Towards Refined Use of Toxicity Data in Statistically Based SAR Models for Developmental Toxicity

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Keywords: toxicity database, developmental toxicity, predictive toxicology, SAR, QSAR

In 2003, an International Life Sciences Institute (ILSI) Working Group examined the potential of statistically based structure-activity relationship (SAR) models for use in screening environmental contaminants for possible developmental toxicants (Birth Defects Research Part A 70:902-911 2004). That Working Group concluded that the predictive capacity of such models would be enhanced with adoption of refined methods for utilizing toxicity data to inform model training sets. Two particular methodological challenges were identified: i) defining the "activity" (i.e., the specific effect to be modeled); and, ii) characterizing activity in an objective and transparent manner. This poster reports on a follow up effort to address those challenges, in which an interdisciplinary group of toxicologists, database developers, and SAR modelers produced a prototype database of published developmental toxicity data from C-section studies in the rat. A prime characteristic of the prototype is its robust and objective data entry scheme, which avoids incorporation of high level summaries or judgments regarding study data. At the same time, the scheme provides potential database users with flexibility to combine specific developmental endpoints into broader, biologically-related groupings. The prototype demonstrates an approach to data collection that is relevant to other types of toxicity characterized by a broad array of endpoints. Another key aspect of this effort is its attempt to tie in to related activities (e.g., efforts to adopt an internationally harmonized glossary of developmental abnormalities), and efforts to generate standardized open access schemas for accessing toxicity data that are linked to chemical structures (ToxML, DSSTox, etc.). Such collaboration is intended to generate synergy across related efforts in computational toxicology. Ultimately, the various individual efforts, which address a range of toxicities (neurotoxicity, developmental toxicity, carcinogenicity, etc.) and a range of study types (in vivo, genomic, etc.), provide pieces of information that, when used together, can potentially solve the puzzle of predicting human response to chemical exposures.

This project was sponsored by Health Canada, Existing Substances Division.

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