Part I Overview Information

Department of Health and Human Services

Participating Organizations
National Institutes of Health (NIH) (http://www.nih.gov)

Components of Participating Organizations
National Institute of Environmental Health Sciences (NIEHS) (http://www.niehs.nih.gov)

Title: Superfund Basic Research and Training Program (P42)

Announcement Type

This is a reissue of RFA-ES-06-003, which was previously released on September 25, 2006

Request For Applications (RFA) Number: RFA-ES-07-006

Catalog of Federal Domestic Assistance Number(s)
93.113, 93.115, 93.143

Key Dates
Release Date: October 19, 2007
Letters of Intent Receipt Date: February 15, 2008
Application Receipt Date: April 15, 2008
Peer Review Date: October 2008
Council Review Date: January 2009
Earliest Anticipated Start Date: April 1, 2009
Additional Information To Be Available Date (Url Activation Date): Not applicable
Expiration Date: April 16, 2008

Due Dates for E.O. 12372

Not Applicable

Additional Overview Content

Executive Summary

- The National Institute of Environmental Health Sciences (NIEHS) is announcing the continuation of the Superfund Basic Research and Training Program [referred to as the Superfund Basic Research Program (SBRP)].
- SBRP grants will support coordinated, multi-project, multi- and interdisciplinary research programs to address the mandates legislated under the Superfund Amendments and Reauthorization Act of 1986. These mandates include the development of 1) methods and technologies to detect hazardous substances in the environment; (2) advanced techniques for the detection, assessment, and evaluation of the effect on human health of hazardous substances; (3) methods to assess the risks to human health presented by hazardous substances; and (4) basic biological, chemical, and physical methods to reduce the amount and toxicity of hazardous substances.
- The objective for the SBRP is to develop a holistic research agenda for the protection of human health. This is accomplished by the establishment of interdisciplinary programs that link and integrate biomedical research with related engineering, hydrogeologic, and ecologic components within the context of unique scientific themes developed by the applicant.
- The NIEHS intends to commit a total of approximately $8.0 million dollars to fund three to four SBRP grants in response to this Funding Opportunity Announcement (FOA).
- This announcement uses the NIH P42 multi-project grant mechanism. Successful applicants must include a minimum of two biomedical projects and two non-biomedical projects.
- Eligible organizations include accredited domestic institutions of higher education.
- Eligible Principal Investigators include any individual with the skills, knowledge, experience and resources necessary to carry out the proposed research. Individuals from underrepresented racial and ethnic groups, as well as individuals with disabilities are always encouraged to apply for NIH support.
- Applicants may submit only one application.
- See Section IV.1 for application materials.
- Telecommunications for the hearing impaired is available at: TTY 301-451-0088.
- Special receipt date, April 15, 2008.
- Initial merit review convened by NIEHS.

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Section I. Funding Opportunity Description

1. Research Objectives

Purpose

The National Institute of Environmental Health Sciences (NIEHS) invites qualified investigators from domestic institutions of higher education to submit an application for a Superfund Basic Research and Training Program (SBRP) multi-project program grant. With the assignment of the SBRP to NIEHS, the emphasis for this Program is the protection of human health. A secondary emphasis which complements the activities of its sister agencies, EPA and ATSDR, is to understand both the potential risk for being exposed to hazardous substances by characterizing environmental fate and movement, and the effects of these exposures on biological processes that determine disease risk. By understanding both components, strategies for mitigating risk can be developed that encompass approaches based on either reducing exposure through environmental remediation methods and/or through public health/ clinical interventions.

Applicants responding to this FOA are expected to develop an over-arching conceptual theme to guide the scientific direction of the program's interdisciplinary/multidisciplinary research team. It is expected that the overall theme will foster collaboration, whereby projects are integrated and specific emphasis is placed on interactions between the biomedical and non-biomedical research projects.

- First, the research team should focus on environmental exposures encountered at hazardous waste sites currently or emerging contaminants of concern.
- Second, a conceptual theme should be developed that encompasses a holistic approach to protecting human health by incorporating the principles of environmental health sciences and the engineering, geochemical and ecological sciences within the framework of a basic research program.
- Third, the scientific approaches to be undertaken should focus on improving our understanding of the multiple aspects of environmental health sciences and environmental sciences research. For example: employing state-of-the-art methods to understand the underlying biology that contributes to the exposure–disease paradigm;

using environmental genetics and genomics to discern the contributions of environmental and genetic factors in relation to disease susceptibility in vulnerable populations or in relation to the impact on microbial communities involved in biodegradation; developing novel computational, statistical, and/or mathematical tools to create risk assessment models that incorporate the complex biological data being generated through high-data content approaches; or employing fate and transport modeling of contaminants in environmental medias as it relates to the development of effective remediation strategies or for predicting exposure risk in humans or ecosystems.

- Fourth, a proactive approach should be developed through a required Research Translation Core for translating the scientific accomplishments emanating from the Program to its many stakeholders -- whether to the public through information dissemination, to industry via technology transfer, or to government through partnerships.

Ultimately, decisions needed to protect human health must be based on mechanistic knowledge gained from the integration of available data from all relevant research disciplines such as toxicology, molecular biology, epidemiology, geology, ecology and engineering. It is expected that the development of integrated multi- and inter-disciplinary research programs will result in an extraordinary level of synergy and technology-transfer opportunities, the outcomes of which have the potential to: (1) improve our understanding of the relationship between exposure and disease; (2) accelerate the development of public health prevention/ intervention strategies to improve human health as well as reduce the risk of exposure to toxic substances found at hazardous waste sites, (3) translate basic non-biomedical research into efficient and cost-effective cleanup strategies, and (4) improve the decision-making process at sites by reducing the uncertainty in human and ecological risk assessments. All are important goals of the SBRP.

Background

The mandates under which the SBRP operates provides a framework that has allowed the NIEHS the latitude to create a university-based, multi-project research program for conducting science to address the wide array of scientific uncertainties facing the national Superfund Program. These mandates include the development of (1) methods and technologies to detect hazardous substances in the environment; (2) advanced techniques for the detection, assessment, and evaluation of the effect on human health of hazardous substances; (3) methods to assess the risks to human health presented by hazardous substances; and (4) basic biological, chemical, and physical methods to reduce the amount and toxicity of hazardous substances. They were created under the Superfund Amendments and Reauthorization Act (SARA) of 1986, when it was realized that that the strategies for the cleanup of Superfund sites and the technologies available to implement these cleanups, were inadequate to address the magnitude and complexity of the problem.

The assignment of the SBRP to the NIEHS underscores an emphasis on human health effects and the evaluation and prevention thereof. However, as noted, the Program has the flexibility to support non-traditional NIH research such as the modeling of fate and transport processes for chemical contaminants and the development of remediation technologies to improve the quality of the environment as a means to reduce exposure and its potential impact on human health. Thus a new paradigm for environmental health research requires the integration of biomedical, ecological, geological and engineering sciences in order to develop and apply a full range of primary prevention strategies. This approach is exemplified by the research being conducted by the Program, see http://www-apps.niehs.nih.gov/sbrp/about/index.cfm.

To ensure that the SBRP meets the strategic goals of the NIEHS (http://www.niehs.nih.gov/about/od/director/strategicplan/index.cfm), the programmatic goals of the national Superfund Program and complements the activities of the U.S. Environmental Protection Agency (EPA, http://www.epa.gov/superfund/index.htm) and the Agency for Toxic Substances and Disease Registry (ATSDR, http://www.atsdr.cdc.gov), the SBRP must provide a fundamentally sound science base that is centered on “use-oriented” objectives. To achieve this, biomedical research is needed which promotes the understanding of the consequences of exposure to environmental agents on human health by elucidating the relationship between exposure and disease etiology, pathogenesis, susceptibility, progression and outcome. Contributing factors that modulate the exposure-disease paradigm include temporal factors (age and developmental stage), spatial factors (geographic locations), genetic factors (SNPS, methylation patterns) and unique circumstances (co-morbid conditions, nutritional status). Ultimately, this information needs to be considered in developing therapeutic strategies to minimize the impact of exposure on disease risk as well as for developing risk assessment models that incorporate these diverse parameters in order to provide the biologically-relevant information needed to make informed choices to protect human health.

The mitigation of potential exposure through the cleanup of contaminated sites is a fundamental goal of the national Superfund Program. While remediation strategies and technologies have been approved for cleanup at many Superfund sites, questions remain. Remediation methods that are appropriate for one site may be inappropriate for other sites. Issues such as site characterization or the effectiveness and appropriateness of existing or new technologies for clean-up of sites can be addressed through a basic research program such as the SBRP. Fundamental research that better defines the characterization of a site will influence the selection and application of appropriate remediation strategies. Considering the biological, chemical and physical characteristics of a site and incorporating this knowledge with an understanding of the molecular, physical or chemical processes involved in various remediation strategies will provide opportunities for the development of newer and more effective remediation approaches. The potential for unforeseen adverse effects on ecosystems, human health and the environment emerging as a consequence of employing new remediation strategies underscores the need to engage toxicologists and other health and wildlife specialists as part of an overall research program strategy.

Clearly integration from many different disciplines is needed to address the complex, interdependent yet fundamental issues that arise in relation to hazardous waste. A holistic approach that borrows theories and methodologies from many diverse scientific disciplines is the future for integrated environmental health as it relates to Superfund. Ultimately, this approach will enable the transitioning of basic research findings into epidemiological, clinical, ecological and remediation studies which will be important for the decision-making process to protect health.

Research Scope

A central premise of the SBRP is that there is a link between chemical exposure and disease outcome, and that understanding/identifying this link will help to establish new or improved prevention/intervention modalities. Therefore, research supported by the SBRP should emphasize basic and applied research, using state-of-the-art techniques to improve the sensitivity and specificity for detecting adverse effects in humans or in ecosystems exposed to hazardous substances, as well as for developing a better understanding of the underlying biology responsible for these adverse effects. Moreover, the applicant should emphasize research that studies the phenomena affecting transport, fate and transformation of hazardous substances, and developing remediation strategies that attenuate and mitigate exposure as necessary to protect human and ecological health.

In addition to the strong basic research focus of the Program, there is an equally important commitment to create an environment that fosters the translation of the scientific accomplishments emanating from the Program to its stakeholders -- whether to industry via technology transfer, to the government through partnerships, or to the public through community outreach. Therefore, research translation is a required element. The training of the next generation of scientists (i.e., graduate, post-doctoral) in interdisciplinary research, and conducting community outreach are highly valued activities and are strongly encouraged.

Goals and Objectives

This FOA encourages the development of multi-project, interdisciplinary research programs with the ultimate purpose of reducing the burden of human illness and dysfunction from environmental causes. The science proposed within an applicant’s program should allow for the evolution and maturation of hypothesis-driven basic research into opportunities for the translation of results into applied, “product-oriented” directions crucial for the protection of the environment and human health. Each interdisciplinary research program should develop an overall conceptual theme that fosters collaborative interactions, whereby projects are integrated, and specific emphasis is placed on interactions between the biomedical and non-biomedical research projects to promote the goals of the SBRP. These goals include

- understanding the biology that underlies the relationship between exposure and disease

etiology, pathogenesis, susceptibility, progression and phenotype
- accelerating the development of prevention/intervention strategies to improve human health as well as to reduce the risk of exposure to toxic substances found at hazardous waste sites
- translating basic non-biomedical research into innovative remediation technologies that are efficient and cost-effective
- advancing the development and use of risk assessment models that incorporate multi-scale data
- improving the decision-making process at sites by reducing the uncertainty in human and ecological risk assessments

Suggested Chemicals

Research must be conducted in the context of

- hazardous substances found with some frequency at Superfund sites.
- hazardous breakdown products of such substances formed in environmental media by physical, chemical or biological (e.g., plants, microorganisms, etc.) processes.
- hazardous metabolites of the above substances or their breakdown products formed in humans or experimental animals.
- chemicals with structural similarity to hazardous substances found at Superfund sites.
- chemicals of emerging interest.

Note: the applicant should refer to the following Web sites for information on hazardous substances that are relevant to Superfund and to the USEPA http://www.epa.gov/superfund/resources/chemicals.htm) and the ATSDR (http://www.atsdr.cdc.gov/cercla).

As technology has advanced over the past decade, the potential for creating new environmental hazards has become a significant concern. Being proactive in identifying these hazards and creating a knowledge base to understand their potential impacts on human health and the environment is a first step towards minimizing future risks from exposure. Therefore, the SBRP encourages applicants to consider studies to: investigate possible health effects; develop new detection, analytical tools and bioassays; and describe the physical and chemical properties that characterize fate and transport parameters for emerging and re-emerging environmental contaminants. Examples include: asbestos, brominated flame retardants, fluorinated compounds such as perfluorooctanoic acid (PFOA), 1,4-dioxane, N-nitrosodimethylamine, nanomaterials, pharmaceuticals and personal care products. Additional resources that the applicant may want to view include: http://www.fedcenter.gov/news/issues/; http://www.epa.gov/nerl/research/2003/g2-1.html.

As there are chemicals of emerging interest and concern, there are also chemicals for which the SBRP has made a significant scientific investment and therefore, these chemicals are not

as high a priority as in years past. Specifically, arsenic and PCB research has received considerable support from the SBRP over the years and the outcomes have contributed to regulatory decision-making. These chemicals remain listed as high priority for CERCLA because of their toxicity and frequency at which they are found at hazardous waste sites. Although the Program will continue to support PCB and arsenic research, new initiatives will be considered very carefully in context of other competing needs. The applicant is strongly encouraged to visit the SBRP website at http://www-apps.niehs.nih.gov/sbrp/ to determine how research that may be proposed fills research gaps or needs not currently addressed within the Program.

Suggested Research Topics

The development of a thematic concept for an SBRP application can be focused in many different ways. It is not uncommon that programs are driven thematically by a particular chemical or class of chemicals; by a common mechanistic pathway such as oxidative stress; by a particular disease, dysfunction or organ system such as the neurological system; or by methodological approaches such as biomarker development or the use of “omic” technologies. In addition, the ability to study biological and environmental processes at the molecular level is providing opportunities to consider research themes that focus on using molecular approaches to stimulate interdisciplinary research. Within this context, the applicant should propose individual biomedical and non-biomedical research projects.

Rather than provide detailed lists of research topics and approaches that are appropriate for study, examples of broad scientific themes relevant to the SBRP are provided. These examples are meant to stimulate the thinking of potential applicants by illustrating interdisciplinary linkages between scientific disciplines, and, ultimately, how this knowledge enhances public and environmental health. These examples are not intended to be exhaustive, and investigators may study these and many other topics that meet the objectives of the FOA. The applicant is also directed to the following site (http://www-apps.niehs.nih.gov/sbrp/rfa/resources.html) for additional research topics and approaches of interest to the SBRP.

In addition to the broad scientific themes provided below, there are some specific research needs and new directions within the Program that applicants may wish to consider. These include

- the incorporation of high throughput screening methods to develop detailed dose-response studies that lead to the development of sensitive biomarkers of biological response anchored to phenotypic characteristic
- the study of the mechanisms and health consequences of exposure to trichloroethylene (TCE) and the development of remediation strategies to mitigate exposure
- the development of analytical, imaging, bioassays and air modeling approaches to study the physical and chemical characteristics of asbestos fiber type and its toxicological

effects on multiple organ systems
- the development of groundwater remediation technologies such as permeable reactive barriers
- the development and application of methods to assess processes leading to vapor intrusion and resultant potential health effects
- the development of sustainable mining-site remediation
- the application of synthetic biology to engineer biological networks (e.g., metabolic, stress response signaling, etc) to create novel functions for remediation applications and/or regulating responses to chemical perturbations
- the development and application of bioengineered devices to study the exposure – response – disease paradigm in living cells and tissues
- the use of comparative genomics and toxicokinetic approaches to study functional consequences of single nucleotide polymorphisms
- the study of the interplay between exposure and epigenetics, genetic variability (SNPs), somatic mutations on influencing the biological processes
- the application of molecular genetic techniques in ecological studies to link evolutionary changes to environmental stressors as a means to identify genetic/phenotypic biomarkers for understanding risk
- the application of nanoscience principles to the geological sciences for studying the environmental fate and transport of environmental contaminants such as metals and to develop novel remediation approaches

Mechanistically-based Biomedical Research

Understanding the mechanisms whereby toxicants induce adverse human health effects is central to the SBRP. It is believed that environmental factors contribute to the etiology of most human diseases/dysfunctions (e.g., reproductive, immune competence, pulmonary/cardiovascular, cancer, neurodevelopment, neurobehavioral, congenital defects, renal, etc.). Therefore, the SBRP seeks to support mechanistic research that includes laboratory-based and population-based studies for unraveling critical biological pathways that contribute to disease when perturbed by environmental contaminants. Research should focus on environmentally related diseases and pathways of toxicological significance in the exposure-disease paradigm. General approaches to consider include

- dissecting the molecular, genetic and biochemical events that describe the normal physiological processes that contribute to good health and the roles hazardous substances play in its disruption by studying these issues at multiple system levels, from in vitro cell, tissue or organ culture, to non-mammalian model organisms to whole animals (including genetically manipulated), and to humans
- developing high throughput cell-based assays to create mechanistically based toxicity profiles for hazardous substances in order to assess risk
- employing integrative or systems biology approaches to study the effects of environmentally relevant levels of hazardous substances on the dynamic nature of

biological systems in order to understand cellular homeostasis; to appraise “biological noise”; and to identify biologically relevant events that lead to disease and dysfunction
- incorporating bio-engineering and synthetic biology to study the regulation, control and modulation of biological processes by small molecules and environmental chemicals
- developing and validating mathematical and computational approaches for physiologically-based mechanistic models for predictive toxicology that incorporate high data content information (e.g., the virtual cell)

A primary goal of the SBRP multi-project program is to integrate knowledge derived from basic mechanistic research into strategies that minimize the impact of exposure on disease risk to develop biologically-relevant risk assessment models that inform decision-making leading to the protection of human health. Accordingly, examples of research that builds on this basic knowledge include

- identifying, developing and validating biomarkers – key molecular or cellular events that link a specific environmental exposure to a health outcome - in population, clinical and ecological-based studies
- developing novel diagnostic or pre-clinical markers of exposure and biological responses
- applying bio-engineering principles to develop therapeutic approaches to mitigate biological consequences of chemical exposures
- developing biomarkers as prognostic indicators of human diseases, as well as therapeutic efficacy
- developing biologically-based risk models that incorporate mechanistic data (see Risk Assessment section)

Susceptibility and Predisposition Research

A critical confounding factor underlying the physiological consequences of exposure to hazardous substances is the genetic variability inherent in the population. This variability can lead to sub-populations with unique genetic characteristics that enhance their sensitivity to environmental contaminants or other external insults. The Program recognizes the importance of identifying susceptible populations in order to develop strategies to reduce their burden of environmentally-influenced diseases.

To address this issue, the SBRP seeks to support research focused on

- clarifying the contribution of genetic and environmental variables in the risk of developing disease by studying the interplay between exposure and intrinsic factors (e. g., genetic polymorphisms, haplotypes, epigenetic factors, gender and age); host factors (e.g., nutrition, co-morbid disease/conditions, lifestyle habits; and timing of exposure
- characterizing altered cellular functions (e.g., metabolic capacity, repair of DNA damage, cell proliferation and apoptosis) critical to modifying susceptibility and predisposition to

disease
- adapting molecular, genetic and or phenotypic approaches into population-based studies to enhance the power to observe associations between exposure and health, or cause and effect relationships
- integrating the factors affecting host susceptibility and resistance into mechanistically-based risk assessment models to identify vulnerable populations
- developing new biostatistical approaches and mathematical algorithms to understand gene-environment, gene-gene or multi-gene-environment interactions

These research efforts provide examples of interdisciplinary approaches and it is encouraged that collaborative efforts between biologists, epidemiologists, statisticians, systems engineers, computer scientists be considered in order to integrate the available information from animal and human studies in such a manner that would inform the risk assessment process.

Exposure Assessment Research

A priori, an environmentally-influenced disease implies that exposure has occurred within some temporal, spatial framework in relation to the development of disease. As such, there should be a direct link between exposure and disease morbidity and/or mortality. Unfortunately, as important as exposure is to the disease paradigm, it is one of the most difficult parameters to measure. This is due, in part, to the lack of precision in the methods to integrate exposure over time, the inability to characterize the attributable risk from multiple exposures experienced over one's lifetime and the lack of statistical and computational approaches to measure complex gene-environment interactions. Because exposure assessment is so integral to decisions related to protecting human health and ecosystems, understanding the complexities that impact the exposure component is an important research focus for the SBRP. Exposure assessment within the context of the SBRP falls within three interconnected research domains, (a) site characterization, (b) bioavailability and (c) accurate body burden and response measurements. These are further discussed below.

a) Site Characterization

The ability to predict the risk of exposure to contaminants at hazardous waste is dependent upon understanding the physical, chemical and geological characteristics of the site. Therefore, site characterization is an integral component of the exposure assessment paradigm. It is critical to understand the nature of contaminants found at a site, the potential for transformation and migration, and eventual uptake by humans and wildlife.

The SBRP seeks to support research that improves site characterization so that the knowledge gained can be incorporated into the exposure assessment paradigm. Examples of research topics include methods to

- identify and quantify chemical forms of the contaminants
- determine the toxicity, concentrations and location of contaminants within a site
- determine the ability of contaminants to be chemically or biologically transformed
- assess the physical, chemical and biological factors that affect movement of these contaminants from the site

The development and application of new and advanced technologies such as nanotechnology–based sensors and probes, biosensors, new imaging modalities, self-contained miniaturized toxicity-screening kits and miniaturized analytical probes and data analysis tools that allow for real-time, on site monitoring, is encouraged. In addition, research that integrates the resulting environmental data within a contextual framework of how contaminants affect nearby populations -- human or wildlife through modeling approaches is also sought.

b) Bioavailability

Another factor that interacts directly with both exposure assessment and site characterization is bioavailability. Bioavailability of a contaminant describes the degree to which it is available for transformation, and transport within environmental media (i.e., soil, sediments and surface and ground water) as well as the degree by which a contaminant eventually is assimilated by organisms. As an integrating principle, bioavailability crosses all scientific disciplines and is an important factor to consider in understanding the fate and transport of hazardous substances; the ability of hazardous substances to be internalized by microbes, wildlife and humans; and the ability once internalized to be available to tissues and organs. Recent technological advances provide new opportunities to study the complex issues surrounding bioavailability. Research approaches that might be considered include

- employing an array of multiple, molecular-scale techniques over a range of temporal scales in combination with macroscopic approaches and computational modeling to understand biogeochemical properties and processes important to chemical bioavailability to organisms
- applying state-of-the-art analytical techniques, such as synchrotron-based technologies (e.g., X-ray absorption fine structure spectroscopy, XAFS), to elucidate reaction mechanisms at a small scale
- characterizing at the molecular scale, the chemical and physical forms and distribution of contaminants in soils, sediments and its interactions with biotic and abiotic systems
- developing reporter systems, biomarkers and/or microbial community bioassays as integrated measures of uptake and response for ecological assessments of risk
- developing nano-enabled and micro-scale platforms to assess the bioavailability of contaminants to microbial and mammalian populations

c) **Quantifying body burden and response**

The integration of available data from site characterization and bioavailability studies into exposure and risk assessment models provides a means to predict potential exposure levels in human populations and ecosystems. The validation of these models requires the development and application of new methods and technologies that can measure the extent of exposure in disparate populations.

Many approaches are available that have the requisite sensitivity and specificity to detect current exposures, or measure contaminants that have a long half-life in biological systems. However, the issues of past exposures and exposure to mixtures are still intractable problems. For example, rarely is one exposed to a single chemical, but rather is exposed either concurrently or sequentially by

various routes of exposure to a large number of chemicals over varying periods of time. Moreover, the concentrations of contaminants found in the environment and in living systems may be at very low levels.

Therefore, research activities of interest for the SBRP are

- the development of improved technological methods such as biosensing materials that detect functional changes in only a few cells that might be predictive of exposure and subsequent disease/dysfunction
- the development of toxicity sensors that rapidly detect and quantify low concentrations of chemicals in cells or tissues
- the development and application of computational approaches to study temporal and spatial factors associated with timing of exposure, and to detect and assess exposure history within the context of biological relevancy
- the application of advances in miniaturization technology to redefine exposure assessment by improving visualization tools, detection methods (such as biosensors), analytical tools and data mining/data analysis tools that can be used for both environmental media and living biological systems
- the development of mathematical, computational and statistical techniques that integrate exposure and biological information into a holistic model for exposure and risk assessment

Remediation Research

The SBRP, in response to its operational mandates, supports research that is beyond the traditional biomedical focus of NIEHS and the NIH in general. Specifically the SBRP supports the application of engineering and microbial sciences as prevention (i.e., remediation) strategies to improve human health by mitigating exposure and reducing toxicity of environmental contaminants at hazardous waste sites. The most common methods used to remediate hazardous waste include thermal treatment, surfactant/co-solvent flushing, in situ

chemical redox reactions, electrochemical treatments, and bioremediation.

As a basic research program, it is important that the SBRP supports research that is focused on the scientific principles and underlying processes that drive different remediation technologies as methods to clean up persistent toxics in groundwaters, sediments and soils. Conversely, it is also important that the SBRP support research that focuses on the translation of these basic principles into efficient and cost-effective technologies to reduce the level of contaminants present in the environment. Moreover, as advanced technologies such as the use of nanoparticles, bio-engineered plants or microbes, are providing new opportunities for remediation research, their presence in the environment may present unexpected hazards which may need to be addressed. By supporting a continuum of research from basic to applied approaches, preventing exposure and mitigating risk from the exposure to hazardous substances, unanticipated by-products of remediation, or from the introduction of engineered microbes or nanomaterials into the environment becomes a realistic goal for the SBRP.

Accordingly, the SBRP encourages research that ranges from basic mechanistic research to technology development. Research examples include

- the investigation of the mechanistic basis for degradation and sequestration of contaminants by microbial, as well as other biological systems, by assessing the physical, chemical and biological factors that affect movement of these contaminants from the site
- the incorporation of molecular, biochemical cellular and/or engineering tools to understand the basic structural and functional properties of microbial and other populations involved in the bioremediation of hazardous substances
- the utilization of visualization and molecular tools to characterize the physical, hydrogeochemical, or biogeochemical properties of sites containing Dense Non-Aqueous Phase Liquid (DNAPLs) and that are typically characterized by extensive, heterogeneous, and persistent source zones of entrapped and pooled organic liquids
- the development of innovative approaches to detect and assess the fate and transport of introduced engineered nanomaterials in the environment and to understand its potential toxicity
- the application of “green technology” to current remediation practices to improve energy-efficiency and reduce waste generation, thereby increasing the usability and sustainability of otherwise effective remediation technologies
- the development of innovative physical, chemical and biological technologies for the remediation of hazardous substances found at waste sites

Ecological Research

Understanding the ecological impacts resulting from exposure to contaminants found at hazardous waste sites is a complex problem, in part, due to the number of species involved

and their interdependencies. Ecological research interfaces biology, ecology, microbiology, bioengineering and engineering sciences. Capitalizing on state-of-the-art methods and genetic approaches that have been primarily applied to human studies provide tools that could be of benefit in advancing the ecological sciences.

Accordingly, the SBRP encourages the application of “omics” tools, new sensor technologies and informatics with the goal of enhancing our understanding of ecological succession and biodiversity as a function of exposure to contaminants. Examples include

- the development of molecular, cellular, biochemical and population-level baseline data describing the components that define an ecosystem and how these individual components are affected by hazardous substances
- the development of informative “biomarkers” that identify stressors, key “sentinel” species, and define the linkages between ecological genetics, and stress responses within the ecosystem
- the identification and validation of genetic markers such as polymorphisms, chromosome inversions, and microsatellites in populations as sensitive indicators of changes in environmental conditions
- the evaluation of the bioavailability/bioconcentration of contaminants in the food web as a basis for predicting bioavailability/bioconcentration in humans
- the use of intact ecosystems in field experiments to model the consequences of bioavailability and sequestration of contaminants. For example, if sequestration of contaminants at a site is an acceptable remediation strategy, what are the potential exposure consequences over time as aging and weathering occurs?

Mixtures

A critical issue related to hazardous waste sites for remediation or health effects research is that the concentrations at which chemicals occur in the environment are extremely low and exposures are long-term, continual, with simultaneous exposure to multiple chemicals. Whether one considers remediation strategies, exposure to humans or ecosystems, site characterization, bioavailability or the development of risk assessment models, chemical mixtures are an issue of concern. Furthermore, biomedical research, exposure assessments or remediation strategies based on exposures to single substances in isolation is rarely reflected in real-life scenarios. This over-simplification fails to consider

- prior exposure history and vulnerability (i.e., susceptibility)
- interactions from other stressors of similar/dissimilar mechanisms of action
- potentiation or sensitization by chemicals not toxic in themselves
- interaction of chemicals that could lead to synergistic or antagonistic effects

The SBRP seeks to support research that considers the effects of mixtures. With the

continued development and refinement in the available repertoire of advanced tools and approaches, the scientific community may be in a better position to assess the impact of mixtures on all areas of research important to the SBRP. Examples include

- the development of computational toxicology approaches to understand dose/effect relationship in the context of chemical interactions
- the application of high throughput functional assays to define critical mechanistic endpoints associated with potential adverse biological consequences of exposure to chemical mixtures
- the integration of diverse datasets to develop biologically-based predictive models for chemical mixtures
- the application of metagenomics to understand the impact of chemical mixtures on the structure and function of microbial communities
- the development of nano-enabled technologies to detect and measure individual components within complex mixtures in real time
- the development of innovative approaches to remediate chemical mixtures in environmental media
- the adaptation and application of fate and transport models to predict and assess the influence of chemical mixtures on the efficiency and effectiveness of applied remediation approaches

Risk Assessment

The risk assessment process defines exposures of concern and potential threats. The more robust the risk assessment, the better one is able to contribute to cost effective and yet protective choices. Historically, risk assessments are focused on developing models for either human health or ecological health and decisions made accordingly. However, within the interdisciplinary framework of the SBRP, opportunities to develop integrated models that incorporate both human and ecological effects need to be encouraged in order to assist in making cost-effective and protective decisions. In addition, the translation of the knowledge gained from high data content approaches, which are increasingly being used to obtain mechanistic data, will require the development of a new generation of risk assessment models. These models will need to take into account biological pathways and networks, susceptible populations, low dose effects and mixtures.

Therefore, the SBRP is interested in innovative research focused on the development of: 1) large datasets to be used in model development, 2) tools to integrate diverse datasets and 3) new risk assessment models that incorporate these diverse datasets. Research examples include

- the development of robust human and/or ecologically-based genomic, proteomic, metabolomic and functional datasets for model development and validation

- the development of new bioinformatic approaches to bridge data from different disciplines and across scales of biological complexity
- the development of multi-dimensional risk models that incorporate exposure data, movement of contaminants within environmental media, bioavailability, uptake by biological receptors (i.e., human or wildlife) and biological responses (e.g., changes in signaling molecules, receptor occupancy, metabolic profiles, etc)
- the development of sophisticated statistical and computational methodologies and improved mathematical algorithms for predictive and computational toxicology to better characterize the lowest dose-response effects that are biologically relevant

CORES

Although novel, innovative, cutting-edge research projects are the nucleus of an SBRP grant, it is the intent of the SBRP that the research activities be integrated into an interdisciplinary program. In support of this goal, NIEHS requires the establishment of cores. Each grant application is required to have an Administrative Core, a Research Translation Core, and at least one Research Support Core. Community Outreach and Training Cores may also be included in support of achieving a truly multidisciplinary approach to hazardous substances research.

Administrative Core (required component)

The Administrative Core is a required component of a program. Through this core the Principal Investigator provides leadership and guidance in fulfilling the stated objective of his or her program. To accomplish this, the applicant should create within the Administrative Core an infrastructure that promotes cross-discipline interactions among all of the projects and cores. The structure of this Core should provide the Principal Investigator with a mechanism for

- planning and coordinating research activities
- integrating cross-discipline research
- overseeing fiscal and resource management

The applicant should include a plan for conducting the administrative functions of the core, a description of the lines of communication among the program scientists, and a description of the mechanisms to be used to encourage and ensure the integration and interaction between the biomedical and non-biomedical projects within the program.

To aid the Principal Investigator in achieving the goals set forth for his or her program, the establishment of an External Advisory Committee is required. Their role is to provide guidance to the Principal Investigator in the following areas:

- the merit of the research

- the relevance and importance of the individual components to the goals of the program
- the integration of research across disciplines
- the appropriateness of outreach activities
- the effectiveness of translating research to appropriate audiences
- the effectiveness of training activities

The composition of the committee should include appropriate scientific expertise as well as represent appropriate stakeholder interests. For example, not only should the academic community be represented on the committee, but also other stakeholders, such as industry, community or government representatives should be selected to serve on the committee.

Research Translation Core (required component)

NIEHS recognizes the importance of translating important research outcomes to appropriate audiences, thereby encouraging the accurate and timely use of these research products. Accordingly, NIEHS requires the inclusion of a Research Translation Core in each SBRP grant. For the purpose of this FOA, the SBRP defines Research Translation to be "communicating and facilitating the use of research findings emanating from the program in the manner most appropriate for their application and the advancement of research objectives." As described below, NIEHS requires that this core be comprised of three specific activities: (a) partnering with governmental agencies, (b) conducting technology transfer and (c) communicating to broad audiences.

It is important that each program be positioned to recognize opportunities for information and technology transfer and be capable of implementing the most appropriate mechanism for the activities proposed.

a) **Partnerships with Government Agencies**: Establishing ongoing communication with the federal, state and/or local agencies charged with protecting human health and the environment is of high importance. In order to address this need, each applicant should:

- Propose a plan explaining how interactions with the appropriate local, regional or national governmental agencies will be achieved. The intent of this is to ensure that governmental offices have first-hand access to the valuable resources the program can provide, and that the investigators have feedback on the real and immediate needs faced by their counterparts in the public sector.

Note: Applicants are not required to conduct Superfund site-specific activities; however, if site activities are planned, these activities, of course, must be conducted in coordination with appropriate federal or state site officials. Therefore applicants should

- propose a procedure for coordinating and documenting site activities including record of

the research being conducted or, on samples being collected
- delineate the steps to be taken to ensure communication with all appropriate site officials, including a final report-back to the site manager indicating the outcome of the activity

b) **Technology Transfer**: It is important that each program establish a mechanism to facilitate the formal transfer of the technologies and other research generated by the grantee into the hands of an end-user.

- e.g., translating research findings quickly into methods and technologies that improve the efficiency of site characterization, remediation and achievement of cleanup goals,
- or identifying biomedical research advances that have potential benefit to specific health effects endpoints or risk assessment applications,
- or identifying non-biomedical research remediation technologies that are ready for field demonstration or commercialization.

In order to meet this objective, each applicant should

- include a plan for identifying opportunities for moving research findings into application. The plan may
- include formal technology transfer (i.e., application for patents), or
- be conducted on a less formal basis (i.e., non-patented application of research advances -– moving research from bench scale to demonstration, developing a new risk assessment paradigm or providing research data to improve upon current risk assessments)
- delineate milestones or benchmarks to demonstrate progress in meeting its goals.

c) **Communicating to Broad Audiences**: Beyond government officials and the market place, there are other stakeholders who should have timely access to SBRP research findings. A variety of mechanisms to reach these stakeholders are appropriate activities for the Research Translation Core.

e.g., Sponsorship of workshops, short symposia, or web-based symposium. These would typically be one-day events that are local or regional in nature and could potentially involve not only academics but also other stakeholders (e.g., industry or local or regional health departments),

or development and use of advanced communication tools or methods such as web-based systems, geographic information systems or other technologically innovative systems

or development and use of more traditional communication tools such as the translation of complex research findings into print and web materials intended for the lay public based on

communication best practices.

In order to demonstrate how the applicant will meet this need, it should

- include a plan that details the mechanisms that will be used for sharing research findings
- identify important stakeholders and propose mechanism for engaging them
- delineate milestones and benchmarks to demonstrate progress in meeting its goals

In addition, NIEHS considers communication with SBRP associated staff to be a high priority and places this responsibility within the Research Translation Core. NIEHS requires that a plan be established for ensuring the effective communication and transfer of important research findings and other program outcomes to NIEHS. This plan should also include a direct line of communication between the Administrative Core and the Research Translation Core.

Research Support Cores (required component)

The SBRP requires at least one Research Support Core. The intent is that this Core will provide essential, centralized services or resources that will result in an economy of effort and/or savings in the overall costs of a program. Well designed cores also serve as a useful tool in promoting interdisciplinary activities. By definition, a Research Support Core must support two or more research projects. Typical Core facilities include laboratory facilities, biostatistics and/or bioinformatics support, or analytical equipment and services. The applicant should include in their description of these cores the services to be rendered, the methodological approaches to be used and a plan for prioritizing the use of the facility by program members.

Community Outreach Core (optional component)

The SBRP strongly encourages the applicant to consider the inclusion of a Community Outreach Core. The Core should be designed with a primary focus on health-related issues; however, other topics of interest to the community such as environmental concerns are also acceptable. Outreach to communities is in line with the Superfund Program's mandate to more actively involve the community in the decision-making process.

For the purpose of this FOA, the SBRP defines community outreach to be "extending support or guidance to communities, community advocates or community organizations. Appropriate target communities include those that (1) are living in proximity to, or affected by hazardous waste sites or (2) are exposed to hazardous substances via other pathways." For example, appropriate community groups could include local government, tribal councils, established groups/organizations focused specifically on local environmental/site issues, or community service groups focused on educating the community about local issues. As an outgrowth of this activity, it is expected that interactions with the community will also serve to enhance the program's research agenda.

Community outreach activities should be conducted in full partnership with the target community. In other words, the community should participate in the design and approach of the activity at the onset of the project. Note: Any activities conducted at Superfund sites should be coordinated with the appropriate offices in EPA or ATSDR. Likewise, activities conducted at state or tribal sites should be coordinated with appropriate state or tribal agencies. This will ensure that the applicant efforts are not in conflict with nor duplicate other agencies activities. However, this coordination should not compromise the independence of the outreach efforts since the community may value the support of a non-regulatory agency.

Community outreach activities may be either very broad or very focused. Examples that are appropriate for a Community Outreach Core are

- sponsoring short courses or workshops to improve the community's awareness and understanding of environmental health issues (e.g., conducting a workshop that provides information on exposure levels that may or may not pose serious health risks and why, and develop an approach for addressing the issues)
- increasing access to relevant information and serving as a resource (e.g., responding to community's questions, assisting them in accessing pertinent information or translating materials into the community's native language)
- education on health and technical issues (e.g., sponsoring a short course, or developing health effects fact sheets)
- establishing collaborative projects among communities, investigators and other colleagues to address environmental problems (e.g., partnering with tribes in determining exposure pathways specific and relevant to their traditional and cultural practices)

It is important that the Community Outreach Core define the approach it will use to identify a community/organizational unit with which it proposes to collaborate. It should develop a plan detailing the objectives and the methods (e.g., conducting small group discussion or listening sessions, producing informational materials, providing leadership mentoring, etc.) that will be used in establishing and maintaining involvement with the community. The SBRP also recognizes that any activity of this nature needs to be reviewed for lessons-learned and outcomes. Accordingly, the SBRP anticipates that each Community Outreach Core should include in its plan how it will measure milestones or outcomes.

The Community Outreach Core is limited to $100,000 direct costs in the first year, with subsequent years subject to the standard cost escalations of three percent. It is expected that the Core will complement the research strengths of the program. Support for appropriate staff positions, consultants, travel and supplies are allowed. The budget must include travel for the Core director or designate to attend the SBRP annual meeting as it is expected that the Community Outreach Core Leaders will convene during this time.

Training Core (optional component)

SBRP strongly encourages applicants to include a Training Core, which supports graduate level training in environmental health, environmental sciences, ecology, and geosciences (including hydrogeology, geologic engineering, geophysics, geochemistry, and related fields) in the setting of the research program.

The Training Core should reflect the interdisciplinary nature of the overall research effort. Of special interest is the cross training of students and post-doctoral fellows in disciplines not traditionally linked in the university structure. Students pursuing degrees in the non-biomedical areas should be encouraged to place their studies in the context of environmental health sciences and biomedical research. Likewise, students of the biomedical sciences should have cross training opportunities in the non-biomedical areas of study.

In addition to providing students with unique opportunities in interdisciplinary research, the SBRP also encourages the Training Cores to provide students with practical opportunities for communicating research outcomes to diverse audiences. For example, all researchers need to know how to explain their work in a manner easily understood by the intended audience – whether the audience be the public or professionals in other areas of science.

Another unique opportunity for students of the SBRP is the participation in the Community Outreach Core. The SBRP encourages the Training Core to formally support cross training of this nature. Opportunities such as this will provide students with valuable insights on the full cycle of the research that they conduct.

It is important to note that the training of pre- and post-doctoral students may be carried on outside the structured Training Core. In these cases, the budgets for these students should be part of the project or core budgets rather than the Training Core budget.

In keeping with the NIH efforts to train members of minority groups, and those with disabilities, applicants are encouraged to consider these candidates in their recruitment efforts.

Individuals in the training positions must be considered employees of the institution and not trainees receiving stipends as in National Research Service Award programs. Salaries and fringe benefits consistent with institutional policies may be requested. Funds may also be requested for tuition, where appropriate, and travel to one scientific meeting per year. The direct costs of the Training Core are not to exceed six percent of the direct costs for the total program budget.

See Section VIII, Other Information - Required Federal Citations, for policies related to this announcement.

Section II. Award Information

1. Mechanism(s) of Support

This funding opportunity will use the NIH P42 award mechanism.

As an applicant, you will be solely responsible for planning, directing, and executing the proposed project.

This funding opportunity uses the just-in-time budget concepts. It also uses the non-modular budget format described in the PHS 398 application instructions (see http://grants.nih.gov/grants/funding/phs398/phs398.html). A detailed categorical budget for the "Initial Budget Period" and the "Entire Proposed Period of Support" is to be submitted with the application.

2. Funds Available

- The NIEHS intends to commit approximately $8.0 million dollars in FY 2009 to fund three to four new and/or renewal SBRP multi- project grants in response to this FOA. An applicant may request a project period of up to five years.
- A new applicant may request a budget for direct costs of up to $2.1 million dollars for the first year. Applicants submitting renewal (competing continuation) applications may request a three percent increase above their last continuation project (non-competitive renewal) year's budget level. For all applicants, budgets submitted in subsequent years may not exceed an escalation of three percent on recurring direct costs.
- Facilities and Administrative (F&A) costs incurred by requesting third party consortia or subcontracts are not included in the direct cost limitation, see NOT-OD-05-004. Applications that exceed the stated allowable budget caps for the first year will be returned as non-responsive to this FOA.
- Although the financial plans of the NIEHS provide support for this program, the funds that are appropriated for the SBRP are determined each year according to the Federal budget process. Because the funding level of this Program may vary from year to year, awards pursuant to this FOA are contingent upon the availability of funds and the receipt of a sufficient number of meritorious applications. The size and duration of each award may vary based on Program balance and the availability of funds, in addition to the scientific merit considerations of the review.

Section III. Eligibility Information

1. Eligible Applicants

1.A. Eligible Institutions

You may submit (an) application(s) if your organization has any of the following characteristic:

- An accredited domestic institution of higher education.

Section 311(a)(3) of SARA limits recipients of awards to "accredited institutions of higher education," which are defined in the Higher Education Act, 20 USC (annotated) 3381. However, grantees are permitted under the law, and encouraged by NIEHS, to subcontract as appropriate with organizations, domestic or foreign, public or private (such as universities, colleges, hospitals, laboratories, faith-based organizations, units of State and local governments, and eligible agencies of the Federal government) as necessary to conduct portions of the research. Examples of other organizations may include generators of hazardous wastes; persons involved in the detection, assessment, evaluation, and treatment of hazardous substances; owners and operators of facilities at which hazardous substances are located; State and local governments and community organizations.

1.B. Eligible Individuals

Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their institution to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH support.

2. Cost Sharing or Matching

Cost sharing is not required.

The most current Grants Policy Statement can be found at:

http://grants.nih.gov/grants/policy/nihgps_2003/nihgps_Part2.htm#matching_or_cost_sharing

3. Other-Special Eligibility Criteria

Applicants must propose a multi-project, inter- and multi-disciplinary research program that addresses a central theme and that is related to the goals of the SBRP. This interdisciplinary/ multidisciplinary effort should bring together investigators from different scientific disciplines to direct discrete Research Projects, each of which is to be related to the central theme developed for the applicant's program. It is expected that the research team will include the expertise required to perform the research proposed and be comprised of scientists that represent the biomedical and non-biomedical (i.e., engineering, geology, microbiology,

ecology, etc.) fields of study.

The applicant must name a Principal Investigator as the designated leader of the SBRP multi-project grant to provide scientific and administrative leadership to the program. The Principal Investigator must commit a minimum of 1.8 person months to the administration of the program.

In order to be considered for funding each applicant must successfully meet the following minimum requirements:

- Two approved biomedical Research Projects (e.g., mechanistic-based studies, epidemiology, human risk assessment, exposure assessment, genetic susceptibility, etc.,) and,
- Two approved non-biomedical Research Projects (e.g., fate and transport, hydrogeology, engineering, remediation, ecology, etc.).
- An approved Administrative Core that oversees organizational, budgeting, and reporting functions and provides intellectual leadership to direct the scientific and programmatic activities of the program. The administrative core must include an external advisory committee which should provide oversight and advice to the Principal Investigator in accomplishing program goals.
- One approved Research Support Core. Research Support Cores are shared facilities that enhance or provide cost effectiveness for services, techniques or instrumentation and must be used by at least two of the research projects.
- An approved Research Translation Core which must include: 1) a plan for partnerships with Government agencies; 2) a plan for technology transfer; and 3) a plan for communicating to broad audiences. The intent of the Research Translation Core is to provide a dedicated mechanism for identifying and acting on opportunities for the basic research findings to be used by the Program's constituencies.

In addition to these required program components, it is important for the applicant to recognize that the SBRP is more than a basic research program and is strongly encouraged to make investments in other areas crucial to the Program. These include:

- A Community Outreach Core, which is intended to position the SBRP to support the nation's Superfund's mandate to more actively involve the community in the decision-making process by translating the scientific accomplishments into a format useful to the needs of the community. The Community Outreach Core is limited to $100,000 direct costs in the first year, with subsequent years subject to the standard three percent cost escalations allowed by NIH.
- A Training Core, which is intended to support graduate and advanced training and should reflect the interdisciplinary nature of the overall research effort proposed within the applicants program. The direct costs for the Training Core are not to exceed six

percent of the total direct costs for the total program budget.

The following size restrictions are applicable for each program:

- The total number of Research Projects and Research Support Cores cannot exceed 12. The Administrative, Research Translation, Community Outreach and Training Cores do not count towards this total.
- The number of Research Support Cores may not exceed the number of proposed Research Projects.

Applicants may submit only one application.

Section IV. Application and Submission Information

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1. Address to Request Application Information

The PHS 398 application instructions are available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. Applicants must use the currently approved version of the PHS 398. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

Telecommunications for the hearing impaired: TTY 301-451-0088.

2. Content and Form of Application Submission

Applications must be prepared using the most current PHS 398 research grant application instructions and forms. Applications must have a D&B Data Universal Numbering System (DUNS) number as the universal identifier when applying for Federal grants or cooperative agreements. The D&B number can be obtained by calling (866) 705-5711 or through the web site at http://www.dnb.com/us/. The D&B number should be entered on line 11 of the face page of the PHS 398 form.

The title and number of this funding opportunity must be typed on line 2 of the face page of the application form and the YES box must be checked.

3. Submission Dates and Times

Applications must be received on or before the receipt date described below (Section IV.3.A). Submission times N/A.

3.A. Receipt, Review and Anticipated Start Dates

Letter of Intent Receipt Date: February 15, 2008
Application Receipt Date: April 15, 2008
Peer Review Date: October 2008
Council Review Date: January 2009
Earliest Anticipated Start Date: April 1, 2009

3.A.1. Letter of Intent

Prospective applicants are asked to submit a letter of intent that includes the following information:

- Descriptive title of proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Number and title of this funding opportunity

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIEHS staff to estimate the potential review workload and plan the review.

The letter of intent is to be sent by the date listed at the beginning of this document.

The letter of intent should be sent to:

Linda Bass, Ph.D.
Scientific Review Branch
Division of Extramural Research and Training
National Institute of Environmental Health Sciences
PO Box 12233, EC-30
111 T.W. Alexander Drive
Research Triangle Park, NC 27709
Telephone: (919) 541-1307
FAX: (919) 541-2503
Email: bass@niehs.nih.gov

3.B. Sending an Application to the NIH

Applications must be prepared using the research grant applications found in the PHS 398 instructions for preparing a research grant application. Submit a signed, typewritten original of the application, including the checklist, and three signed photocopies in one package to:

Center for Scientific Review

National Institutes of Health
6701 Rockledge Drive, Room 1040, MSC 7710
Bethesda, MD 20892-7710 (U.S. Postal Service Express or regular mail)
Bethesda, MD 20817 (for express/courier service; non-USPS service)

Personal deliveries of applications are no longer permitted (see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-040.html).

At the time of submission, two additional copies of the application and five copies of collated appendix materials (Appendix material should be clearly identified and collated by project and core; do not staple or bind) must be sent to:

Linda Bass, Ph.D.
Scientific Review Branch
Division of Extramural Research and Training
National Institute of Environmental Health Sciences
PO Box 12233, EC-30
111 T.W. Alexander Drive
Research Triangle Park, NC 27709
Telephone: (919) 541-1307
FAX: (919) 541-2503
Email: bass@niehs.nih.gov

Using the RFA Label: The RFA label available in the PHS 398 application instructions must be affixed to the bottom of the face page of the application. Type the RFA number on the label. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2 of the face page of the application form and the YES box must be marked. The RFA label is also available at: http://grants.nih.gov/grants/funding/phs398/labels.pdf.

3.C. Application Processing

Applications must be **received on or before the application receipt date** described above (Section IV.3.A.). If an application is received after that date, it will not be reviewed. Upon receipt, applications will be evaluated for completeness by the CSR and responsiveness by the National Institute of Environmental Health Sciences. Incomplete and non-responsive applications will not be reviewed.

The NIH will not accept any application in response to this funding opportunity that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. However, when a previously unfunded application, originally submitted as an investigator-initiated application, is to be submitted in response to a funding opportunity, it is to be prepared as a NEW application. That is, the application for the funding opportunity must

not include an Introduction describing the changes and improvements made, and the text must not be marked to indicate the changes from the previous unfunded version of the application.

Information on the status of an application should be checked by the Principal Investigator in the eRA Commons at: https://commons.era.nih.gov/commons/.

4. Intergovernmental Review

This initiative is not subject to intergovernmental review.

5. Funding Restrictions

All NIH awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The Grants Policy Statement can be found at http://grants.nih.gov/grants/policy/policy.htm.

Pre-award costs are allowable. A grantee may, at its own risk and without NIH prior approval, incur obligations and expenditures to cover costs up to 90 days before the beginning date of the initial budget period of a new or renewal award if such costs: are necessary to conduct the project, and would be allowable under the grant, if awarded, without NIH prior approval. If specific expenditures would otherwise require prior approval, the grantee must obtain NIH approval before incurring the cost. NIH prior approval is required for any costs to be incurred more than 90 days before the beginning date of the initial budget period of a new or competing continuation award.

The incurrence of pre-award costs in anticipation of a competing or non-competing award imposes no obligation on NIH either to make the award or to increase the amount of the approved budget if an award is made for less than the amount anticipated and is inadequate to cover the pre-award costs incurred. NIH expects the grantee to be fully aware that pre-award costs result in borrowing against future support and that such borrowing must not impair the grantee's ability to accomplish the project objectives in the approved time frame or in any way adversely affect the conduct of the project. See NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part6.htm.

6. Other Submission Requirements

A. Application Guidelines. The applications submitted in response to this FOA are complex, and the scientific and programmatic information needed to adequately assess a grant proposal is not fully accommodated within the instructions accompanying the PHS 398 form. Therefore, applicants need to follow the detailed guidelines that are provided at http://www-apps.niehs.nih.gov/sbrp/rfa/ to supplement the PHS 398 instructions.

In general an SBRP grant proposal will consist of the following categories of information:

Section I. This section consolidates the budget information, the list of all professional and non-professional personnel, biosketches for all key personnel, institutional environment and resources and tables of core utilization and use of human subjects/vertebrate animals for the entire applicant's program.

Section II. This section is unique to a multi-project application. The information requested in this section, for the most part, is not covered in the PHS 398 and includes: an overall introduction and description of the program that incorporates the major theme, goals and objectives, the inter- and multi-disciplinary nature of the program and the interactions between the projects and cores; a description of the role of the Principal Investigator; a description of the organizational structure of the applicant's program including an administrative and management plan to achieve an integrated coordinated research program; and for competing renewals, a general progress report.

Section III- VIII. These sections contain the research plans for the individual research projects, research support cores, administrative, community outreach and training cores and follow the guidelines established in the PHS 398.

Section IX-XI. These sections include the Plan for Data Sharing, the Checklist and Appendix materials.

B. Quality Assurance Statement. Quality Assurance Statements will be necessary ONLY for Research Support Cores that provide analytical, quantitative services to the applicant's program.

EPA regulations as stated in 40CFR30.54 require the inclusion of a Quality Assurance Narrative Statement (QANS, OMB # 2080-0033, approved 8/14/97) for any project application involving data collection or processing, environmental measurements, and/or modeling. The QANS provides information on how quality processes or products will be assured. NIEHS cannot consider applications incomplete without this statement, however, it requests that the QANS be included with all applications that contain analytical and quantitative cores. For awards that involve environmentally related measurements or data generation, a quality system that complies with the requirements of ANSI/ASQC E4, "Specifications and Guidelines for Quality Systems for Environmental Data Collection and Environmental Technology Programs," must be in place. The Quality Assurance Statement should not exceed two pages. This Statement should, for each item listed below, present the required information, reference the specific page and paragraph number of the project description containing the information, or provide a justification as to why the item does not apply to the proposed research.

1. Discuss the activities to be performed or hypothesis to be tested and criteria for determining acceptable data quality. (Note: Such criteria may be expressed in terms of precision, accuracy, representativeness, completeness, and comparability or in terms of data quality objectives or

acceptance criteria. Furthermore, these criteria must also be applied to determine the acceptability of existing or secondary data to be used in the project. In this context secondary data may be defined as data collected for other purposes or from other sources, including the literature, compilations from computerized data bases, or results from mathematical models of environmental processes and conditions.)

2. Describe the study design, including sample type and location requirements, all statistical analyses that were or will be used to estimate the types and numbers of samples required for physical samples, or equivalent information for studies using survey and interview techniques.

3. Describe the procedures for the handling and custody of samples, including sample collection, identification, preservation, transportation, and storage.

4. Describe the procedures that will be used in the calibration and performance evaluation of all analytical instrumentation and all methods of analysis to be used during the project. Explain how the effectiveness of any new technology will be measured and how it will be benchmarked to improve an existing process, such as those used by industry.

5. Discuss the procedures for data reduction and reporting, including a description of all statistical methods with reference to any statistical software to be used to make inferences and conclusions; discuss any computer models to be designed or utilized with associated verification and validation techniques.

6. Describe the quantitative and/or qualitative procedures that will be used to evaluate the success of the project, including any plans for peer or other reviews of the study design or analytical methods prior to data collection.

ANSI/ASQC E4, "Specifications and Guidelines for Quality Systems for Environmental Data Collection and Environmental Technology Programs," is available for purchase from the American Society for Quality, phone 1-800-248-1946, item T55. Only in exceptional circumstances should it be necessary to consult this document.

C. Annual Meetings. It is the intent of the NIEHS to hold annual grantee meetings. Funds for travel by appropriate staff (i.e., Principal Investigator, Business Manager, and three students) to attend a three-day meeting should be included in the Administrative Core's budget for each year. It is also anticipated that the Outreach Core and Research Translation Core Leaders will convene at the annual meeting, and expenses for this travel should be included in their individual budgets. The location of the meeting site will rotate among the different grantees.

Plan for Sharing Research Data

The precise content of the data-sharing plan will vary, depending on the data being collected

and how the investigator is planning to share the data. Applicants who are planning to share data may wish to describe briefly the expected schedule for data sharing, the format of the final dataset, the documentation to be provided, whether or not any analytic tools also will be provided, whether or not a data-sharing agreement will be required and, if so, a brief description of such an agreement (including the criteria for deciding who can receive the data and whether or not any conditions will be placed on their use), and the mode of data sharing (e.g., under their own auspices by mailing a disk or posting data on their institutional or personal website, through a data archive or enclave). Investigators choosing to share under their own auspices may wish to enter into a data-sharing agreement. References to data sharing may also be appropriate in other sections of the application.

All applicants must include a plan for sharing research data in their application. The data sharing policy is available at http://grants.nih.gov/grants/policy/data_sharing. All investigators responding to this funding opportunity should include a description of how final research data will be shared, or explain why data sharing is not possible.

The reasonableness of the data sharing plan or the rationale for not sharing research data will be assessed by the reviewers. However, reviewers will not factor the proposed data sharing plan into the determination of scientific merit or the priority score.

Sharing Research Resources

NIH policy expects that grant recipients make unique research resources readily available for research purposes to qualified individuals within the scientific community after publication (NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps_2003/index.htm and http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part7.htm#_Toc54600131). Investigators responding to this funding opportunity should include a plan for sharing research resources addressing how unique research resources will be shared or explain why sharing is not possible.

The adequacy of the resources sharing plan and any related data sharing plans will be considered by Program staff of the funding organization when making recommendations about funding applications. The effectiveness of the resource sharing will be evaluated as part of the administrative review of each non-competing Grant Progress Report (PHS 2590, http://grants.nih.gov/grants/funding/2590/2590.htm). See Section VI.3. Reporting.

Section V. Application Review Information

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1. Criteria

Only the review criteria described below will be considered in the review process.

The following will be considered in making funding decisions:

- Scientific merit of the proposed project as determined by peer review
- Availability of funds
- Relevance of program priorities

2. Review and Selection Process

Applications that are complete and responsive to the FOA will be evaluated for scientific and technical merit by an appropriate peer review group convened by the National Institute of Environmental Health Sciences in accordance with the review criteria stated below.

As part of the initial merit review, all applications will:

- Undergo a selection process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed and assigned a priority score.
- Receive a written critique.
- Receive a second level of review by the National Advisory Environmental Health Council.

The goals of NIH supported research are to advance our understanding of biological systems, to improve the control of disease, and to enhance health. Within this context, the goal of the SBRP is to improve public health by supporting integrative research that is multi- and interdisciplinary in nature and includes the ability to identify, assess, and evaluate the potential health effects of exposure to hazardous substances and to develop innovative chemical, physical and biological technologies for reducing potential exposure to hazardous substances.

In their written critiques, reviewers will be asked to comment on each of the following criteria in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. Each of these criteria will be addressed and considered in assigning the overall score, weighting them as appropriate for each application. Note that an application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. For example, an investigator may propose to carry out important work that by its nature is not innovative but is essential to move a field forward.

The initial review for scientific and technical merit will emphasize two major aspects: (1) the multi-project grant as an integrated research effort of projects and support cores focused on a central theme; and (2) the review of each research project, research support core and other core components independently.

Review Criteria for the Overall SBRP Application

The scientific review panel will evaluate the scientific merit of the program as a whole as well as the inter-relationship and contributions of the research projects and cores to an overall conceptual theme.

The overall multi-project grant application will be based on the following criteria:

Significance: Does the overall program address an important problem?

- If the program is successful, would it lead to incremental advance, or would it provide a substantial step forward that would likely not be achieved through mechanisms other than this multi-project program? If successful, will the program result in knowledge or resources that could be utilized to improve human health, risk assessment, or improve the quality of the environment?
- Is the importance of the proposed research program sufficient to further the knowledge of environmental health sciences to understand the physical, chemical and biological properties of hazardous substances in the environment?

Approach: Are the research projects and cores well integrated, well reasoned, and appropriate to the overall theme and goals of the proposed program? Is there strong synergy among the combined efforts of the various investigators within the overall program?

Innovation: Is the overall program original and innovative? For example: Does the program challenge existing paradigms; address an innovative hypothesis or critical barrier to progress in the field? Does the program develop or employ novel concepts, approaches, methodologies, tools, or technologies for this area?

Investigators: Are the investigators appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the Principal Investigator and other researchers? Does the investigative team bring complementary and integrated expertise to the overall program?

Environment: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the scientific environment, or subject populations, or employ useful collaborative arrangements? Is there evidence of institutional support?

In addition to the five criteria used to judge the scientific merit of the program as a whole, the following criteria should be considered in reviewing the integration of the overall program.

Multidisciplinary and Interdisciplinary Nature of the Program

- Interdisciplinary nature of the proposed research activities. Is there integration of the

projects around a central theme? Are there plans to effectively pursue interdisciplinary research objectives? Does the program propose a plan for the development of interdisciplinary collaboration between all components of the program?

- Coordination and Cohesiveness. Is there evidence of the integration of the Administrative, Research Translation, Community Outreach and Training Cores with the Research Projects and Research Support Cores? Is there evidence for the translation and delivery of the research findings to appropriate audiences?
- Synergy of the program. Is there evidence of meaningful interdisciplinary/ multidisciplinary collaboration and synergistic potential between the research projects and cores? Is the whole greater than the sum of the parts? Is the size of the program sufficient to afford effective interaction focused on a specific central theme, but diverse in scientific disciplines in order to achieve meaningful contributions to protecting human health and the environment?
- Is there evidence of integration and interaction of the non-health related research with the health-based research as it contributes to the central theme of the program?
- For competing renewals, is there evidence that there was integration and synergy among the projects and cores within the program?

Principal Investigator

- The experience and scientific leadership of the Principal Investigator to effectively direct a large complex multidisciplinary program. Does the Principal Investigator demonstrate the appropriate ability and experience to coordinate the interactions of the Research Projects with effective utilization of cores to achieve programmatic goals?
- Is the level of commitment and ability to develop a well-defined central research focus adequate?

Review Criteria for Renewal Applications

In addition, for competing renewal applications the following will be considered:

- Is there evidence of progress and achievements specific to this program since the previous competitive review? Is there documentation through publications, conferences, etc. that demonstrates that collaboration between or among projects has occurred?
- Is there evidence that the cores have met their objectives and been well utilized by the individual research projects?
- Is there adequate justification for adding new projects or cores or for deleting components previously supported?
- Is there evidence that the aims of the Research Translation Core for developing approaches for transferring research findings to appropriate audiences such as EPA, EPA Regions, ATSDR, State and local professionals or other professionals working in the field of hazardous waste management been met? Is there evidence that the transfer

of research findings to these audiences has occurred?

Review Criteria for the Research Projects

The review of the individual Research Projects is similar to the review of investigator-initiated individual project grant applications (R01). Accordingly, these projects must have substantial scientific merit. Reviewers will evaluate the individual projects against five review criteria. The four technical review criteria (Significance, Approach, Innovation and Environment) are intended to encourage reviewers to focus on the global impacts of each project, rather than concentrating on the experimental details and their critiques. The review criteria are as follows:

Significance: Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced? What will be the effect of these studies on the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field? If the study is successful, would it lead to incremental advance, or would it provide a substantial step forward that would likely not be achieved through mechanisms other than this multi-project program? If successful, will the project result in knowledge or resources that could be utilized to improve human health, risk assessment, or improve the quality of the environment?

Approach: Are the conceptual or clinical framework, design, methods, and analyses adequately developed, well integrated, well reasoned, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics? Is there strong synergy among the combined efforts of the various investigators within the program?

Innovation: Is the project original and innovative? For example: Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools, or technologies for this area?

Investigators: Are the investigators appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the Principal Investigator and other researchers? Does the investigative team bring complementary and integrated expertise to the project (if applicable)?

Environment: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the scientific environment, or subject populations, or employ useful collaborative arrangements? Is there evidence of institutional support?

In addition to the standard criteria listed above, reviewers will evaluate each project for its contribution to the overall goals of the SBRP application:

- Does the project contribute scientifically to the overall proposed programmatic theme (i. e., the importance of the ideas or aims, the rationale and originality of the approach, the feasibility of the methods and the value of the result)?
- Will the specific scientific objectives of each project benefit significantly from, or depend upon, collaborative interactions with other projects in the program (i.e., objectives that can be uniquely accomplished, specific contributions to the accomplishments of objectives in other projects, objectives that can be accomplished with greater effectiveness and/or economy of effort, etc.).
- For competing renewals, reviewers will evaluate whether previous specific aims, as funded, have been accomplished and that the new research goals are logical extensions of ongoing work.

In addition to the review criteria described above for research projects, the following will be considered by the review panel in evaluating the cores, the multidisciplinary and interdisciplinary nature of the program and the principal investigator.

Review Criteria for the Research Support Cores

The Research Support Cores will be assessed based on the following criteria:

- The Core's utility to the Program. Does each Research Support Core provide essential facilities or service for two or more of the Research Projects judged to have substantial scientific merit? Is the projected use sufficient to warrant establishment of the core? Are the core facilities contributing to the overall research activities of the program?
- The quality of the facility or service provided. Is the Quality Control and Quality Assurance plan for cores providing quantitative analyses adequate?
- Is there a prioritization plan for core usage?
- The cost effectiveness/enhanced efficiencies afforded by the Core. Are the requests for equipment, supplies and other items to support the activity of the core appropriate and justified?
- The qualification of the personnel involved. Does the staff have the appropriate experience and level of commitment?
- For competing renewals, is there evidence that the previous aims, as funded, were accomplished?

Review Criteria for the Administrative Core

The Administrative Core will be assessed based on the following criteria:

- Evidence that the lines of authority and the administrative structure are designed for effective management of the program. Is there a decision-making process for the management of funds and resources? Is there an ability to provide administrative

support to the project and core leaders?
- Evidence of an internal plan to promote integration and coordination. Does the program's internal plan promote coordination of interdisciplinary research, stimulate collaborations among constituent Research Projects and Cores, and evaluate research productivity?
- External advisory committee. Is there an appropriate plan to establish and use an external advisory committee? Do the members of the committee have the expertise required to evaluate all projects and cores and appropriately represent the applicant's stakeholders?
- Qualifications of the senior leaders of the administrative core. Does the senior leadership have appropriate experience and have they demonstrated effective and responsible leadership in the past? Is the percent effort requested adequate?
- Qualifications of the administrative staff. Are the qualifications, duties and time commitments of administrative staff appropriate to contribute to the needs and conduct of the program's research activities?
- Adequacy of program resources. Are the resources committed to the Administrative Core adequate?

Review Criteria for the Research Translation Core

The Research Translation Core will be assessed based on the following criteria:

- Are the qualifications of proposed personnel to conduct the activities described for the Core?
- Is the proposed plan to partner with governmental agencies adequate?
- Is the proposed plan to identify technology transfer opportunities and to assist in the advancement of technologies into application appropriate?
- The adequacy of the proposed plan to communicate to broad audiences. Is there a plan for identifying and engaging target audiences? Is there adequate commitment and support for the approach being developed? Are the communication tools selected appropriate for the intended audience?
- Are milestones delineated, realistic and appropriate?
- Adequacy of the program's coordination with NIEHS. Is there a plan to coordinate and exchange information with SBRP staff?
- Adequacy of program resources. Are the resources committed to the Research Translation Core appropriate for the proposed activities?
- For competing renewals, is there evidence that the previous aims, as funded, were accomplished?

Review Criteria for the Community Outreach Core

The Community Outreach Core will be assessed based on the following criteria:

- The adequacy of the approach. Is the proposed approach appropriate, adequate and feasible? Is there evidence of community involvement in the development of the core's goals?
- Is there evidence that sensitivity to socioeconomic and cultural factors have been adequately addressed?
- Is there evidence that the coordination and collaboration with appropriate community groups, and state, local and federal agencies is adequate?
- Are milestones delineated, realistic and appropriate?
- Are the qualifications of proposed personnel to conduct the activities described appropriate?
- For competing renewals, is there evidence that the previous aims, as funded, were accomplished?

Review Criteria for the Training Core

The Training Core will be assessed based in the following criteria:

- The appropriateness of the objectives, design, and direction for the research-training program. Are the approaches and methods proposed adequate to develop training curriculum and courses that provide opportunities to interface with different scientific disciplines? Does the training program reflect the interdisciplinary nature of the program?
- Is there evidence for, and the appropriateness of, plans for the recruitment and selection of individuals participating in the Training Core?
- Adequacy of the training environment. Is there institutional commitment? Is the quality of the facilities and the availability of courses appropriate to the SBRP? Is there an availability of research support for post-doctoral training?
- For competing renewals, is there evidence that the previous aims, as funded, were accomplished?

2.A. Additional Review Criteria:

In addition to the above criteria, the following items will continue to be considered in the determination of scientific merit and the priority score:

Resubmission Applications (formerly "revised/amended" applications): Are the responses to comments from the previous scientific review group adequate? Are the improvements in the resubmission application appropriate?

Protection of Human Subjects from Research Risk: The involvement of human subjects and protections from research risk relating to their participation in the proposed research will be assessed (see the Research Plan, Section E on Human Subjects in the PHS Form 398).

Inclusion of Women, Minorities and Children in Research: The adequacy of plans to include subjects from both genders, all racial and ethnic groups (and subgroups), and children as appropriate for the scientific goals of the research will be assessed. Plans for the recruitment and retention of subjects will also be evaluated (see the Research Plan, Section E on Human Subjects in the PHS Form 398).

Care and Use of Vertebrate Animals in Research: If vertebrate animals are to be used in the project, the five items described under Section F of the PHS Form 398 research grant application instructions will be assessed.

Biohazards: If materials or procedures are proposed that are potentially hazardous to research personnel and/or the environment, determine if the proposed protection is adequate.

2.B. Additional Review Considerations

Budget: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research. The priority score should not be affected by the evaluation of the budget.

2.C. Sharing Research Data

Data Sharing Plan: The reasonableness of the data sharing plan or the rationale for not sharing research data will be assessed by the reviewers. However, reviewers will not factor the proposed data sharing plan into the determination of scientific merit or the priority score. The presence of a data sharing plan will be part of the terms and conditions of the award. The funding organization will be responsible for monitoring the data sharing policy.

2.D. Sharing Research Resources

NIH policy expects that grant recipients make unique research resources readily available for research purposes to qualified individuals within the scientific community after publication (See the NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps/part_ii_5.htm#availofrr and http://www.ott.nih.gov/policy/rt_guide_final.html). Investigators responding to this funding opportunity should include a sharing research resources plan addressing how unique research resources will be shared or explain why sharing is not possible.

Program staff will be responsible for the administrative review of the plan for sharing research resources.

The adequacy of the resources sharing plan will be considered by Program staff of the funding organization when making recommendations about funding applications. Program staff may negotiate modifications of the data and resource sharing plans with the awardee before recommending funding of an application. The final version of the data and resource sharing plans negotiated by both will become a condition of the award of the grant. The effectiveness

of the resource sharing will be evaluated as part of the administrative review of each non-competing Grant Progress Report (PHS 2590). See Section VI.3. Reporting.

3. Anticipated Announcement and Award Dates

Not applicable

Section VI. Award Administration Information

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1. Award Notices

After the peer review of the application is completed, the PD/PI will be able to access his or her Summary Statement (written critique) via the eRA Commons.

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant. For details, applicants may refer to the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General (http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_part4.htm).

A formal notification in the form of a Notice of Award (NoA) will be provided to the applicant organization. The NoA signed by the grants management officer is the authorizing document. Once all administrative and programmatic issues have been resolved, the NoA will be generated via email notification from the awarding component to the grantee business official (designated in item 12 on the Application Face Page). If a grantee is not email enabled, a hard copy of the NoA will be mailed to the business official.

Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NoA are at the recipient's risk. These costs may be reimbursed only to the extent considered allowable pre-award costs. See Also Section IV.5. Funding Restrictions.

2. Administrative and National Policy Requirements

All NIH grant and cooperative agreement awards include the NIH Grants Policy Statement as part of the NoA. For these terms of award, see the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General (http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part4.htm) and Part II Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities (http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_part9.htm).

The following Terms and Conditions will be incorporated into the award statement and will be

provided to the Principal Investigator as well as to the appropriate institutional official, at the time of award.

- An annual grantee meeting, to be held at one of the grantees sites or in Research Triangle Park, NC is planned for the exchange of information among investigators. Applicants must budget travel costs associated with this meeting for the Principal Investigator, Business Manger, at least four students (minimum of $4000 for student travel), the Research Translation and Community Outreach Core Leaders for each year. These funds are restricted and may not be used for any other purpose without written prior approval from NIEHS.
- The multi-project P42 grant mechanism is under expanded authorities. However, carry-over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

3. Reporting

Awardees will be required to submit the PHS Non-Competing Grant Progress Report, Form 2590 annually (http://grants.nih.gov/grants/funding/2590/2590.htm) and financial statements as required in the NIH Grants Policy Statement.

Section VII. Agency Contacts

We encourage your inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants. Because of the complexity of the SBRP, applicants are strongly encouraged to contact NIEHS staff early in the grant preparation process. Inquiries may fall into three areas: scientific/research, peer review, and financial or grants management issues:

1. Scientific/Research Contacts:

Claudia Thompson, Ph.D.
Center for Risk and Integrated Sciences
Division of Extramural Research and Training
National Institute of Environmental Health Sciences
P.O. Box 12233 MD EC-27
Research Triangle Park, NC 27709
Telephone: 919-541-4638
FAX: 919-541-4937
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FAX: 919-541-4937
Email: tainer@niehs.nih.gov

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P.O. Box 12233 MD EC-27
Research Triangle Park, NC 27709
Telephone: 919-541-5330
FAX: 919-541-4937
Email: henryh@niehs.nih.gov

2. Peer Review Contacts:

Linda Bass, Ph.D.
Scientific Review Branch
Division of Extramural Research and Training
National Institute of Environmental Health Sciences
PO Box 12233, EC-30
111 T.W. Alexander Drive
Research Triangle Park, NC 27709
Telephone: (919) 541-1307
FAX: (919) 541-2503
Email: bass@niehs.nih.gov

Leroy Worth, Ph.D.
Scientific Review Branch
Division of Extramural Research and Training
National Institute of Environmental Health Sciences
PO Box 12233, EC-30
111 T.W. Alexander Drive
Research Triangle Park, NC 27709
Telephone: (919) 541-0670
FAX: (919) 541-2503

Email: worth@niehs.nih.gov

3. Financial or Grants Management Contacts:

Susan Ricci
Grants Management Branch
Division of Extramural Research and Training
National Institute of Environmental Health Sciences
P.O. Box 12233, EC-30
Research Triangle Park, North Carolina 27709
Telephone: 919-316-4666
Fax: 919-541-2860
E-mail: ricci@niehs.nih.gov

Lisa Archer
Grants Management Branch
Division of Extramural Research and Training
National Institute of Environmental Health Sciences
P.O. Box 12233, EC-30
Research Triangle Park, North Carolina 27709
Telephone: 919-541-0751
Fax: 919-541-2860
E-mail: archer@niehs.nih.gov

Section VIII. Other Information

Required Federal Citations

Use of Animals in Research:
Recipients of PHS support for activities involving live, vertebrate animals must comply with PHS Policy on Humane Care and Use of Laboratory Animals (http://grants.nih.gov/grants/olaw/references/PHSPolicyLabAnimals.pdf) as mandated by the Health Research Extension Act of 1985 (http://grants.nih.gov/grants/olaw/references/hrea1985.htm), and the USDA Animal Welfare Regulations (http://www.nal.usda.gov/awic/legislat/usdaleg1.htm) as applicable.

Human Subjects Protection:
Federal regulations (45CFR46) require that applications and proposals involving human subjects must be evaluated with reference to the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained (http://www.hhs.gov/ohrp/

humansubjects/guidance/45cfr46.htm).

Data and Safety Monitoring Plan:
Data and safety monitoring is required for all types of clinical trials, including physiologic toxicity and dose-finding studies (phase I); efficacy studies (Phase II); efficacy, effectiveness and comparative trials (Phase III). Monitoring should be commensurate with risk. The establishment of data and safety monitoring boards (DSMBs) is required for multi-site clinical trials involving interventions that entail potential risks to the participants (NIH Policy for Data and Safety Monitoring, NIH Guide for Grants and Contracts, http://grants.nih.gov/grants/guide/notice-files/not98-084.html).

Sharing Research Data:
Investigators submitting an NIH application seeking $500,000 or more in direct costs in any single year are expected to include a plan for data sharing or state why this is not possible (http://grants.nih.gov/grants/policy/data_sharing).

Investigators should seek guidance from their institutions, on issues related to institutional policies and local IRB rules, as well as local, State and Federal laws and regulations, including the Privacy Rule. Reviewers will consider the data sharing plan but will not factor the plan into the determination of the scientific merit or the priority score.

Access to Research Data through the Freedom of Information Act:
The Office of Management and Budget (OMB) Circular A-110 has been revised to provide access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are (1) first produced in a project that is supported in whole or in part with Federal funds and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm. Applicants may wish to place data collected under this funding opportunity in a public archive, which can provide protections for the data and manage the distribution for an indefinite period of time. If so, the application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

Sharing of Model Organisms:
NIH is committed to support efforts that encourage sharing of important research resources including the sharing of model organisms for biomedical research (see http://grants.nih.gov/grants/policy/model_organism/index.htm). At the same time the NIH recognizes the rights of grantees and contractors to elect and retain title to subject inventions developed with Federal funding pursuant to the Bayh Dole Act (see the NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps_2003/index.htm). All investigators submitting an NIH application or

contract proposal, beginning with the October 1, 2004 receipt date, are expected to include in the application/proposal a description of a specific plan for sharing and distributing unique model organism research resources generated using NIH funding or state why such sharing is restricted or not possible. This will permit other researchers to benefit from the resources developed with public funding. The inclusion of a model organism sharing plan is not subject to a cost threshold in any year and is expected to be included in all applications where the development of model organisms is anticipated.

Inclusion of Women And Minorities in Clinical Research:
It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects unless a clear and compelling justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43). All investigators proposing clinical research should read the "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html); a complete copy of the updated Guidelines is available at http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm. The amended policy incorporates: the use of an NIH definition of clinical research; updated racial and ethnic categories in compliance with the new OMB standards; clarification of language governing NIH-defined Phase III clinical trials consistent with the new PHS Form 398; and updated roles and responsibilities of NIH staff and the extramural community. The policy continues to require for all NIH-defined Phase III clinical trials that: a) all applications or proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable; and b) investigators must report annual accrual and progress in conducting analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

Inclusion of Children as Participants in Clinical Research:
The NIH maintains a policy that children (i.e., individuals under the age of 21) must be included in all clinical research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines" on the inclusion of children as participants in research involving human subjects (http://grants.nih.gov/grants/funding/children/children.htm).

Required Education on the Protection of Human Subject Participants:
NIH policy requires education on the protection of human subject participants for all investigators submitting NIH applications for research involving human subjects and individuals designated as key personnel. The policy is available at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html.

Human Embryonic Stem Cells (hESC):
Criteria for federal funding of research on hESCs can be found at http://stemcells.nih.gov/index.asp and at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html. Only research using hESC lines that are registered in the NIH Human Embryonic Stem Cell Registry will be eligible for Federal funding (http://escr.nih.gov). It is the responsibility of the applicant to provide in the project description and elsewhere in the application as appropriate, the official NIH identifier(s) for the hESC line(s)to be used in the proposed research. Applications that do not provide this information will be returned without review.

NIH Public Access Policy:
NIH-funded investigators are requested to submit to the NIH manuscript submission (NIHMS) system (http://www.nihms.nih.gov) at PubMed Central (PMC) an electronic version of the author's final manuscript upon acceptance for publication, resulting from research supported in whole or in part with direct costs from NIH. The author's final manuscript is defined as the final version accepted for journal publication, and includes all modifications from the publishing peer review process.

NIH is requesting that authors submit manuscripts resulting from 1) currently funded NIH research projects or 2) previously supported NIH research projects if they are accepted for publication on or after May 2, 2005. The NIH Public Access Policy applies to all research grant and career development award mechanisms, cooperative agreements, contracts, Institutional and Individual Ruth L. Kirschstein National Research Service Awards, as well as NIH intramural research studies. The Policy applies to peer-reviewed, original research publications that have been supported in whole or in part with direct costs from NIH, but it does not apply to book chapters, editorials, reviews, or conference proceedings. Publications resulting from non-NIH-supported research projects should not be submitted.

For more information about the Policy or the submission process please visit the NIH Public Access Policy Web site at http://publicaccess.nih.gov/ and view the Policy or other Resources and Tools including the Authors' Manual (http://publicaccess.nih.gov/publicaccess_Manual.htm).

Standards for Privacy of Individually Identifiable Health Information:
The Department of Health and Human Services (DHHS) issued final modification to the "Standards for Privacy of Individually Identifiable Health Information", the "Privacy Rule", on August 14, 2002 . The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information, and is administered and enforced by the DHHS Office for Civil Rights (OCR).

Decisions about applicability and implementation of the Privacy Rule reside with the researcher and his/her institution. The OCR website (http://www.hhs.gov/ocr/) provides information on the Privacy Rule, including a complete Regulation Text and a set of decision

tools on "Am I a covered entity?" Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, funding, and progress monitoring of grants, cooperative agreements, and research contracts can be found at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html.

URLs in NIH Grant Applications or Appendices:
All applications and proposals for NIH funding must be self-contained within specified page limitations. For publications listed in the appendix and/or Progress report, internet addresses (URLs) **must** be used for **publicly** accessible on-line journal articles. Unless otherwise specified in **this** solicitation, Internet addresses (URLs) should **not** be used to provide any **other** information necessary for the review because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.

Healthy People 2010:
The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This FOA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at http://www.health.gov/healthypeople.

Authority and Regulations:
This program is described in the Catalog of Federal Domestic Assistance at http://www.cfda.gov/ and is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review. Awards are made under authority of the Superfund Amendments and Reauthorization Act of 1986, Title 1, Section III, and Title II, Section 209 (Public Law 99-499); and are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92. All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The NIH Grants Policy Statement can be found at http://grants.nih.gov/grants/policy/policy.htm.

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

Loan Repayment Programs:
NIH encourages applications for educational loan repayment from qualified health professionals who have made a commitment to pursue a research career involving clinical, pediatric, contraception, infertility, and health disparities related areas. The LRP is an important component of NIH's efforts to recruit and retain the next generation of researchers by

providing the means for developing a research career unfettered by the burden of student loan debt. Note that an NIH grant is not required for eligibility and concurrent career award and LRP applications are encouraged. The periods of career award and LRP award may overlap providing the LRP recipient with the required commitment of time and effort, as LRP awardees must commit at least 50% of their time (at least 20 hours per week based on a 40 hour week) for two years to the research. For further information, please see: http://www.lrp.nih.gov.

Weekly TOC for this Announcement
NIH Funding Opportunities and Notices

Department of Health and Human Services

National Institutes of Health (NIH)
9000 Rockville Pike
Bethesda, Maryland 20892