The Integrated Chemical Environment: Tools and Data to Support Toxicity Assessments

S Bell1, J Phillips2, N Cariello1, P Ceger1, K Chang1, F Hermes1, A L Karmans1, K Mansouri1, E McAfee2, R Rai1, D Allen1, W Casey3, N Kleinstreuer1

1ILS, RTP, NC, USA; 2Sciome LLC, RTP, NC, USA; 3NIH/NIEHS/DNTP/NICEATM, RTP, NC, USA

The Integrated Chemical Environment

<table>
<thead>
<tr>
<th>Users</th>
<th>Resources</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method Developers</td>
<td>High-Quality Data</td>
<td>- Identify opportunities to develop new methods</td>
</tr>
<tr>
<td>Chemical Producers</td>
<td>Reference Chemicals</td>
<td>- Compute method performance</td>
</tr>
<tr>
<td>Risk Assessment</td>
<td>Computational Tools</td>
<td>- Identify data gaps</td>
</tr>
</tbody>
</table>

ICE provides free online access to:
- Curated in vivo and in vitro data related to toxicity testing
- In silico toxicity predictions and chemical property data
- Curated lists of chemicals with defined assays (reference chemical lists)
- Computational tools related to chemical characterization and predicting toxicity
- Updated tools
- Expand your search by adding chemicals in ICE with the same QSAR-ready structures

New Features in ICE 2.0:
- FAIR (findable, accessible, interoperable and reusable)
- Data analysis: allows characterization of data using online workflows
- Results exploration: enables dynamic, graphical extrapolation from chemical quick list and/or entering CASRN
- Data integration: brings together available data, including data on formulations
- Machine learning: includes data accessible, interoperable and reusable

ICE supports:
- Data integration: brings together available data, including data on formulations
- Results exploration: enables dynamic, graphical extrapolation from publication-quality graphics
- Data analysis: allows characterization of data using online workflows
- FARR (findable, accessible, interoperable and reusable) data access

ICE Integrator

Machine Learning

Use the machine learning tool for hypothesis generation and to explore different machine learning approaches using ICE data. Selected endpoints (for classification and regression modeling) and algorithms are available through ICE to facilitate ease of use by those with limited background in computational toxicology.

Performance statistics of the model including the confusion matrix (classification) and RMSE (regression) are available to compare method performance

Stand-alone version available for use with custom datasets: F https://github.com/NIEHS/Machine-Learning-Pipeline

Chemical Space Characterization

Leverage ICE models to characterize a user-supplied chemical list, getting information on the chemical space covered based on different physicochemical properties.

Future plans for Chemical Characterization tool:
- Generate physchem and other structure-based predictions from user-provided chemical lists
- Prediction of chemical parameters for use in modeling (example: fraction unbound, pKa)
- Machine learning tool uses imputation and/or removes sparse assays/chemicals to permit use of methods requiring complete cases

In Vivo to In Vivo Extrapolation

Use high-throughput in vitro data available from ICE to estimate external dose.

Choose from:
- One-compartment pharmacokinetic (1C PK) model including population simulation
- Two-three compartment physiologically-based pharmacokinetic (PBPK) models
  - 3C Glu: incorporates gut glucuronidation for BPA-family compounds
  - 3C HTTK: uses the httk package model
- Three-compartment models include gut, liver, and kidney Rat and human predictions

Contact Us

Visit ICE https://ice.niehs.nih.gov/

To get announcements of ICE updates and other NICEATM activities, visit the NIH mailing list page for NICEATM News at https://list.nih.gov/cgi-bin/wa?A1=1

Acknowledgements

ICE has been funded in whole or in part with federal funds from the National Institute of Environmental Health Sciences, National Institutes of Health, Department of Health and Human Services, under Contract No. HHSN2762010010C.

The views expressed above do not necessarily represent the official positions of any federal agency. Since the poster was written as part of the official duties of the authors, it can be freely copied.