Presentation Abstracts and Background Materials

SCIENTIFIC ADVISORY COMMITTEE ON ALTERNATIVE TOXICOLOGICAL METHODS

Session 4: Update on NICEATM Computational Resources
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NICEATM's Integrated Chemical Environment (ICE; https://ice.ntp.niehs.nih.gov/) provides user-friendly access to data and tools needed to explore and contextualize chemical bioactivity profiles. ICE contains curated in vivo and in vitro toxicity testing data and experimentally measured physicochemical property data, gathered from publications, publicly available databases, or validation studies. ICE also contains computationally generated in silico toxicity models and physicochemical property and environmental fate parameter predictions from the OPEn structure–activity/property Relationship App (OPERA; https://github.com/NIEHS/OPERA) open-source/open-data suite of QSAR models, including applicability domain and confidence assessments.

Updates to ICE include substantial improvements to interactive computational tools that can characterize, analyze, and predict bioactivity for user-defined chemicals. The ICE Search tool provides the opportunity to select and merge datasets for user-defined, or established, lists of chemicals and mixtures, yielding summary-level information with new visualization features, additional curated reference data, and bioactivity details mapped to mechanistic targets and modes of action, which can be automatically ported to other tools within ICE. In vitro activity can now be examined using the Curve Surfer tool, where the user can explore concentration-response relationships of curated high-throughput screening assays. The new Physiologically Based Pharmacokinetics (PBPK) tool predicts tissue-level concentrations resulting from in vivo doses. The updated In Vitro–In Vivo Extrapolation (IVIVE) tool allows users to translate in vitro activity concentrations to equivalent in vivo dose estimates for an expanded list of exposure routes. The Chemical Characterization tool displays distributions of physicochemical properties, bioactivity- and structure-based projections relative to large chemical libraries, and consumer product use cases from a recently developed interface that relies upon information from the EPA's Chemicals and Products Database (CPDat). Chemical Quest, another new ICE feature, allows users to query the ICE database for structurally similar compounds based on molecular fingerprints. This includes >800,000 chemicals from EPA's DSSTox database with OPERA predictions. These similar chemicals can then be used to query other ICE tools and datasets. Additionally, ICE links to the NTP's Chemical Effects in Biological Systems and the U.S. Environmental Protection Agency's CompTox Chemicals Dashboard and Chemical and Products Database, expanding ICE's capacity to examine and compare chemicals based on physicochemical properties, bioactivity, and product use categories.

Background

- An Integrated Chemical Environment to Support 21st-Century Toxicology
- An Integrated Chemical Environment with Tools for Chemical Safety Testing

- Saagar – A New, Extensible Set of Molecular Substructures for QSAR/QSPR and Read-Across Predictions
- NICEATM Integrated Chemical Environment v3.4
- HTTK: EPA's Tool for High-Throughput Toxicokinetics
- EPA: Chemical and Products Database (CPDat)