

Suggested Research Topics Superfund Hazardous Substance Research and Training Program (P42)

This document contains suggested research topics for the NIEHS Superfund Hazardous Substance Research and Training Program (P42) RFA-ES-10-010 (<http://grants.nih.gov/grants/guide/rfa-files/RFA-ES-10-010.html>) referred to as the Superfund Research Program (SRP) Center grant. The P42 supports coordinated, multi-project, interdisciplinary research Centers to address the mandates legislated under the Superfund Amendments and Reauthorization Act of 1986. Hence, research and supporting activities from each Center should address at least one or more of these mandates:

- 1) Advanced techniques for the detection, assessment, and evaluation of the effect of hazardous substances on human health.**
- 2) Methods to assess the risks to human health presented by hazardous substances.**
- 3) Methods and technologies to detect hazardous substances in the environment.**
- 4) Basic biological, chemical, and physical methods to reduce the amount and toxicity of hazardous substances.**

The following research topics represent themes that are responsive to Program mandates and illustrate interdisciplinary linkages between scientific areas. These examples are not intended to be exhaustive, and investigators may utilize these and many other topics for the minimum two biomedical and two non-biomedical research projects in order to meet the objectives of RFA ES-10-010.

Stakeholder Research Needs / Interests

The SRP Strategic Plan encourages stakeholder involvement in the development of research proposals as a means to increase Program relevancy. SRP's key stakeholders are the sister Superfund programs at the U.S. Environmental Protection Agency and the Agency for Toxic Substances and Disease Registry as well as other Federal agencies, State, local, and Tribal entities responsible for sites impacted by hazardous substances. In addition, SRP considers the individuals and communities living near these sites as key stakeholders.

As a part of the development of an SRP Center's problem-based, solution-oriented research, the Center may wish to consider the following issues which have been identified by colleagues at EPA and ATSDR. Although not an exhaustive list, these include:

- **Asbestos:** the study of asbestos (and related mineral fibers or elongated mineral particles) including: fiber size distribution and mineralogy and their relation to adverse health effects; determinants of fiber toxicity and mechanisms leading to disease; dosimetry in animal and epidemiological studies; studies on cancer and non-cancer effects (especially pleural changes); immunotoxicity; mutagenicity; effects of variable levels of exposure (shorter term and/or lower levels); risk factors including early life exposures, smoking, lung diseases, and medical intervention; and biomarkers of exposure and disease.
- **Contaminated Sediments:** the study of contaminated sediments including the development, demonstration, and validation of technologies or methods to remediate and/or monitor contaminated sediment exposures and adverse biologic effects, and to assess the effectiveness of contaminated sediment remediation in reducing the exposure risk to humans. Also needed are new sediment amendments and reactive caps to reduce the toxicity and bioavailability of contaminated sediments.

- **Trichloroethylene:** the study of the mechanisms and health consequences of chronic, low level (sub-Maximum Contaminant Level)exposure to trichloroethylene, and the development of remediation strategies to mitigate exposure.
- **Vapor Intrusion:** the development and application of methods to assess processes leading to vapor intrusion and resultant potential health effects; development of cost-effective methods to detect vapor intrusion and/or assess cumulative human exposures; development of rapid, cost-effective source treatment of vapor intrusion in groundwater.
- **Green and Sustainable Remediation:** 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
- **Combined Remedies:** the optimization of sequential, compatible remediation strategies for different phases of a clean-up process, also known as “combined remedies” or “treatment train,” to maximize the degradation/removal of hazardous substances at complex sites.
- **Mixtures:** the investigation of effects of complex mixtures including chemical, mineral, or radionuclide contaminants on humans or biota in order to identify patterns of synergism, antagonism, or cumulative effects involved in a toxic response; development of computational toxicology approaches to understand dose/effect relationship in the context of chemical interactions.
- **Biomarkers of Response:** the incorporation of high throughput screening methods to develop detailed dose-response studies leading to identification and validation of sensitive biomarkers of biological response anchored to a phenotypic characteristic.
- **Cumulative Risk:** methods to integrate risks of all chemical stressors (in addition to stressors related to nearby hazardous waste sites) in communities exposed to contaminants. This type of research is particularly needed for tribal and environmental justice communities.
- **Susceptibility and Predisposition:** the performance of research on susceptible populations (children, elderly, minority) in order to develop strategies to reduce their burden of environmentally-influenced diseases.

Investigators are also encouraged to refer to the following resources for more information about stakeholder needs:

- EPA Office of Research and Development (ORD) Multi-Year Plans:
 - Human Health: <http://www.epa.gov/hhrp/hhmyr.html>
 - Human Health Risk Assessment: <http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=161757>
 - Land: <http://www.epa.gov/ord/npd/pdfs/Land-MYP-Final-07-19F.pdf>
 - Other Plans: <http://www.epa.gov/OSP/myr.htm>
- ATSDR’s Congressionally mandated Substance-Specific Applied Research Program (SSARP): <http://www.atsdr.cdc.gov/pdns/unfilled.html>

SRP also encourages applicants to involve community stakeholders as a means to identify and address science-based questions relevant to the SRP’s mandates. The research themes identified within this document may be a useful reference for researchers and their community partners to understand the scope of the Program; however, applicants should utilize community-based participatory processes to identify community engagement research projects. Applicants should refer to RFA ES-10-010 for a description of community based participatory processes. In addition, the following website provides links to additional resources that may be useful in establishing community engagement projects: http://www.niehs.nih.gov/research/supported/srp/funding/rfa_community_involvement.cfm.

Broad Research Themes

In addition to the specific needs and interests listed above, the following Broad Research Themes may be useful for applicants developing Center proposals. The following list consists of examples of research themes organized by the four SRP mandate areas. These examples are not intended to be exhaustive.

1) Health Effects Research. Advanced techniques for the detection, assessment, and evaluation of the effect of hazardous substances on human health.

- dissect 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
- use and interpret high throughput cell-based assays (e.g., “omics techniques”) to create mechanistically based toxicity profiles for hazardous substances
- employ 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
- incorporate bioengineering and synthetic biology to study the regulation, control, and modulation of biological processes by small molecules and environmental chemicals (e.g., toxicity sensors that rapidly detect and quantify low concentrations of chemicals in cells or tissues)
- develop, validate, and interpret mathematical and computational approaches for physiologically-based mechanistic models for predictive toxicology that incorporate high data content information (e.g., the virtual cell or organ)
- identify, develop, and validate novel diagnostic or prognostic biomarkers of exposure, biological response, disease, and therapeutic efficacy (human or animal studies)
- clarify the contribution of genetic and environmental variables in the development of disease (e.g., genetic polymorphisms, somatic mutations, haplotypes, epigenetic factors, gender and age) and host factors (e.g., susceptibility, nutrition, co-morbid disease/conditions, lifestyle habits; and timing of exposure)
- characterize altered cellular functions (e.g., metabolic capacity, repair of DNA damage, cell proliferation and apoptosis) critical to modifying susceptibility and predisposition to disease
- develop new biostatistical approaches and mathematical algorithms to understand gene-environment, gene-gene, or multi-gene-environment interactions using of comparative genomics and toxicokinetic approaches to study functional consequences of genetic polymorphisms
- explore the role of non-chemical stressors (e.g., psychological) as a factor in susceptibility to environmental insult

2) Risk Assessment Research: Methods to assess the risks to human health presented by hazardous substances.

- interpret robust human and/or ecologically-based genomic, proteomic, metabolomic, and functional datasets in risk assessment (i.e., model development and validation)
- develop multi-dimensional risk models that incorporate exposure data, movement of contaminants within environmental media, bioavailability, uptake by biological receptors, and biological responses (e.g., molecular, genetic and/or phenotypic alterations, changes in signaling molecules, metabolic profiles, etc) to determine cause and effect relationships
- interpret virtual tissues and systems biology data and determine of how this data should be used in risk assessment

- developed 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
- assess the uncertainty in risk assessment associated with differences in species, gender, extrapolation of high to low dose, acute to chronic exposure, in vitro to in vivo data
- evaluate the interface of pharmacokinetic studies with pharmacodynamic models to describe key physiological and biological processes leading to adverse health outcomes
- conduct studies of human health effects, mechanisms of toxicity, and toxicity pathways (mode-of-action) to support risk management decisions
- develop new risk assessment methods or frameworks (e.g., develop biologically-based predictive models) that incorporate chemical mixtures or that characterize cumulative risk (e.g., extrapolation from single chemical to multiple chemicals or mixtures)
- clarify 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) and host factors (e.g., susceptibility, nutrition, co-morbid disease/conditions, lifestyle habits, and timing of exposure)

3) Detection Research: Methods and technologies to detect hazardous substances in the environment.

- develop advanced technologies that allow for real-time, on site monitoring 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
- integrate the site environmental data within a contextual framework of how contaminants affect nearby populations (human or wildlife) through modeling approaches
- develop analytical technologies for rapid evaluation of hydrophobic organic contaminants such as PCBs in sediment and fish tissues
- develop methods to detect and quantify nanomaterials in environmental media including detection methods for groundwater, surface water, and soil for nanomaterials used for site remediation
- develop mobile techniques or tools with field data exchange capabilities such as solar powered sensors embedded with wireless transmitters for real time remote monitoring of conditions, or technologies that automatically geo-reference collected data
- improve methods for assessing physical characteristics of the environmental matrix (e.g. hydraulic conductivity, bedrock fractures, etc.) within the context of hazardous substance detection, characterization, and remediation efforts
- identify and validate genetic markers such as polymorphisms, chromosome inversions, and microsatellites in populations as sensitive indicators of changes in environmental conditions
- evaluate the bioavailability/bioconcentration of contaminants in the food web as a basis for predicting bioavailability/bioconcentration in humans

4) Basic biological, chemical, and physical methods to reduce the amount and toxicity of hazardous substances.

- investigate the mechanistic basis for microbial degradation and sequestration of contaminants by assessing the physical, chemical, and biological factors that affect movement (or reduction) of site contaminants
- develop sustainable mining-site remediation
- identify hazards resulting from the use of advanced remediation technologies (such as the use of nanoparticles, bioengineered plants or microorganisms)

- utilize 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
- perform research on the potential effects of the remedy on characteristics of the aquifer (including soil microbial populations, hydraulic conductivity, pH, etc.)
- develop innovative physical, chemical and biological technologies for the remediation of hazardous substances found at waste sites
- utilize visualization and molecular tools to characterize the physical, hydrogeochemical, or biogeochemical properties of sites containing dense non-aqueous phase liquid (DNAPLs) and sites that are typically characterized by extensive, heterogeneous, and persistent source zones of entrapped and pooled organic liquids
- develop new technologies for in situ remediation of contaminated sediments, soils, and groundwater
- optimize combined remedies for clean-up on complex contaminated sites
- develop innovative approaches to remediate chemical mixtures in environmental media
- adapt fate and transport models to predict and assess the influence of chemical mixtures on the efficiency and effectiveness of applied remediation approaches
- assess the health benefits resulting from or related to the clean-up of contaminated sites
- apply metagenomics to understand the impact of chemical mixtures on the structure and function of microbial communities involved in site bioremediation
- optimize and validating simplified food chain bioaccumulation models for predicting long-term changes in tissue contaminant concentrations, particularly as a gauge of remediation success in sediment clean-up activities