peer-reviewed journals, U.S. EPA documents and reports, membership in professional societies, and participation in workgroups and committees. Communication within the scientific community maximizes the exchange of ideas and approaches to support the Agency's mission. Measures of success in this area include peer-reviewed publications and reports rated as highly-cited and publications rated as high-impact.

NERL will ensure that its research is used by the Agency by delivering high-quality, high-impact products to its clients. Working cooperatively, scientists, Division Directors, Associate Directors, and Assistant Laboratory Directors must make certain that NERL research products, which include peer-reviewed software, methods, reports, and journal articles, are strategically provided to its customers. NERL must promote implementation of its tools in the Agency by providing workshops, internet downloads, and user's manuals that advance these tools and models. NERL will also demonstrate the intended use of its high-quality methodology through case studies and pilot programs with its partners.

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Appendix A
Example Approach for Developing Research Questions

Broad Agency Problem:

- Does exposure to PM2.5 in ambient air cause death and hospitalizations?
- Should the 1997 revision to the NAAQS by upheld?

Need for Exposure Information:

- Time series epidemiology studies were used for risk assessment. Exposure to PM2.5 was estimated using ambient monitoring data.
- Previous studies had shown no relationship between PM2.5 and ambient exposure.

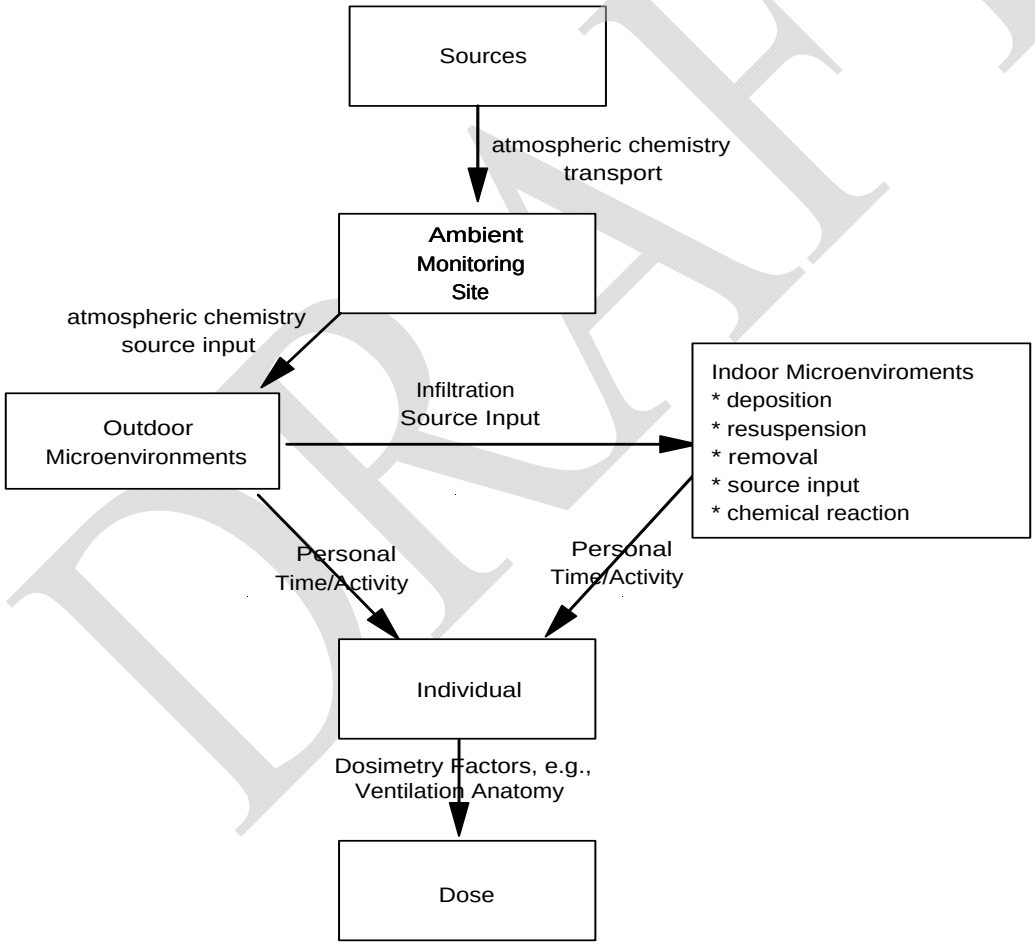

Figure A-1. Conceptual research design for human exposure to PM2.5 of ambient origin.

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Research Question:

- Is PM2.5 measured at the ambient site an appropriate estimate for exposure?

Table A-1 shows the key exposure research questions considered in this program.

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Table A-1. Key exposure research questions.

Questions				
	What is currently known	What research is ongoing	What additional research is needed	What impact will it have
Related to Ambient				
What are the characteristic of ambient PM in different U.S. regions?				
Outdoor Microenvironments				
What are the outdoor concentrations of PM/gases and their spatial distribution?				
What are the characteristics of outdoor PM in various outdoor microenvironments?				
What are the outdoor microenvironmental sources of PM/gases? What are their characteristics?				
What are the key outdoor microenvironments of concern for exposure to PM/gases?				
What are the factors that influence these distributions?				
Indoor Microenvironments				
What are the concentrations and of PM/gases in indoor microenvironments?				
What are their characteristics?				
What is the relative contribution of ambient PM to indoor PM?				
What are the indoor sources of PM/gases? What are their characteristics? Source strengths?				
What are the penetration rates of PM/gases indoors?				
What are the factors that influence penetration of PM/gases indoors?				
What changes occur during penetration?				

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Questions				
	What is currently known	What research is ongoing	What additional research is needed	What impact will it have
What is the spatial distribution of PM (of ambient origin) throughout a building or residence?				
What are the effects of deposition, reaction, resuspension, and removal of PM/gases indoors?				
Activity Pattern				
What are the time/activity patterns that effect exposure to PM/gases indoors and outdoors?				
How do these activities vary over time for the same individual? In the general population? In susceptible populations?				
What are the personal sources of PM/gases? What are their characteristics? Source strength?				
Personal Exposure				
What are exposures of the general population, susceptible populations, and individuals to PM/gases from ambient, indoor, and personal sources?				
How do these exposures vary over time?				
What is the correlation over time between ambient, indoor, and personal exposures to PM/gases on a community basis or for subpopulations?				
How does this vary across subpopulations, environments, seasons, and geographic areas?				

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Appendix B
NERL's Research Within the Context of ORD

The U.S. EPA's research agenda is determined by means of a research planning process involving every organizational level within the Agency. Figure B-1 is a simplified diagram for this process. ORD's research is driven by the five Agency goals described in the U.S. EPA's Strategic Plan. Within each goal, ORD works in partnership with many stakeholders to identify the highest priority research topics. The objective is to focus on environmental problems that pose the greatest risk to people and the environment, to reduce uncertainties which will improve our ability to identify risks, and to clearly help the Agency fulfill its regulatory mandate. For each goal, ORD commits to reaching certain milestones and delivering specific products within a given time period.

ORD's Multi-Year Plans (MYP) provide the long-term (5 to 10 year) focus for a given area of research, integrating efforts across all of ORD's Labs and Centers. For each MYP, an ORD team conceptualizes a framework for the research with long term goals that will be addressed across ORD. NERL plays a vital role in the development of the MYPs. All of NERL's research is included in these plans, and the Laboratory is held accountable for meeting commitments contained in MYPs.

NERL develops research Implementation Plans, using ORD's MYPs as roadmaps. The Implementation Plans bring the planning process to the operational level within the Laboratory. Separate plans are developed for each of ORD's MYPs and are intended to develop focused and integrated programs. For each Implementation Plan, steering committees made up of scientists, Associate Laboratory Directors, and Managers within NERL and across the Agency are charged with identifying the important programmatic research questions. Scientists across the Laboratory are then tasked with developing specific research programs to address these questions.

In summary, while the problems NERL is tasked to solve are defined by the Agency's planning process, the research agenda for solving those problems is determined by NERL and its staff. Although the relative emphasis in topic areas may change as ORD priorities and budgets shift, substantial efforts are made by NERL to build and maintain research programs that are relevant to the scientific problems and responsive to the Agency needs.

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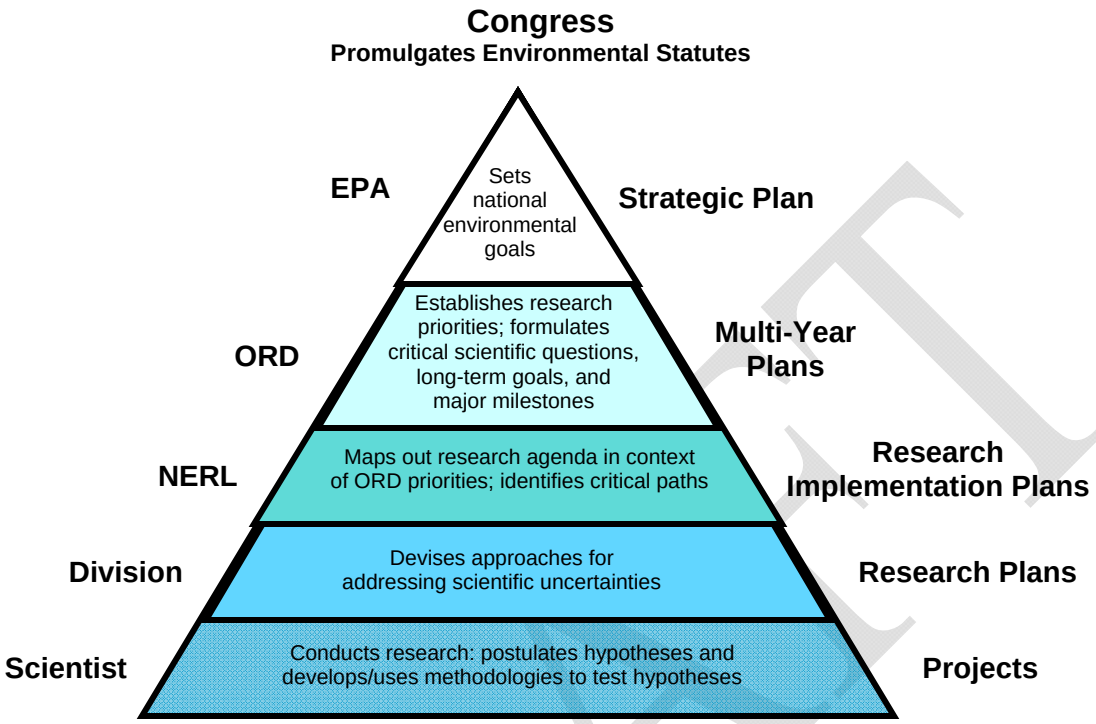

Figure B-1. Research planning in EPA.

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