Application of a Controlled Vocabulary to Curated Databases of In Vivo Developmental Toxicity Data

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Developing alternatives to traditional in vivo developmental toxicity tests presents many challenges. First, reference data from high-quality studies meeting specific regulatory guideline-like criteria must be identified and compiled. These data also must be standardized and harmonized so that the in vivo endpoint descriptions are sufficiently homogeneous to be integrated across sources and ultimately provide a benchmark for silico and in vitro model endpoints. This requires use of knowledge organization systems (KOS) such as controlled vocabularies and ontologies. The U.S. National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) extracted data from in vivo mammalian developmental toxicity studies performed by the NTP and from the available relevant chemical registration dossiers available from the European Chemicals Agency. NICEATM used the National Library of Medicine's Unified Medical Language System's controlled vocabulary in a first pass to standardize extracted study endpoints as initial mapping to KOS. Mapping to KOS enables data accessibility and cross-species comparisons that will increase the usability of these developmental toxicity data. The curated dataset will be made available to the public as a resource for evaluating the performance of alternative methods that measure key events in developmental toxicity pathways. In parallel, NICEATM is coordinating the analysis of data currently being generated in multiple laboratories using an embryonic zebrafish model of developmental toxicity. As part of this effort, these data will undergo a similar process to the in vivo mammalian studies, including standardization and application of a controlled vocabulary. Using the controlled vocabularies and a multi-species ontology such as Uberon, endpoints between the two methodologies will be compared and used to evaluate the usefulness and limitations of zebrafish models as an alternative to in vivo mammalian developmental toxicity tests.

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