

National Children's Study Follow-Up Concept Clearance

Title of proposed program: National Children's Study Transition

What is the major obstacle/challenge/opportunity that should be addressed?

The National Children's Study (NCS), a national longitudinal study of environmental influences (including physical, chemical, biological, and psychosocial) on child health and development, was reviewed recently by an expert working group of the Advisory Committee to the NIH Director (ACD). The ACD working group recommended that, while the overall goals of the NCS should remain a priority for future scientific support, the NCS was not feasible as outlined currently. As such, the NCS was closed, and NIH efforts to address challenges at the intersection of pediatric and environmental health through another approach are proposed here. All proposed activities must be supported using FY 2015 funds, as it is unclear whether these funds will be appropriated in FY 2016.

What would the goals of the program be?

As described for the NCS above, the focus of the program will be on environmental influences on child health and development. To the extent possible, we would like to create a comprehensive program by using FY 2015 NCS funds to: (i) start compelling new initiatives, (ii) integrate projects within and across these initiatives that could deliver more than the sum of their component parts and/or (iii) enhance otherwise important (extant) programs by incorporating (more comprehensive) environmental assessments. There are three general initiatives that are being proposed, which are not mutually exclusive:

- Develop tools to enhance studies of environmental influences of pediatric diseases.
- Study the influence of environment on *in utero* development with the goal of identifying the "seeds" of future diseases and conditions.
- Expand examination of environmental influences on later child development by leveraging extant programs.

As tool development would facilitate research in the remaining two areas, we view Initiative 1 as a core effort and would launch multiple complementary projects within this initiative during FY15. Strategically, we will then outline a number of projects in the remaining two initiative areas as examples of what could be accomplished over time, and then implement only a small subset of projects from this larger set of possibilities in FY15, with the promise of pursuing others in future years, if funds were made available.

Why is a trans-NIH strategy needed to achieve these goals?

In keeping with the spirit of the NCS, the proposed program necessitates a trans-NIH strategy to be successful. While NIEHS and NICHD clearly are the two Institutes and Centers (ICs) most vested in understanding environmental influences and their impact on pediatric health and development, this topic overlaps with the missions of numerous ICs. Further, the complexity required to undertake such a program will require transdisciplinary efforts.

What initiatives might form the strategic plan for this topic?

Initiative 1: Develop new tools to enhance the measurement of a broad range of environmental exposures throughout development to increase understanding of the intersection of environment and genes.

- (New Project) *Biosensor Based Integrated Health Monitoring Systems for Environmentally and Behaviorally Related Pediatric Health Problems* (NIBIB, NIEHS, NIA, NICHD, NIGMS) – Initiative to develop wearable, in-household, in-community, and *in utero* sensors to couple standardized data to a wireless integrated health monitoring system. The sensors will be designed for application-specific sensing of various parameters and produce a rich bio-database for ease of analysis. The approaches and devices that emerge from this project will be used to expand and strengthen a number of extant and future clinical research studies to produce a very rich bio-database that can be mined across a large number of target parameters (location, age, exposure

history, genomics profiles, EHR data) to help establish and gain new insights into environmental determinants of pediatric diseases.

- (New Project) Children's Health Exposure Analysis Resource (CHEAR) (NIEHS) – Launch a new NIEHS program, CHEAR, that is designed to provide an infrastructure for the characterization and integration of environmental exposures in banked or fresh specimens in studies of children's health across studies. The program will provide technical expertise, validation of measures, data integration, and a system for sample tracking. However, the goal would be to go well beyond current, "classical" exposure methodology to develop unique analytical tools to interrogate samples in an unbiased manner and feed into data streams generated by other efforts, including the biosensor project described above.
- (Expansion of Extant Program) Clinical Validation of Patient Reported Outcomes (PROMIS) Items Banks in Children (NIAMS) – Expand the PROMIS CF initiative by validating PROMIS measures for children with inclusion of environmental components (albeit more related to environmental stressors as opposed to substances in the environment). This program will utilize existing pediatric banks for several chronic conditions (e.g., obesity, asthma, juvenile arthritis).

Initiative 2: Enhance understanding of in-utero development, and effects on post-natal development to illuminate the "seeds" of chronic disease, developmental origins of health and disease, and provide a critical window to research. In each of these efforts, ensure the appropriate representation of the most vulnerable populations, including members of racial and ethnic minority groups.

- (Expansion of Extant Program) Tox21 Developmental Toxicity Program (NCATS) – Expand the Tox21 program to understand the effects of environmental chemicals on human development, both *in utero* and postnatally. Derive biological signatures (i.e., developmental pathways and cellular phenotypes) of environmental chemicals using the 10,000 chemical collection. The program would simultaneously invest in developing more efficient and scalable test platforms and computational tools.
- (Expansion of Extant Program) Human Placenta Project Expansion (NICHD) – Develop methods to assess human placental function and metabolism in real-time. New resources also would be used to include studies on the impact of environmental influences on placental function and *in utero* development.

Initiative 3: Expand examination of environmental influences on later child development by leveraging extant programs.

- (Expansion of Extant Program) Supplemental Support for Existing Children's Environmental Health Cohorts (NIEHS) – This program aims to add proteomic, metabolomics, and epigenetic analyses to existing cohort studies, and enhance GxE interaction studies. Resources available through the proposed CHEAR network also will be utilized.

If a program or multiple initiatives on this topic achieved its objectives, what would be the impact?

The NIH will employ the proposed initiatives to address the critical goal of understanding the impact of environmental influences on pediatric health and development. The overarching goal of the FY15 NCS funds will be to develop novel and technologically advanced tools to enhance the measurement of environmental exposures throughout development as a means to increase understanding of the intersection of environment and genes. These new tools will collect standardized, integrated data that can readily be shared and analyzed. A further focus will be on gathering information to better understand developmental pathways and influences, and to incorporate an environmental component to existing pediatric studies. In doing so, the data collected from this initiative will not only be informative, but also will rely on uniform, standardized collection methods to advance the field of pediatric environmental health.