Standardization of SOPs to Evaluations: Impacts on Regulatory Decisions using Learning and Memory as Case Studies

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In an era of global trade and regulatory cooperation, consistent and scientifically based interpretation of developmental neurotoxicity (DNT) studies is essential, particularly for non-standard assays and variable endpoints. Because there is flexibility in the selection of test method(s), standardization can be especially challenging for learning and memory tests required by US EPA and OECD DNT test guidelines (chemicals and pesticides) and recommended in ICH prenatal/postnatal guidelines (pharmaceuticals). No one cognitive test is clearly superior, yet detection of treatment effects may depend on this choice. An understanding of the purpose behind the tests and expected outcomes is critical, and attention to elements of experimental design, conduct, and reporting can improve data collection by the investigator as well as accuracy and consistency of interpretation by regulatory evaluators. This understanding also directs which information must be clearly described in study reports. Standard operating procedures (SOPs) may contain important experimental features, but if not clearly reflected in thorough report submissions there may be questions and misunderstandings by evaluators which could impact risk assessments. A practical example of learning and memory tests will be presented to provide insights into important experimental variables, reporting methods, and approaches for data assessments. Cognitive functions most often tested in DNT guidelines studies include associative, positional, sequential, and spatial learning and memory in weanling and adult animals. These complex behaviors tap different brain areas and develop at different rates. The relative involvement of different neural systems depends on the specific task; however, there is considerable overlap across brain areas during the process of acquisition (learning) and consolidation of memory. Evaluation should include integration of treatment data including performance assessments (motor, sensory), control data (concurrent, historical, positive), and additional measures of neuro- or other toxicity. Doing so can empower consistent and defensible risk evaluations. These considerations provide a stronger scientific basis for standard evaluation approaches for review and interpretation of DNT studies. *This is an abstract of a proposed presentation and does not reflect US EPA policy.*