

## Concept Clearance

**Branch:** Population Health Branch

**Council Period:** 201505

**Concept Title:** Infrastructure and Methodological Research Support for Environmental Epidemiology Cohorts

### Introduction

At the February 2011 National Advisory Environmental Health Sciences Council meeting, David Balshaw presented a concept to establish a program to provide support for the sharing of technological resources to the environmental health sciences community.

Complementary to this effort, the NIEHS is proposing to expand this original concept to meet another identified infrastructure need expressed by the epidemiology community: a mechanism to ensure the maintenance of existing and new cohorts and their often extensive biorepositories. By providing support for cohort maintenance, the NIEHS will maximize and protect its large investment that has been made over the years.

The NIEHS is proposing the creation of a mechanism to provide support for the maintenance of environmental epidemiology cohorts and their associated biorepositories and for the collection or development of additional measures, in existing Environmental Epidemiology Cohorts. The goal of this mechanism is to support the retention of trained personnel, ongoing longitudinal data collection, follow-up among study participants, and preserved integrity and quality of specimen collection that could otherwise be lost with breaks in funding. This mechanism will reduce the depreciation of invested resources and enable a greater continuity of research in the field.

### Research Goals and Scope

Environmental Epidemiology Cohorts (EECs) are defined as large observational population studies in which groups of people with a set of characteristics or exposures are followed over time for the incidence of environmentally-related health outcomes. This definition includes large cohorts of pregnant women and their offspring, children, and adults with longitudinal assessment of responses to environmental exposures and short- and long-term health outcomes occurring after environmental exposure measurement. The EECs have helped advance our understanding of the complex etiology of environmentally-related diseases and have provided insights into other behavioral, lifestyle, and genetic determinants of disease. Findings from EECs may also serve as a basis for risk prediction models and/or the design and testing of preventive and therapeutic intervention strategies to mitigate harm. These EECs have established large biorepositories, support genomic and epigenetic studies, and are beginning to support proteomic, metabolomics, and microbiome studies along with a few multigenerational studies.

Each infrastructure grant is expected to focus on activities that will enable efficient planning and operation of cohorts in preparation to: (1) prepare for future scientific needs; (2) address cutting edge research questions related to population environmental health; (3) promote engagement of new disciplines in the field; and (4) facilitate scientific collaborations across cohorts.

Specific maintenance functions that can be supported for the existing cohorts include, but are not limited to:

- Follow-up or additional accrual of the target population, and/or enrollment of special populations in the catchment area to enhance the breadth or power of the cohort;
- Measurement of high-throughput genetic/genomic, epigenetic/epigenomic, metabolomic or other biological markers in additional cohort samples, where measurements have already been funded or completed for a subset of the cohort, and where measurements in additional samples would substantially enhance the validity of research findings. For example, this may include the collection of additional –omic data that would ensure a more robust laboratory design (e.g. the avoidance of batch effects) or an increased sample size to examine hypotheses with greater statistical power.
- Validation, quality control, standardization, harmonization, and/or calibration of data across environmental health cohorts;
- Biospecimen collection and management of biorepositories as well as environmental sample repositories, including ongoing quality control, application of standards, and inventory maintenance, and
- Data management and data sharing activities, and administrative and communication tasks in preparation for collaborative analyses across cohorts.

Methodologic activities may include, but are not limited to the following:

- Novel statistical methods development for integration of systematic, high-throughput assessment of genetic or other biological markers;

- Validation of exposures and health outcomes. For example, the comparability of self-reported data versus medical record or biomarker information, or the assessment of how well a biomarker measured through non-invasive means compares to gold standard or other target tissue;
- Development and improvement of quality control and quality assurance activities related to laboratory work, data use, biospecimen and environmental sample repository standards, etc.;
- Development and application of tools to support interoperability of data generated in the parent cohorts with other relevant data sets (e.g. implementation of common data and metadata standards and evaluation of their utility to support data integration);
- Methods for biospecimen collection, processing, and repository management; and
- Development of informatics systems to promote wider access/use of the samples from these cohorts.

### **Mechanism and Justification**

The Cohort Infrastructure program will be solicited through a broadly focused FOA with a single annual receipt date for three consecutive years. Applicants will be encouraged to submit a letter of intent to determine eligibility. Projects will be funded for up to five years, with competitive renewal possible. Individual projects may not exceed \$500K direct and funds requested must be well justified. It is anticipated that 1-3 awards will be made annually.

We will consider the U01 mechanism since there will be substantial NIEHS project scientist involvement in the coordination of the resources funding under this FOA such data sharing activities, potential collaborative analyses, and harmonization of data end points across awarded infrastructure grants. Program scientists will assist in reviewing all major transitional changes that the awardees might propose as well as technical assistance and advice to the awardees as appropriate; and organize and conduct regular meetings to share progress either by teleconference, videoconference, or face-to-face, as needed between the awardees.

Since the FOA will also allow for the fragmented infrastructure components of environmental epidemiology cohorts to be consolidated under a single cooperative agreement (U01) award, the transition of the consolidated infrastructure support may be initiated when a grant that contains infrastructure components becomes eligible for renewal. If the application is selected for funding, the overlap with other grants will be administratively adjusted, if necessary

Research projects relying on the ECC's infrastructure are NOT appropriate for this FOA and should seek support through appropriate research project mechanisms such as investigator-initiated R01s.

### **Program Management**

Although this infrastructure support is awarded to an applicant with an existing cohort, opportunities will be developed to reach out to the broader scientific community by requiring the awardees to provide regularly updated descriptive and meta-data to the NIEHS, including cohort characteristics, study protocols, basic counts of study participants, availability of biospecimens, and study variable definitions.

The NIEHS will document the data that has been collected across cohorts and make the information available online. This will assist the research community in identifying potential cohorts to address specific research questions and facilitate cross-cohort efforts such as replication and meta-analyses. Awardees will be required to contribute to a cross-EEC data harmonization with NIEHS staff and other awardees through participation in working groups.

Documentation of use of the resource by the broader environmental health sciences research community will be a vital aspect of the annual non-competitive renewal process. The solicitation will make clear that under-utilized resources will not receive non-competitive renewals; awardees will be expected to document utilization beyond their institution and known collaborators in the non-competitive renewal.