**Innovation in Risk Assessment—Using Time-Dependent Models to Interpret Neurobehavioral Toxicity Studies**

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Estimates indicate that approximately 25% of the chemicals used in the United States are neurotoxic (OTA, 1990), although many of them have not been tested for this endpoint. To aid in evaluating these chemicals, the EPA has adopted the functional observational battery (FOB) as a standardized list of noninvasive tests designed to evaluate sensory, motor, and autonomic responses of the nervous system in response to chemical exposure. Data from these studies represent repeated measurements of individual animals over time to determine the magnitude and duration of adverse effects. The dose-response modeling of such neurotoxicity data poses challenges that include dealing with repeated measurements, multiple endpoints with both continuous and ordinal scales, and time dependence of risk characterization. To support the understanding and correct interpretation of this disparate information, the Agency has developed new statistical methods and models for the estimation of benchmark doses (BMDs) from such time-dependent studies. Models were developed by Dr. Yiliang Zhu of the University of South Florida in conjunction with NCEA, NHEERL and OPP personnel. These models allow application of the benchmark dose method, a more quantitative approach, to behavioral neurotoxicity data, thus allowing for better use of data generated from these noninvasive tests. An external review panel concluded that these models will be useful for determining BMDs from neurobehavioral data, and work is currently underway to further develop and expand these models for use on other types of repeated-measures data. Our long-range goal is to support risk assessors across EPA programs and regions as well as assessors in states and in the international community by incorporating these models into the existing BMD software offered by EPA [www.epa.gov/NCEA/bmds.htm].