OECD/EFSA Workshop on Developmental Neurotoxicity (DNT): The use of non-animal test methods for regulatory purposes

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Alternative Test Methods for Developmental Neurotoxicity: A History and Path Forward Questions

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Exposure to environmental contaminants is well documented to adversely impact the development of the nervous system. However, the time, animal and resource intensive EPA and OECD testing guideline methods for developmental neurotoxicity (DNT) are not a viable solution to characterizing potential chemical hazards for the thousands of untested chemicals currently in commerce. Thus, research efforts over the past decade have endeavored to develop cost-effective alternative DNT testing methods. These efforts have begun to generate data that can inform regulatory decisions. Yet there are major challenges to both the acceptance and use of this data. Major scientific challenges for DNT include development of new methods and models that are "fit for purpose", development of a decision-use framework, and regulatory acceptance of the methods. It is critical to understand that use of data from these methods will be driven mainly by the regulatory problems being addressed. Some problems may be addressed with limited datasets, while others may require data for large numbers of chemicals, or require the development and use of new biological and computational models. For example mechanistic information derived from in vitro DNT assays can be used to inform weight of evidence (WoE) or integrated approaches to testing and assessment (IATA) approaches for chemical-specific assessments. Alternatively, in vitro data can be used to prioritize (for further testing) the thousands of chemicals used in commerce for which there is no data at all on their potential to cause DNT. The focus of this problem-dictated strategy is that testing is driven by decision-making needs, and the amount of resource utilization is adjusted to provide efficient and timely data to address the needs. As the health and environmental impacts of the decision increase, data needs increase, resource use increases, and the need increases for reduced scientific uncertainty in estimates of risk. Recent advances in testing methods and models hold great promise for the development and use of efficient testing strategies for DNT that are capable of initial prioritization and screening, hazard characterization, and hazard prediction. *This abstract does not necessarily reflect U.S. EPA policy.*

Both of these needs require the development and use of a battery of DNT in vitro assays (and possible inclusion of alternative species). However, this battery must be designed in a fit for purpose manner for the above two different requirements. This means, for example, that use of the battery for screening and prioritization purposes may necessitate a broader acceptance of uncertainty in the assays and resulting data compared to use in chemical specific assessments. The latter will require a higher degree of validation due to regulatory decisions that may restrict chemical production and use, while the former will only suggest that further testing may be required. Thus, as development of the battery proceeds, the use of the assays, and the state of their validation may vary depending on problem formulation, i.e. screening purposes versus hazard identification and risk assessment.

In order to accelerate the development and facilitate regulatory use of such tools, a workshop is co-organized by EFSA and the OECD.