Suggested Research and Activities for the Superfund Hazardous Substance Research and Training Program Center Grants (P42)

This document contains suggested research topics and activities for the NIEHS Superfund Hazardous Substance Research and Training Program (P42) Notice of Funding Opportunity RFA-ES-27-004 referred to as the Superfund Research Program (SRP) Center grant. SRP Center grants support problem-based, solution-oriented research Centers that consist of multiple, integrated projects representing both the biomedical research (BMR) and environmental science and engineering (ESE) disciplines; as well as cores tasked with administrative (which includes data management and training) and translational research and engagement, and as applicable, research support functions. The research and activities from each Center are expected to address the SRP 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.

Because of the complexity of the P42 application, applicants are highly encouraged to consult with SRP staff listed in the NOFO to discuss the theme/focus of the proposed Center application as they are developing their P42 grant proposal.

SRP considers key stakeholders to be the U.S. Environmental Protection Agency (USEPA), the Agency for Toxic Substances and Disease Registry (ATSDR), U.S. Geological Survey (USGS), U.S. Department of Defense (DOD), and the U.S. Department of Energy (DOE), other NIH Institutes, and/or end-users of research and technology that assess, manage, and mitigate sites impacted by hazardous substances. SRP also considers important stakeholders to be federal, state, local, and Tribal governments, owners/operators of facilities at which hazardous substances are located, and communities impacted by hazardous substances. Other stakeholders to be considered include formal/informal educational groups, hazardous waste practitioners, the general public, and other academic researchers. Therefore, investigators should seek input from end-users mentioned above (and on the SRP webpage) during application development and identify critical issues for which fundamental science is needed. In addition, the NIEHS Strategic Plan serves as a basis for prioritizing research topics and activities.

This document contains the following sections:

- ***A. Suggested Research Needs***
- ***B. Hazardous Substances of Interest***
- ***C. Exposure Scenarios of Interest***
- ***D. Suggestions for the Administrative Core's Data Management and Training Activities***
- ***E. Suggestions for Translational Research and Engagement Core Activities***

A. Suggested Research Needs

This section divides research topics by SRP's mandate areas to demonstrate how fundamental and applied research can be directed to solve problems relevant to SRP's mandates. For any given topic, applicants are encouraged to integrate knowledge and results from multiple projects and cores to achieve a holistic resolution (e.g., involving biomedical, environmental and engineering, data management, training, and translational research and engagement approaches) to solve complex environmental problems. Likewise, topics within one mandate area are likely to be synergistic with topics in other mandate areas. Applicants, therefore, should take into consideration the relationships between mandate area topics to develop an integrated, problem-solving SRP Center.

The following list consists of topics meant to direct P42 applicants to areas in need of research that would be responsive to SRP mandates and could be accomplished through interdisciplinary research. These examples are not intended to be exhaustive, and applicants may utilize these and many other topics to meet the objectives of the NOFO.

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

- Dissection of the roles that hazardous substances play in the disruption of biological responses (e.g., molecular, genetic, epigenetic, nucleic acid and protein metabolism, biochemical events, and/or progression of complex disease/dysfunction (e.g., cancer, neurocognitive decline, cardiovascular disease, metabolic syndrome, birth outcomes, etc.).
- Use and interpretation of high throughput cell-based assays (e.g., New Approach Methodologies (NAMs)) that consider biological complexity (e.g. organotypic models that utilize multi-omic approaches to uncover the intricacies of biological response).
- Determination of the contribution of genetic and environmental variables in the development of disease (e.g., genetic variation, epigenetic factors, sex, and age) and host factors (e.g., windows of susceptibility, nutrition, co-morbid/chronic disease/conditions, lifestyle habits, psychosocial stressors, allostatic load, timing of exposure, resilience).
- Utilization, combination, and integration of varied epidemiological data sets to determine relationship(s) between environmental exposures and effects on human health.
- Development, validation, and interpretation of advanced artificial intelligence (AI)-assisted machine learning (ML) approaches and AI models for analysis of high-density and multi-modal data and data used to predict toxicity (e.g., integration of various data types from high throughput assays and data in silico studies to uncover biological pathways leading to toxicity).
- Identifying and elucidating the interaction between environmental toxicants and the human microbiome including changes in bioavailability, shifts in microbiome community structure associated with a disease pathway, assessment of small molecule metabolites as biological response indicators (e.g., biomarkers) of microbiome interactions, and/or identification of patterns indicative of protective microbiome communities/consortia.
- Identification and validation of sensitive and novel diagnostic or prognostic biological response indicators (e.g., biomarkers) of exposure and disease, that can be easily detected (in blood, urine, saliva, sweat, and exhaled breath condensate, etc.) and anchored to a biological response (e.g. phenotype, disease) and/or therapeutic efficacy.
- Evaluation of effects from hazardous substances on local tissue compartments (e.g., eye, skin, lung, gastrointestinal tract) and organ systems (e.g., brain, heart, liver, kidney, bone) and its role in chronic diseases.
- Investigation of the internal and external exposome, which will require: the validation, and implementation of characterization of exposure and biological response; exposure assessment for multiple analytes; utilization of computational tools and resources for analyzing; and conducting non-targeted analysis and screening analysis to identify connections between an exposure(s) and biological response(s).
- Investigation of disease/dysfunction related to environmentally relevant (low dose) exposures, using human biomonitoring data and/or other large databases to develop testable hypotheses

(e.g. National Health and Nutrition Examination Survey (NHANES), ToxCast, disease registries, etc.).

2) Methods to assess the risks to human health presented by hazardous substances.

- Development of multi-dimensional and multi-scale models that incorporate: exposure data; fate and transport; transformation of contaminants in the environment; contaminant bioavailability in the environment and in biological systems to determine individual and population-based biological responses.
- Development of novel methods, models, machine learning, or generative AI approaches to integrate exposure over time, determining windows of susceptibility, and to characterize the attributable risk from multiple exposures experienced over one's lifetime.
- Development of models for integrating connections and interdependence between environmental exposures and psychosocial factors (e.g., stress, mental health, etc.).
- Development of appropriate AI-assisted/ML algorithms for predictive toxicology to characterize low dose-response effects and disease latency.
- Provide innovative strategies to address uncertainty in risk associated with:
    - Extrapolation from *in vitro* to *in vivo* to human data, differences in species, extrapolation from virtual tissue/systems biology studies, individual susceptibility and predisposition, sex, age, extrapolation of high to low dose, and acute to chronic exposure.
    - Combined exposures or cumulative risk (e.g., component and whole mixture approaches, extrapolation from single chemical(s) to multiple exposures or mixtures; inclusion of non-chemical stressors).
    - Development, characterization, and validation of biological response indicators (e.g., biomarkers) of exposure and/or disease that can be applied to gain additional mechanistic insight(s) into disease pathogenesis.
    - High throughput screening tests relevant to human toxicity, pathways, and endpoints (e.g., network/systems/pathway biology and knowledge graphs).
    - Predisposition based on current or past disease states (e.g., immune related-diseases, cardiovascular disease, cancer, endocrine disruption, etc.).
    - Factors that affect bioavailability.
- Determination of how exposome methodologies (i.e., untargeted analysis of biological response and exposure indicators (e.g., biomarkers of response and exposure)) including metabolomics, proteomics, transcriptomics and epigenomics) can be utilized and combined with geospatial tools to assess risk of disease.
- Pathway/computational modeling that incorporates the dynamic interplay of external and internal factors (e.g., diet, microbiome, genetic/macromolecular variations and alterations, etc.) with the route of exposure(s) (e.g., dermal, respiratory, oral) to identify individual susceptibility or resilience.
- Development of methods to determine exposure rates and different routes of exposure (e.g. tracer methods to identify the amount of soil ingested by children; exposure metrics of toxicants from fish or other foods in diet; contribution of soil to indoor and dust due to human activities (e.g., tracking soil indoors).

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

- Development of fast, accurate, robust, low-cost, minimally invasive, and advanced detection technologies and assays that optimize sampling; allow for portable real-time, on-site monitoring; and characterize hazardous substances (especially multi-analyte) and their breakdown products.
- Development of advanced sensors and probes such as biosensors, molecular diagnostic tools, new imaging modalities (e.g., geophysical imaging), self-contained miniaturized toxicity-screening kits (e.g., tissue/organ/lab-on-a-chip), miniaturized analytical probes, and in situ devices that are capable of multi-analyte readings.

- AI/ML, computational, geographical information system-based, or modeling approaches/products for predicting fate and transport of contaminants, rates of remediation, bioavailability, or for identifying contamination sources.
- Development of tool/assay designs that consider device reuse, waste generation, and utilization of non-toxic components (particularly for *in situ* devices).
- Development of detection technologies that are easily deployable for environmental disaster response and can be used at sites complicated by multiple contaminant streams or complex environmental media (e.g., soil, sediments, and groundwater).
- Integration of environmental data within a contextual framework of how contaminants affect nearby populations (human or wildlife) through modeling approaches, such as:
    - Utilization of bioassays or ecological indicators as measures of disturbance due to hazardous substances in the environment as well as recovery of ecosystems following remediation (e.g. natural succession, changes in food web uptake, etc.).
    - Development of innovative generalizable methods to assess impacts of hazardous substances based on sentinel species.
    - Utilization of environmental mapping databases for understanding impacts of hazardous substances on ecosystem functioning.
    - Molecular and genetic endpoints in invertebrates, fish, birds, and wildlife that can serve as early predictors of toxicity and diminished reproduction/fecundity, that may impact normal wildlife population levels and/or ecological restoration/succession.
- Improvement of methods to assess complex sites: physical characteristics of the environmental matrix (e.g. hydraulic conductivity, bedrock fractures, etc.).
- Utilization of subsurface visualization and molecular diagnostic tools to characterize the physical, hydrogeochemical, or biogeochemical properties of complex sites (e.g. sites containing dense non-aqueous phase liquids (DNAPLs) and sites that are typically characterized by extensive, heterogeneous, and persistent source zones of entrapped and pooled organic liquids).
- Development of innovative methods and tools for analyzing specific vapor-phase chemicals in indoor air and gas samples to inform sampling strategies such as sample collection time-periods to capture maximum indoor exposure(s).
- Development of techniques to improve analytical detection limits, particularly where current methodology detection limits exceed action levels for site cleanup, risk action, or screening benchmarks, or where it is unclear what is the background level of the contaminant.
- Development of cost-effective techniques and approaches for identifying contamination in fractured rock including understanding the mechanisms of contaminant diffusion in/out of rock matrices; the fate of certain contaminants within rock matrices (i.e., sorption onto the rock matrix, influence of biodegradation/chemical transformation; role of rock type in influencing these factors); properties that affect back diffusion, which may limit remediation effectiveness.
- Development of tools to support rapid assessment of bioaccessible fractions of hazardous substances in the environment including relevant exposure times and locations in complex environments (e.g., groundwater/surface water interaction zones, etc.). In particular, there is a need for the development and validation of inexpensive, laboratory-based, in vitro tests of bioaccessibility for common contaminants of concern and exposure scenarios.
- Development and standardization of low effort sampling (e.g., passive) methods, particularly for determining bioaccessibility of hazardous substances in sediments and water.
- Application of innovative sensors or sampling devices that can be used to validate remediation performance and/or conduct post-remedial monitoring, comparing these innovative approaches with conventional biomonitoring organisms or analytical methods.
- Collaboration with field practitioners (e.g. engineering firms, site managers) for testing, refining, or validating new detection strategies through use of real-world contaminated media, and/or testing on sites; as well as developing technoeconomic analysis (e.g. comparative cost estimates) of new technologies.

4) **Basic biological, chemical, and physical methods to reduce the amount and toxicity of hazardous substances. (**Please note that at least one ES&E project should support mandate 4.)

ESE Prevention and Intervention Approaches:

- Development of novel materials, amendments, and approaches to remediate contaminated sediments, soils, and groundwater.
- Optimization of sequential and compatible remediation strategies for different phases of a clean-up process (i.e., “combined remedies” or “treatment train”) to maximize the degradation/removal of hazardous substances, including mixtures, at complex sites.
- Optimization of cleanup technologies, components, and strategies to develop resilient remediation solutions that are effective, energy efficient, economically feasible, cost-effective, technologically sound, and reduce ecosystem impacts.
- Remediation processes to recover/reuse valuable constituents or developing regenerable adsorbents for multiple uses.
- Utilization of new computational or data-mining approaches to improve remediation outcomes (including optimizing design of novel adsorbent materials, assessing optimal conditions for remedial success, etc.).
- Development of innovative approaches to remediate complex contaminated sites (e.g., karst environments, fractured bedrock, rock matrix diffusion, heterogeneous sedimentary deposits, complex contaminant mixtures, groundwater/surface water interactions) and to address back diffusion.
- Utilization of molecular, biochemical, cellular, and/or engineering tools to understand the structural and functional properties of microorganisms or plants involved in the bioremediation of hazardous substances.
- Development of new technologies for source zone treatment, including delivering agents *in situ* for remediation of contaminated sediments, soils, and groundwater.
- Development of robust remediation strategies resilient to the impacts of extreme weather events.
- Development of low cost and effective soil immobilization approaches to prevent transport of contaminants indoors, translocation into plants, or re-entrainment.
- Development of new innovative passive remediation technologies (particularly for in situ groundwater remediation and mining influence waters), with potential for reduced treatment costs, treatment waste volumes, and energy usage.
- Collaboration with field practioners (e.g. engineering firms, site managers) for testing, refining, or validating new remediation strategies through use of real-world contaminated media, and/or testing on sites; as well as developing technoeconomic analysis (e.g. comparative cost estimates of new technologies.

Biomedical Prevention/Intervention Approaches:

- Development of prevention/intervention strategies (e.g., diet, nutrition, exercise, vitamin supplements, pharmacological, microbiome/pre- and probiotic, behavioral intervention) to reduce toxicity of hazardous substances (NOTE: Prevention/Intervention activities involving human subjects may be classed as a clinical trial. Need help determining whether you are doing a clinical trial?).
- Development of mechanistic/fundamental studies to assess how diet, nutrition, exercise, vitamin supplements, pharmacological, microbiome/pre- and probiotic, and behavioral intervention, etc. may reduce toxicity of hazardous substances.
- Development of biological monitoring studies to assess the effectiveness of remediation strategies in preventing exposures in humans.

B. Hazardous Substances of Interest

Applicants are highly encouraged to consult with SRP staff for specific questions about the relevancy of a hazardous substance as the presence of a compound on one of the lists mentioned below does not automatically make it relevant to the SRP. ***Per SARA Mandates, hazardous substances do not include petroleum nor natural gas, natural gas liquids, liquefied natural gas,***

or synthetic gas usable for fuel. With regard to specific hazardous substances, please refer to the following areas of interest:

- **Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) Priority List**: these are hazardous substances that are relevant to the US Environmental Protection Agency (EPA) Superfund Program and to the Agency for Toxic Substances and Disease Registry. These hazardous substances are ranked based on frequency of occurrence at NPL sites, toxicity, and potential for human exposure.
- **EPA Superfund Website**: provides information about current and previously listed National Priorities List sites and their contaminants. In addition, EPA's Integrated Risk Information System (IRIS) develops IRIS Assessments for many compounds relevant to Superfund and identifies hazard endpoints for which there is insufficient data to derive reference values.
- **Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profiles:** By Congressional mandate, the Agency for Toxic Substances and Disease Registry (ATSDR) produces "toxicological profiles" for hazardous substances found at National Priorities List (NPL) sites. Toxicological profiles are developed from a priority list of substances and include a "Data Needs" section, which is a useful resource to identify gaps/needs in toxicological testing.
- **Co-Exposures and Mixtures:** Commonly occurring mixtures of contaminants found at Superfund sites and relevant to human exposure are of high interest to the SRP and its stakeholders/end-users. Examples include but are not limited to: methylmercury and PCBs (potential co-exposures due to fish/shellfish consumption); polycyclic aromatic compounds and metals; co-occurrences of endocrine disrupting chemicals; metal/metalloid mixtures associated with mining operations, etc.); apparent co-exposures/mixtures identified in national databases (e.g., NHANES, National Center for Environmental Health) and databases from state/community biomonitoring programs. Applicants are encouraged to visit the ATSDR's Interaction Profiles for Toxic Substances.
- **Emerging Contaminants (ECs)**: There are many contaminants that are of emerging concern to Superfund for reasons such as increased prevalence of a compound on Superfund sites or in human biomonitoring studies together with a lack of data about the hazards of the compound. These compounds may not be on the CERCLA Priority List; however, there is uncertainty about the safety of these compounds in the environment. ***Applicants considering a focus on emerging contaminants are strongly encouraged to contact SRP staff early in the application development process to discuss the programmatic relevancy of the proposed hazardous substance(s).*** Resources regarding emerging contaminants include:
    - The Interstate Technology Regulatory Council
    - Provisional Peer Reviewed Toxicity Value
    - Federal Facilities Restoration and Reuse Office
    - High Production Volume
    - National Academies of Science and Medicine

C. Exposure Scenarios of Interest

SRP Centers present a unique opportunity to understand the science and address the complex problems associated with Superfund or other similar sites impacted by hazardous substances. Hence, applicants are highly encouraged to investigate exposure scenarios relevant to SRP and Superfund – meaning there is a point source of hazardous substances that have the potential to reach human receptors, but that can be intercepted through engineering/remedial processes. Work on a Superfund site (or other sites with hazardous substances) is not a requirement; however, these sites can serve as a valuable conceptual site model to understand risks of human exposure, fate and transport, and remediation opportunities to guide a Center to asking practical questions for scientific research. ***Applicants are encouraged to speak with SRP Staff about potential exposure scenarios that might fall outside of Superfund relevance such as ambient air pollution, consumer product-based, or occupational exposure scenarios – as these studies may be more appropriate for other funding opportunities.***

The following examples have been identified as scenarios that may be opportunities for research efforts.

- **Susceptible Populations and Predisposition:** research on susceptible populations (e.g., pregnant women, children, elderly, disease states) in order to develop strategies to reduce their burden of environmentally-influenced diseases; investigation of windows of susceptibility (e.g., pre-pregnancy, development, infancy, early childhood, puberty, and aging) that are sensitive to environmental exposures and may lead to disease; identification of biologically relevant models to accurately predict disease from exposure during critical life stages in human populations; development of biological indicators (e.g., biomarkers) of exposure and disease to predict disease later in life; determination of the role of genetic variability and the mechanism(s) responsible for the latency of effect/disease; determination of how exposure to environmental contaminants during windows of susceptibility can be used to predict risk of disease; identification of other potentially susceptible populations.
- **Vapor Intrusion (VI):** development of sustainable remediation strategies to mitigate exposure; development of innovative method(s) for assessing effectiveness of VI mitigation systems; evaluation and optimization of site investigation methods to improve the conceptual site model and assess the VI pathway including source forensics and sitewide preferential pathways; development of cost-effective, real-time, and validated methods to detect VI and/or assessment of exposures; innovative methods to assess spatial/temporal/seasonal fluctuations in soil VI and strategies to incorporate fluctuations into risk assessment modeling; development of non-invasive sampling techniques; development of hand-held or remote-capable air monitoring tools to detect volatile substances and compounds in air at low (i.e., relevant) risk-based detection limits; development of studies to understand mechanisms and health consequences of chronic, low level exposure of chemicals associated with VI.
- **Combined Exposures and Cumulative Risk Assessment:** investigation of effects of combined exposures/mixtures which include any combination of chemical and/or nonchemical stressors that act jointly to elicit a measurable adverse effect; examples include: whole mixtures; mixtures of multiple environmental toxicants (where the individual toxicants are well-defined), combinations of environmental toxicants and nonchemical stressors (e.g. physiological stressors, psychosocial stress), or the interactions between diet, or infectious agents, with environmental toxicants; development of computational toxicology approaches to understand the interactions among combined exposures, which may include mathematical and statistical models/approaches, to predict human health effects associated with combined exposures and to support cumulative risk assessment); development of innovative detection and/or remediation technologies for combined exposures in the environment; assessment of strengths/weaknesses of various approaches used to determine cumulative impacts including understanding the advantages/disadvantages of including certain data sources, geographic scales, and methods of statistical analysis; determination of environmental exposures that may be unique to particular communities, including mitigation approaches for those communities. (In addition, applicants may wish to visit the EPA's Community-Focused Exposure and Risk Screening Tool (C-FERST) webpage for ongoing efforts to integrate information about community exposure to multiple stressors. Combined exposures selected for study should have relevance to Superfund and human exposure, with an emphasis on investigating relevant contaminant exposure and dose concentrations.)
- **Emerging Exposure Pathways:** Examples include but not limited to: new exposure pathways from legacy contaminants; the emerging concern posed by metals/metalloids inhalation from mining sites; and the human health and environmental effects associated other reclamation and recovery activities.
- **Exposome:** investigation of the exposome, which describes the totality of human exposures in an integrated temporal, spatial, and biological framework (see Vermeulen et al., 2020 and Wild, 2012); exposome research requires the development, validation, and implementation of characterization of exposure and biological response. Exposome research topics include: comprehensive assessment of external exposure, internal dose, and biological response; assessment of multiple analytes in biological samples; computational//artificial intelligence/machine learning tools and resources for analyzing and providing centralized access to information on the associations between exposure and disease; development of objective measures of historical exposures to inform investigations of latent effects of exposures or diseases arising from exposures during windows of susceptibility; assessment of

exposure before, during, and after remediation; development and validation of exposure assessment tools to determine the incorporation of bioavailability/bioaccessability of environmental contaminants; use and refinement of environmental monitoring and geographic information system (GIS) for spatial exposure assessment.

D. Suggestions for the Administrative Core's Data Management and Training Activities

The RFA-ES-27-004 details the requirement for P42 applicants to include an Administrative Core with Data Management and Training functions. The role of the Data Management Coordinator is to support the management and integration of data assets across the Center and to foster and enable the interoperability of data between the BMR and ESE projects, accelerating the impact of the Center's research. In addition to data management activities, the Core should include training functions, led by a Training Coordinator, to support scientific workforce develop, with a focus on graduate and postdoctoral level cross-disciplinary training in fields related to environmental health and environmental science/engineering. (Note: the SRP defines "trainees" within the core as graduate students and post-doctoral researchers that perform research/activities that are supported by the Center).

Data Management Activities

Depending on the research goals of the center, the following activities may be useful to demonstrate how the Data Management Coordinator can support effective data management, analysis, and integration across the center:

- **Coordinating with Project and Core Leaders:**
    - Ensuring data management and sharing efforts align with the NIH Data Sharing Policy.
    - Developing and/or implementing tools that enable/standardize the collection of metadata during the research process to ensure consistency with community standards to support rigor and reproducibility and to facilitate interoperability and reuse of data.
    - Identifying appropriate data sharing platforms (within and outside the Center and to SRP staff) or strategies for sharing prioritized data sets outside the Center and reporting to SRP staff (e.g., via the optional SRP Data Collection Tool) and establishing timelines for deposition.
    - Providing support for research projects so that handling of sensitive and restricted data (e.g., human population studies) is described and appropriately anonymized with formal consent agreements in place (for more information, please visit Data Privacy).
    - Providing data analytical/statistical support for research projects/core leaders, as appropriate.
    - Providing support to enhance data integration and interpretation through visualization approaches (e.g., computational modeling support combined with GIS mapping to reveal geographic patterns to characterize exposure) and through graphical approaches to represent knowledge.
    - Encouraging and providing strategies for project and core leaders/trainees to analyze shared datasets to explore new linkages between data and the formation of new hypotheses.
    - Working with the Administrative Core's Training Coordinator to support training and education on data management practices.
- **Fostering Data Sharing and Interoperability.** Examples include:
    - Development of schema that collects sufficient metadata and their relationships to other data generated in the Center to enable interoperability and compatibility across the Center, creating the potential to advance the understanding of relationships between multiple datasets to advance the research goals of the Center.
    - Developing visualization and other application tools to facilitate data sharing and integration (e.g., graphical interfaces and dashboards).
    - Standardizing data documentation (metadata), and/or analysis tools (leveraging community-based ontologies and semantic resources as applicable) to enable

interoperability and compatibility across the Center creating the potential to advance the understanding of relationships between multiple datasets to advance the research goals of the Center.
    - Developing strategies to foster and enable the interoperability of data between BMR and ESE projects.
- **Data Quality Assurance and Quality Control**. Examples include:
    - Developing a strategy for implementing and monitoring quality assurance/quality control (QA/QC) measures for each data type across the Center.
    - Assessing QA/QC measures for effectiveness.
    - Training project/core staff and trainees on QA/QC best practices.

Note: Per NOT-OD-22-189, peer reviewers will not be provided with the separate Data Management and Sharing Plan (DMSP) attachment. However, all projects must provide, in their "Resource Sharing Plan," plans for interaction with the Center's Data Management Coordinator. Hence, Data Management Coordinators may wish to work collaboratively with project leaders do develop their section, drawing from the best practices outlined in the bullets above.

Training Activities

The following activities may be useful to demonstrate how the Training Coordinator may support effective training opportunities for the Center's trainees:

- Promoting trainees to participate in the Center's overall research program, projects, and cores.
- Conducting and promoting interdisciplinary research/activities among the trainees within the Center, and as appropriate, with other trainees from outside the Center.
- Providing trainees with opportunities to enhance their professional career development and mentoring of SRP and non-SRP trainees (e.g., other graduate students, undergraduates, high school students).
- Providing opportunities for trainees such as: serving in leadership/mentoring roles, presenting research or activities to the Center's institution and/or outside organizations, and participating in workshops/conferences that promote professional development (e.g., resume or scientific writing, interviewing skills, and oral/poster presentation skills).
- Facilitating practical opportunities for coordination or collaboration among other grant recipients and for communicating research outcomes to various audiences (e.g., the public, their peers, and experts in the field) so that the trainees learn 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.
- Facilitating opportunities for grant writing and recruitment of Center trainees for fellowship/externship/award opportunities (e.g., KC Donnelly Externship; SRP Karen Wetterhahn Memorial Award).
- Hosting events within their Center and among Centers to promote collaboration among the trainees (e.g., workshops, in-person/online courses, conferences, seminars, or field days).
- Providing training and education on data management practices and data sharing opportunities with the Center's Data Management Coordinator.
- Coordinating trainee participation in the Translational Research and Engagement Core (TREC).
- Participating in the SRP-hosted quarterly webinars (e.g., trainee professional development webinars).
- Coordinating with the Center's Administrative Core to ensure that the Center's trainees' activities/accomplishments are added to the optional SRP Data Collection Tool to inform SRP staff about trainee publications, awards, patents, presentations, seminars, etc.

Note: Projects must provide, in their "Resource Sharing Plan", plans for interaction with the Center's Training Coordinator (e.g., identifying opportunities for trainee career development and cross-training research experiences). It is recommended that Training Coordinators work closely with projects to detail any training opportunities relevant to that project.

E. Suggestions for Translational Research and Engagement Core Activities

The RFA-ES-27-004 details the requirement for P42 applicants to include a Translational Research and Engagement Core (TREC)*.* The TREC Coordinator(s) has/have a critical role in assisting project/core leaders in translating research emanating from the Center to appropriate audiences, thereby encouraging the accurate and timely use of the Center's research products to end-users/stakeholders. The SRP also considers the individuals and communities living near impacted sites as key end-users and recognizes the opportunity for SRP Center's to achieve positive public health benefits through bidirectional interactions with the communities and promote prevention and intervention strategies to reduce the amount and toxicity of hazardous substances (whether in their homes, their schools, their community, and/or their environment). (For the purposes of this RFA, the SRP refers to prevention and intervention as "basic biological, chemical, and physical methods to reduce the amount and toxicity of hazardous substances.")

The SRP also encourages interaction between project leaders and stakeholders/end-users throughout the proposal development, the project duration, and conclusion of research activities to increase project and Center relevancy (stakeholders may include federal, state, local, and Tribal agencies, owners/operators of facilities at which hazardous substances are located, the commercial sector, affected communities, etc.). To address this, the TREC is expected to work with each project leader to develop a **Translational Research Plan (TRP)** as part of the Project/Core Resource Sharing Plan. Plans should outline a strategy for the translation of their research beyond typical methods to share research findings (i.e. the publication of research findings in scientific journals, oral/poster presentations at scientific meetings, etc.) and engagement with a community(ies), as applicable.

The following examples demonstrate some of the various tools and activities that can be used for effective translational research and engagement. This list is not meant to be exhaustive. (Note: the TREC is not meant to be a pilot project/activity program).

Translational Research Activities:

- Coordinating with Project leaders to develop plain language description(s) of research project(s) for dissemination to broad audiences (e.g., elevator pitches, lightning talks, website summaries, factsheets, YouTube videos, webinars, social media, podcasts).
- Coordinating with Project Leaders in identifying potential stakeholders and assisting in developing TRP. Examples could include:
    - Assisting in opportunities such as identifying appropriate sites for testing detection and remediation technologies and assisting field practitioners in site monitoring and remediation technologies when developing these technologies.
    - Sharing of anticipated project-generated resources such as: detection/remediation technology, specimen sharing, field sample sharing, development and distribution of analytical protocols/methodologies, data generated from BMR and ESE projects (e.g. adding data to federal/state data repositories).
    - Creating and sharing open-source data sharing repositories/knowledgebases and analytic resources in coordination with Data Management Coordinator.
    - Refining technologies/demonstration research to make more applicable to end-users.
    - Quantifying health, well-being, environmental, and economic benefits resulting from application of a relevant technology (e.g., biological and/or ESE technology).
    - Advancing and validating biological indicators of exposure and response (e.g., biomarkers), remediation strategies, detection technologies, etc. research into application with consultation from technology transfer offices and/or stakeholders and technology transfer offices.
    - Coordinating with formal technology transfer mechanisms (e.g., patents, licenses, Small Business Innovation Research/Small Business Technology Transfer Research grants).

    - Sharing research findings to inform current risk assessments and remediation practices.
- Developing audience appropriate educational in-person/online courses/curricula/learning material, relative to the Center's theme and hazardous substances under investigation.
- Communicating and providing information about various activities to SRP staff on the results of activities through utilization of the optional SRP Data Collection Tool about publications, press releases, awards, patents, presentations, meetings seminars, etc.
- Participating in SRP TREC webinars and focus groups as appropriate to the Center.
- Developing and participating in workshops, meetings, and networking groups with the various SRP Centers/investigators/stakeholders to advance scientific themes of the Center and translation of new scientific research.
- Participating in biological and environmental sample and data-sharing with other SRP Centers/investigators/stakeholders.
- Helping to identify opportunities for SRP Center trainees to interface with the TREC Coordinator(s) on activities relevant to their research.

Stakeholder Engagement:

- Establishing connections at the federal, state, local, and Tribal health and environmental departments (e.g., planning visits to communicate scientific findings and participate in seminars/conferences/workshops to meet agency staff to learn about programs and potential data gaps, as well as identify future collaborations).
- Identifying opportunities to work with or leverage resources from stakeholder agencies such as, but not limited to: U.S. Environmental Protection Agency, U.S. Geological Survey, U.S. Department of Defense, U.S. Department of Energy, National Science Foundation, and the National Institutes of Health. (Note: when work is proposed for Superfund Sites, the site Remedial Project Manager as well as appropriate EPA and ATSDR regional staff, should be contacted and incorporated into the plan.)
- Establishing a plan for unanticipated opportunities for stakeholder engagement relevant to the Center's activities – including notifying local networks, the SRP Program Staff, and leveraging strengths among the SRP network.
- Identifying appropriate Center expertise for serving on External Advisory Panels (e.g., EPA or ATSDR panels; National Research Council, National Academies of Science, Engineering, and Medicine (NASEM)).
- Participating during Public Comment periods on Superfund relevant environmental health related documents at local, regional, state, and federal government levels (e.g., reviewing documents, submitting public comments when appropriate). A few examples of regularly posted documents include:
    - ATSDR's Toxicological Profiles
    - EPA's Integrated Risk Information System (IRIS)
    - State products (e.g. from state environmental health and quality departments)
    - Other Federal Agencies: To find other public comment opportunities related to hazardous waste, Centers may find it helpful to monitor the Federal Register, Grants.gov, and/or Regulations.gov.
- Plans for promotion of solution-oriented research and activities that are intervention and prevention-related (and that are consistent with SRP's fourth mandate) that could include:
    - Coordinating and partnering with federal, state, local, and Tribal agencies regarding community-based needs and exposure assessments to identify prevention and intervention strategies to reduce exposures.
    - Coordinating with Center's researchers and relevant federal, state, local, and Tribal agencies to provide communities with information that may help with the decision process for cleanup of sites.
    - Coordinating with the community to conduct an inventory of community-level environmental and health resources/needs to help prioritize and inform prevention strategies.

    - Developing ways to improve the community's resilience to natural disasters or extreme events, especially related to contaminated sites including improved methods for assessing and preventing cumulative impacts of these events.
    - Applying lessons learned from prevention and intervention activities specific for one community to other communities. Note: because SRP is not a site-specific program, it is expected that engagement activities, though focused on one community, would be generalizable to other communities living around or near sites affected by hazardous substances.
    - Working with the community to understand what increases the risk of exposure to hazardous chemicals and ways to reduce/avoid exposure, which may include, but is not limited to:
        - Identifying how dietary choices, including specific nutrients, vitamins, and supplements can mitigate the effects of exposure to hazardous substances.
        - Identifying food sources that may pose greater risks and identifying/recommending safer alternatives (e.g., evaluating which fish (or their tissues) have high contaminant levels).
        - Recommending/providing exposure reduction strategies (e.g., water filtration, air filters, etc.).
- Plans to engage with communities impacted by sites with hazardous substances (especially those that the Center is focused upon), which may include:
    - Assisting a community or an individual in accessing information regarding the Center's research and providing responses to a community's questions.
    - Participating in local community or health events (e.g., health fairs, school-based programs, science cafes, etc).
    - Training and education for communities and individuals, including tools that facilitate in data collection and sampling methodologies (e.g., teaching community members how to use personal sensors or exposure assessment devices).
    - Providing workshops and informal educational outreach opportunities for information sharing within the community group.
    - Attending EPA or ATSDR community meetings related to the community(ies) of interest.
- Coordinating with the TREC Coordinator(s) and the Training Coordinator for opportunities for the Center's trainees to participate in community meetings and/or opportunities for other Center-community interactions.

F. Other Resources

As mentioned above, SRP has provided Additional Resources here, which includes SRP and NIEHS Resources, USEPA and ATSDR Resources, Tips for Applicants, and Electronic Application Process information. Applicants are highly encouraged to utilize these resources as they are developing their applications.

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