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**Advancing Neurodevelopmental Evaluation in Children: An Interdisciplinary  
Scientific Approach**

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***Final project summary – December 2009***

**Background:** With published research suggesting that growing numbers of children are affected by an array of neurodevelopmental disorders, questions regarding etiology will continue to be raised. These questions can be addressed in part by well-designed epidemiological studies. While the uses of neurodevelopmental function tests in studies of environmental chemicals and pediatric neurodevelopmental disorders have been reviewed, a comprehensive critical examination of methodologies commonly used in past studies has not been conducted. There are limitations associated with currently used tests and many neurodevelopmental tests are available that have not been used in the environmental chemical study arena. In addition, differences in methods for conducting neurodevelopmental epidemiologic studies of environmental chemicals can lead to difficulties in performing weight-of-evidence assessments.

**Objectives:** The objectives of this project were to:

- (i) critically review commonly used neurodevelopmental tests in epidemiological studies of associations between environmental chemical exposure and adverse health effects, and identify tests that should be considered for use in future studies,
- (ii) evaluate the feasibility of conducting a systematic review of environmental epidemiology studies of an exemplar chemical class,
- (iii) hold an interdisciplinary workshop to discuss innovative paths forward for neurodevelopmental testing, and
- (iv) develop guidelines and/or criteria for selection, administration, and interpretation of neurodevelopmental tests in studies of environmental chemical exposures.

**Results:** We reviewed the outcome measures used to assess neurodevelopmental effects of environmental toxicants using PCBs as a case study. While a large number of global and more narrowly-focused measures have been used, newer measures as well as revised core measures warrant consideration for inclusion in new studies due to their superior psychometric properties. In addition, entirely new domains should be explored due to their importance in real world functioning

and/or the possibility that they would be sensitive to toxicants' effects (e.g., adaptive functioning, executive functioning, articulation). The most commonly documented psychometric properties for measures are only indirectly relevant to the main objectives of epidemiological studies of toxicants. Our review of measures revealed that the most relevant psychometric features for measures used in toxicant studies (such as retest stability or sensitivity to exposure effects) have been reported only rarely. We also note that the selection of covariates in these studies has been largely focused on demographics and confounders, whereas the inclusion of other covariates (e.g., IQ) that are highly correlated with the dependent variable (e.g., language) would further improve estimation of the effects of toxicants. In terms of the feasibility of conducting a systematic review across studies, we found that differences in methods for estimating exposures and in reporting of outcomes preclude conducting a quantitative systematic review across the cohorts (based on a case study of the PCBs literature).

**Conclusions:** A series of recommendations were developed to enhance the state-of-the-science of neurodevelopmental function testing in environmental epidemiologic studies. These are described in a series of publications and are summarized here:

- (i) Future research should include comparable measures used by past researchers; otherwise, our ability to conduct weight-of-evidence assessments will be hindered.
- (ii) A broad effort is needed to ensure that raw study data are available for weight-of-evidence assessments.
- (iii) An interdisciplinary panel should develop guidelines for best practices for selection of statistical methods for analyzing data from the complex data sets generated by neurodevelopmental epidemiologic studies.
- (iv) Study publications should be accompanied by archived tables of summary statistics, such as unadjusted correlations, means, and standard deviations, perhaps augmented by a description of patterns of missing data.
- (v) A formal set of reporting guidelines is needed to help the design of future studies, as has been done with clinical trials, studies of diagnostic assessment tools, and medical epidemiological studies (<http://www.strobe-statement.org/>; <http://www.stard-statement.org/>; <http://www.consort-statement.org/>).

Publications:

- Youngstrom E, LaKind JS, Kenworthy L, Lipkin PH, Goodman M, Squibb K, Mattison DR, Anthony BJ, Gutermuth Anthony LG. 2010. Advancing the selection of neurodevelopmental measures in epidemiological studies of environmental chemical exposure and health effects. *Int J Environ Res Public Health*. 7:229-268.
- Goodman M, Squibb K, Youngstrom E, Gutermuth Anthony L, Kenworthy L, Lipkin PH, Mattison DR, LaKind JS. Using systematic reviews and meta-analysis to support regulatory decision-making for neurotoxicants: lessons learned from a case study of PCBs. Submitted to *Environ Health Persp*. December 2009.