National Institute of Environmental Health Sciences
Division of Extramural Research and Training

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Concept Clearance

Validation and Field Testing of New Tools for Characterizing the Personal Environment and Biological Response Indicators

Overview:

One of the primary challenges in the study of environmental health is the ability to comprehensively characterize an individual's environment including simultaneous assessment of exposures to multiple chemical toxicants, dietary intake, physical activity, psychosocial stress, the use of addictive substances and the biological response to those factors. The NIEHS and our partner institutes on this concept have supported several projects to develop new technologies to address these shortcomings including efforts supported by the Superfund Research Program, the SBIR Program, the Genes Environment and Health Initiative (GEI) and investigator initiated R21 and R01 projects, which have resulted in the creation of prototype tools for characterizing the personal environment. This concept will support a highly focused program to facilitate the acceptance of these new tools and candidate biomarkers in studies of environmental epidemiology and gene-environment interactions. The effort will include rigorous evaluation of the sensitivity and specificity of the prototypes and candidate markers under controlled laboratory conditions as well as validation of their usability and scientific value in field tests integrating them into existing epidemiological projects.

Background:

Application of emerging tools for characterizing the personal environment and the biological response to exposure in epidemiological studies depends on the validation of these products in terms of the feasibility, reliability, and robustness of the application of these new approaches as well as the ability of the new measures to add valuable new information to the study. Acceptance by the epidemiology community of new devices (including measures of chemical exposures, diet, activity and stress) will require extensive documentation of the sensitivity and specificity of their measures carefully under controlled conditions and in comparison to existing gold standards, where such standards exist. In addition, it is essential that there be an evaluation of the ease-of-use, reliability under real-world conditions, compliance, and feasibility of use in the target population. For candidate biomarkers of exposure and response, questions that must be addressed are: Does the biomarker correctly identify exposed and unexposed populations (or heavily exposed vs. ambient exposures)? Does the biomarker have the necessary sensitivity and specificity to detect whether an exposed person carries a phenotype of adverse response? Does the biomarker represent the underlying biological mechanism being studied? Does the biomarker correlate with other relevant (*e.g.,* physiologic)

characteristics. For example, if allergy incidence declines with age, does the biomarker also decline with age?

Although the topic of biomarker validation was included in the ARRA Challenge grant announcement, a more comprehensive program is needed to bridge the gap between biomarker/sensor development and the application to environmental epidemiology and gene-environment interaction studies. We propose a two-year program that leverages existing studies with banked biospecimens or ongoing studies to validate prototype sensor devices and candidate biomarkers developed in the GEI Exposure Biology Program and in other projects supported by NIEHS and our partner Institutes and Centers. Successful applicants would need to provide preliminary evidence in the application that sensor device reliably measures the targeted environmental variables with a high degree of specificity and sensitivity and performs under a variety of conditions (changes in humidity, temperature, dust, interferent exposures, etc.). For biomarker validation, applicants would need to provide compelling evidence that the markers are biologically relevant, robust (can be detected in population with samples collected under "real-world" conditions), and are relatively cost-effective (*i.e.,* could reasonably be scaled up for large epidemiology studies).

Objectives:

The goal of this two-year program is to validate promising candidate biomarkers and devices by taking advantage of existing NIH-supported epidemiological studies. Studies can include biomarker testing in stored samples (*e.g.,* blood, serum, plasma, urine, or buccal cells) or in on-going population studies. Validation of sensor devices can include application of sensor devices to cohort studies in which exposure assessment is currently conducted via questionnaire or through ambient or other personal exposure monitors. In addition, ongoing chamber studies of inhaled toxicants may provide opportunities for testing the sensitivity and specificity of personal sensors.

For candidate biomarkers, the goals will be:

- to verify that the markers or signatures can be detected in multiple populations with similar exposures. In addition, it will be important to determine whether changes in the response marker represent adaptive or adverse responses to environmental stresses including diet activity, stress and toxicant exposures.
- to evaluate the performance of biomarker tools and assays with archived samples collected under real world conditions (collection, storage, freezing, shipping, etc.)
- to test candidate markers in studies with repeated sampling, when possible, to understand how the biomarkers change over time and whether a subset of these represent persistent changes associated with exposure.
- to compare results from novel biomarker profiles to current methodologies or existing reference measures where appropriate.

For prototype personal sensors or biosensor devices, opportunities are needed to test devices in both controlled settings and existing prospective population studies:

- to verify that devices accurately and reliably measure the set of environmental variables (toxicants, diet, activity, psychosocial stress and use of addictive substances) that they

were designed to measure with sensitivity and specificity appropriate to large scale population based studies
- to demonstrate that devices can be used by study participants with minimal burden and oversight, and that the data can be effectively collected, stored and analyzed.
- to compare results from sensors to current sensor technology with respect to acceptability, cost, completeness, and accuracy of the measures.
- to determine the utility of the technologies in different study phases (for example recruitment and follow-up; deployment methodologies; user training) and populations including appropriate developmental stages
- to assess the validity of strategies for intensive monitoring of subpopulation and extrapolation to course measures (i.e. by questionnaire or ambient measures)

The goal of this program is to establish the validity, reproducibility, feasibility and utility of these new approaches in better defining exposure and response in population-based studies or other clinical settings.

Program Management, Implementation, and Budget:

This program will be overseen by a trans-NIH team of project scientists including representatives from each of the funding ICs; to include at a minimum NIEHS (lead), NHLBI, NCI, NIDA, NIAAA, and OBSSR. Participation from other ICs is actively being sought. This group will work cooperatively to develop solicitations and coordinate all programmatic decision making using similar processes to those implemented by the NIH Genes, Environment and Health Initiative's Exposure Biology Program.

The projects will be supported as two year R01/R21 projects with a limited budget. Applicants will be expected to clearly describe the capabilities of their prototype devices and candidate biomarkers and to integrate them into existing cohort studies (biomarker validation can rely on banked samples but field deployable tool validation must be performed on prospective studies with on-going recruitment or follow-up). Direct costs for projects funded by this initiative will be limited to $300k per year for a two year maximum duration. NIEHS intends to contribute up to $5M (10 awards) to this program with other ICs contributing in line with their needs; expected to total approximately another $5M combined.