ICE Tools to Facilitate PBPK Modeling and IVIVE for Various Exposure Scenarios

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Physiologically based pharmacokinetic (PBPK) modeling and in vitro to in vivo extrapolation (IVIVE) are computational methods that help put in vitro assay data into a human-relevant context to facilitate comprehensive chemical safety assessments. The Integrated Chemical Environment (ICE) provides easy and open access to high-quality curated data and interactive PBPK modeling and IVIVE tools to explore and contextualize chemical bioactivity. The PBPK tool uses pharmacokinetic models from the U.S. Environmental Protection Agency's high throughput toxicokinetics (httk) R package and other pharmacokinetic parameters to predict dynamic plasma and tissue concentrations resulting from given external doses. The IVIVE tool uses both experimental and predicted parameter information to translate in vitro activity concentrations to equivalent in vivo dose estimates. This tool gives users the option to either provide their own data or use data provided in ICE. Both PBPK and IVIVE tools were recently updated to accommodate the latest release of the httk R package. ICE data can be further explored with the Search tool, which provides summary-level information of chemical bioactivity, curated reference data, and in vitro assay data mapped to mechanistic targets and various modes of action. This presentation will highlight how ICE can be utilized to support PBPK modeling and IVIVE under various exposure scenarios, including intravenous injection, oral ingestion, gas inhalation, and gestational exposures. This project was funded with federal funds from NIEHS, NIH under Contract No. HHSN273201500010C.