Concept Clearance

Branch: Exposure, Response, and Technology Branch

Council Period: 202001

Concept Title: SBIR Technologies for Environmental Health Research

Introduction

As with most federal agencies with an R&D budget over $100M the NIEHS is required to allocate a portion of its extramural R&D budget to support small businesses through the SBIR programs. With the reauthorization of the SBIR program by Congress in December 2018 for FY18-FY22, several key provisions were implemented, including the SBIR set-aside to remain at FY17 levels (i.e. 3.2%), reauthorization of Direct to Phase II and the Commercialization Readiness Pilot program.

In order to focus on development and commercialization of technologies that support the NIEHS mission of reducing the exposure to environmental stressors to promote healthier lives, several new SBIR RFAs concepts are proposed here:

1 Developmental Neurotoxicity Related Assays and Tools for Environmental Sciences
2. Biomarkers/ Biomonitoring of Biological Response to Environmental Exposures
3. Artificial Intelligence and Machine Learning Approaches to Advance Environmental Health Sciences
4. Environmental Exposure Assessment Sensor Validation - Phase II/IIB

Given the increase in funds set aside for SBIR program, soliciting applications through selected RFAs will help to focus research and development of technologies and tools that have high priority for the NIEHS mission.

The NIEHS has two current RFAs for SBIR applications for FY20. RFA-ES-20-005, Organotypic Culture Models Developed from Experimental Animals for Chemical Toxicity Screening (R43/R44 Clinical trial not allowed) was re-released in October 2019 to allow Phase II applications from the previous RFA (RFA-ES-17-008) as well as new Phase I and Fast-track applications. A total of 5 Phase I and one Fast track grants were funded through the previous RFA to develop kidney, neuronal, corneal, peripheral nerve, blood brain barrier and multiorgan organotypic culture models. RFA-ES-20-005 supports develop novel, physiologically-relevant *in vitro* screening systems (*e.g.,* engineered 3-dimensional or organotypic models) using cells derived from animal species typically utilized for toxicological testing, which will replicate biological interactions and toxicological responses observed in animal tissues or organs, will produce assay data suitable for comparisons between *in vitro* and *in vivo* animal toxicology studies, and may ultimately provide alternative methods to reduce the use of animals in toxicity testing.

A second RFA (ES-20-008), New Approaches for Incorporating Genetic Diversity into Toxicity Testing R43/R44 Clinical Trail not allowed) released in November 2019 aims to provide support to develop resources and approaches that reflect the variability in responses to chemical exposures based on genetic diversity in the human population. These can include panels of human cells or cell lines, rodent panels, including cell lines generated from rodent diversity panels, lower organism strains with well-characterized genetic backgrounds, or *in silico* approaches to enhance the ability to characterize the effects of genetic variation in toxicity testing.

In addition to proposals submitted to NIEHS through the general Omnibus Solicitation of the NIH, CDC, FDA and ACF for Small Business Innovation Research Grant Applications (Parent SBIR [R43/R44]), soliciting SBIR applications through additional RFAs over the next 4-5 years will help to enhance the development of technologies and approaches by small businesses that support many aspects of the NIEHS mission.

Research Goals and Scope

The following topics are proposed for SBIR RFAs in the next 4-5 years.

1. Developmental Neurotoxicity Related Assays and Tools for Environmental Sciences

The potential for developmental neurotoxicity (DNT) following exposure to environmental chemicals remains a high public health priority due to concerns that recent increases in the prevalence of neurological disorders in children (e.g., ADHD, and autism spectrum disorders) may in part be due to chemical effects. The National Toxicology Program (NTP) /NIEHS recently has initiated the Developmental Neurotoxicity Health Effect Innovation (DNT-HEI) program which aims to have a global public health impact by identifying environmental chemicals that have the greatest potential to affect susceptible populations and thereby prevent neurodevelopmental disorders. Thus, the need for reliable, relevant, and efficient screening tools to identify, prioritize, and evaluate chemicals for their potential to induce DNT is well recognized. Towards this end, the NTP as part of Tox21 Phase III's effort to "Improve on Biological Coverage and Human Relevance", created an 80+ compound library of known DNTs, developmental toxicants (DTs), and adult neurotoxicants (NTs), as well as compounds of interest to the NTP with unknown DNT, DT or NT activity (e.g., flame retardants, polycyclic aromatic hydrocarbons). This library is available for small business and other researchers interested in evaluating their effects on DNT. NIEHS, through the SBIR program, is interested in supporting development of high-content and/or high-throughput cell culture assays for DNT screening and encouraging use of these test chemicals. These efforts can involve application of 3-D culture models, brain on chip and microfluidic systems. NIEHS is also interested in supporting development and application of DNT-related predictive toxicology methodologies and modeling such as, *in vitro- in vivo* exposure (IVIVE) extrapolation, cross-species extrapolation and other *in silico* approaches for data profiling. Additional areas of interest include developing or applying real imaging techniques and novel biomarkers for clinically relevant neurodevelopmental disorders such as autism and ADHD and others.

2. Biomarkers/ Biomonitoring of Biological Response to Environmental Exposures

Common human diseases such as asthma, cardiovascular disease, cancer, and neurodegenerative diseases, are known to result from a complex interplay between genes and environmental factors, including chemical toxicants and biological toxins. There is a continued need for developing and applying specific biomarkers and/or biomonitoring technologies of exposure or response. Availability and application of well-characterized biomarkers and biomonitoring tools in population studies aimed at investigating the role of gene-environment interaction in human health and disease could provide significant insights about the person's exposure and response to environmental exposures. NIEHS is interested in the further validation of previously identified biomarkers/ indicators of a biologic response to environmental stressor that can be objectively measured and adequately define exposure or response. These biomarkers could be at cellular, molecular, tissue or physiologic level, and preferably multiple markers to characterize the full response of the pathway to the environmental stressor. The biomarkers may include circulating markers, exosome related, inflammation, oxidative stress, DNA damage, mitochondrial perturbations, endocrine disruption, immune activation, and epigenetic regulation and others. For the development of point-of-care devices or markers, emphasis will be on pathways known to be perturbed by environmental stressors and related to disease pathogenesis. Development of point-of-care biomonitoring devices focus on approaches that are low-cost, compact, sensitive, non-invasive or minimally invasive, user-friendly and robust, using blood, saliva, urine or exhaled breath to detect environmental exposures or specific markers of exposure.

3. **Artificial Intelligence and Machine Learning Approaches to Advance Environmental Health Sciences**

Leveraging the tremendous growth in data collection, availability as well as computing power and accessibility, Artificial Intelligence (AI) and Machine Learning (ML) applications are now broadly applied in many scientific disciplines. In June 2019, the National Academies of Sciences, Engineering, and Medicine's Standing Committee on the Use of Emerging Science for Environmental Health Decisions held a 2-day workshop to explore emerging applications and implications of AI and ML in environmental health research and decisions. This workshop was sponsored by NIEHS and in the closing thoughts it was concluded that AI and ML have the potential to revolutionize environmental health. This RFA concept is to apply the AL and ML approaches to address some of the challenges and potential environmental health-related applications. NIEHS interest areas include curating, annotating and integrating environmental health datasets, such as legacy data and high-throughput screening assay results, and incorporating details about specific chemical features, automation of these processes and generating algorithms for better understanding of differential susceptibility, identifying biomarkers of exposure. Additional specific applications could include predicting the toxicology of chemicals, estimating exposures, helping to characterize the exposome, understanding the interactions between genes and environmental exposures, supporting systematic reviews of scientific literature, applying AI to epidemiology and exposure science, and addressing the research challenges with studying health effects of chemical mixtures.

4. **Environmental Exposure Assessment Sensor Validation - Phase II/IIB**

A major focus of the NIEHS Exposure Biology and Exposome Program is to support the development, validation, and application of exposure assessment technologies or approaches that will enable to focus on the total personal environment exposure. The 2018-23 NIEHS Strategic Plan places a significant emphasis on transforming exposure science through the development and application of new approaches to exposure assessment, the definition and dissemination of the exposome concept, and the development and demonstration of the exposome as a tool for both epidemiological and mechanistic research. NIEHS is interested in continuing to support such developments through the SBIR program with a goal to promote the use of innovative technologies for the fundamental research and translation science. Towards this end, a two-pronged approach is proposed. One approach, using the Phase IIB mechanism, is to promote environmental exposure assessment sensor technologies that were previously developed with SBIR or STTR funding from NIEHS, other Institutes of NIH, or other federal agencies. The focus of the Phase IIB effort will be on evaluating the sensor performance characterization, benchmark validation, certification from EPA if applicable, pilot-scale validation, and development of usability protocols and testing the sensors in additional pilot studies or field tests that may involve a variety of end users to demonstrate the value of the technology and its usability across a range of real world conditions. The other approach is to support through the Direct to Phase II mechanism for exposure assessment technologies that are in prototype or under development at academic labs with non SBIR funding to further advance their development, validation and application through collaboration with small business companies who are eligible to apply for SBIR grants. This RFA will also support the development of statistical and machine-learning methods for data extraction, integration and analysis of data from personal and public sources and citizen science related activities.

Mechanism and Justification

Phase I (1R43), Fast Track (1R44) and Direct to Phase II (1R44) applications will be solicited for initial development of technologies for the first three topic areas. For the environmental sensor validation Direct to Phase II or Phase IIB applications will be solicitated.

Soliciting applications from small businesses through selected RFAs in these scientific areas will help to focus technology development in areas that support many aspects of the NIEHS mission.