May 15, 2007

Dr. Kristina Thayer National Institute of Environmental health Sciences Research Triangle, N.C. <u>Thayer@niehs.nih.gov</u>

Dear Dr. Thayer:

I am writing to express my concern about the April 6, 2007 Review Panel Report on the Centers for Children's Environmental Health and Disease Prevention Research Program.

During almost 10 years of the current Children's Centers program, remarkable progress has been made in identifying the etiologic factors of some of the most important childhood diseases, including asthma and other respiratory diseases, autism and other neurodevelopmental impairments, and birth defects, and of the effects on children of common environmental toxins like air pollution, pesticides, lead, endocrine disruptors and second hand smoke exposure. Progress has been possible in part because NIEHS has invested in the creation of population-based cohorts of children and of repositories of biological and environmental samples that have been used by epidemiologists, basic scientists, and molecular epidemiologists in transdisciplinary approaches to the investigation of environmental effects. The Community Outreach and Translation Cores have facilitated and promoted access to the scientific results of the Centers' efforts that have translated into both primary and secondary prevention. Examples include the reliance of regulators on Center results in phasing out harmful organophosphate insecticides and in setting standards for air pollution that affect the health of millions of children.

The Report reflects a lack of appreciation of the importance of the NIEHS investment in population studies in the development of a strong scientific basis for primary prevention in children's environmental health. The two examples of how the new centers would look after the radical restructuring recommended by the reviewers are illustrative. In one, an existing population study would be the target of opportunity for basic scientists interested in pesticide-induced DNA methylation. In the other, existing case-control studies would be linked to examine a common mechanism for different childhood diseases. There are some important historical examples of progress that has been made by exploiting opportunities using existing population resources. However, this approach is no substitute for developing research populations in which there is careful consideration of the covariates relevant to environmental exposures and of the exposure assessment necessary to do credible population studies of environmental causes of disease. In the second example, environment is a topic that is "eventually" addressed and appears to be an afterthought to the investigation of mechanism. NIEHS has had the foresight to develop cohorts of children designed to evaluate the effect of environmental exposure, and I believe the proposed restructuring to focus on basic science to the exclusion of carefully planned population studies is a step backward that may result in findings that do not provide the scientific foundation required for public health translation.

The Report also reflects a lack of appreciation of the importance of primary prevention and an apparent lack of understanding of the scope of secondary prevention in environmental health. It argues for a "move beyond exclusive primary prevention (i.e. reducing exposures) toward... the development of therapeutics". It is generally recognized that the largest environmental health benefits have resulted from reducing exposures, and the Report's proposed restructuring of the Centers that relegates this approach to a secondary role requires strong evidence to support the proposal that the reviewers have not provided. A shift away from primary prevention is also arguably a dangerous precedent that could relegate NIEHS to a less relevant role in protecting the country's children. The reviewers apparently consider drug discovery to be secondary prevention, but not the intervention trials to reduce exposure that have been a major focus of several Centers, for example the study of model programs for reducing exposure to indoor asthma triggers in preventing asthma exacerbation that have been developed by the community based participatory research projects.

The proposed restructuring of the program to require three interrelated existing R01s with a focus on basic science as a prerequisite for developing a new Center is problematic in several ways. The timing of funding resulting from reviews on different cycles from different study sections limits the feasibility of this approach. In addition, establishing multidisciplinary teams through independent R01s is not consistent with the goals of integrated research that the reviewers purport to promote. It is worth noting that the current structure of the Centers requires that each center have a basic science project and that this requirement has fostered the transdisciplinary approaches that have been important in making scientific progress without relegating population-based approaches to environmental science to the status of an optional enhancement to the basic science.

Finally, I would like to comment on the Reports' treatment of the Community Outreach and Translation Cores. These Cores have been critical to the success of many Centers, as acknowledged by the Report, and should be supported in any new Center program.

Sincerely,

Rob McConnell, M.D. Professor of Preventive Medicine Keck School of Medicine University of Southern California