Strategic Roadmap Goal

Foster the use of efficient, flexible, and robust practices to establish confidence in new methods

- Identify and collate sources of high-quality human toxicological data.
- Create centralized data access points that are publicly available and easily accessible.
- Actively solicit the submission and collation of parallel data from animal studies and alternative methods.
- Leverage partnerships and complimentary initiatives
  - FAIR Principles, NIH Data Commons, NCATS Data Translator, EPA Chemistry Dashboard, NLM Databases, Biomed21 recommendations, SEND reporting, etc.
Developing Web-based Data Resources

- Who needs them?
  - NTP & ICCVAM scientists
  - Researchers from other institutes/companies
  - Regulators looking for information
  - Assay/model developers looking for data (or opportunities)

- What do they need?
  - Data supporting chemical evaluation and model development
  - High quality and open access
  - Context and meta data available
  - Centrally available (one stop shop)
  - Easy to use, free, transparent
Integrated Chemical Environment: ICE

https://ice.ntp.niehs.nih.gov/

- **Data integrator:**
  - Structured format designed for ease of use
  - Allows access to data for multiple regulatory endpoints
  - Query by CASRN or established reference chemical lists
  - Flexible, exportable results

- **Workflows:**
  - Property predictions, Chemical space characterization, IVIVE, Mechanistic models, AOP mapping

Bell et al. 2017 EHP
Goals of ICE

• Uphold FAIR principles for ICCVAM Data

• Provide intuitive access to high quality (curated) data and tools to support:
  – chemical evaluations,
  – data integration, and
  – model development

• Enable wider community to engage in the use of alternative and computational approaches for assessing chemical safety
Integrated Chemical Environment (ICE)
https://ice.ntp.niehs.nih.gov/

- Provides FAIR for ICCVAM data
- Communication with other applications and data systems
  - Chemical Effects in Biological Systems (CEBS)
  - NIEHS Data Commons
  - EPA Dashboard, CTD, NLM databases, etc.

- Significant ongoing efforts to improve data and tool utility
  - Intuitive user interface
  - Web-based visual analytics
  - Improved search functionality
  - Improving capture of data provenance
  - Web application programming interfaces (APIs)
  - Interactive web-based workflows
  - Many more...
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<th>Endpoint</th>
<th>In vitro</th>
<th>In vivo animal</th>
<th>In vivo human</th>
<th>In silico</th>
<th>Chemicals (+ AIs)</th>
<th>Formulations</th>
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Data Curation Process

Example: Uterotrophic Data (endocrine in vivo)

- Systematic literature review of publically available data
- Extract all study protocol and effect details
- Identify chemical activities measured in “guideline-like” uterotrophic studies
- Identify a subset of in vivo reference chemicals

Kleinstreuer et al. 2015 EHP
https://ice.ntp.niehs.nih.gov/
Backup Slides

Download reference chemical lists
Filter results
ICE Workflows

NICEATM and partners have generated several software programs and workflows designed to improve predictions of chemical safety. Currently available workflows:

- Physicochemical property predictions
- Skin sensitization potency
- AOP overlay and ontology

**Physicochemical property predictions**

Generates in silico predictions of octanol-water partition coefficient (logP), water solubility (logS), boiling point (BP), melting point (MP), vapor pressure (logVP), and bioconcentration factor (logBCF) using QSAR models developed in R. These constants are useful in the calculation of some modeling parameters as well as for chemical characterization.


Software Requirements: Requires R version 3.4 or above

How to access: [Physicochemical Property Prediction Github](#)

Data inputs: a data frame with pdCheM descriptors for each chemical to be predicted

Returns: a data frame with predictions of the desired physicochemical property for each chemical
Reference Chemical Lists

Reference chemicals are chemicals that cause a specific well-characterized biological effect and therefore can be used to assess the performance of an assay designed to measure that effect. NICEATM compiled reference chemical lists in the context of assay validation studies conducted or sponsored by NICEATM and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM). These lists are available on the NICEATM website. "ICCVAM reference lists" were compiled through ICCVAM activities or working groups, while the other lists were developed for studies conducted by NICEATM or other partners. Reference chemical lists may be issued as part of protocols or best guidelines describing accepted procedures for specific tests, or in performance standards documents describing essential test method components for tests intended to measure similar biological outcomes. Some reference chemical lists are designed to assess the performance of assays conducted for a specific regulatory purpose, and thus may not be entirely applicable for assessing the performance of similar assays applied to different endpoints or used in different contexts. Please consult the background references listed below to determine the suitability of these reference chemical lists for a particular purpose.

Download Reference Chemical Lists

The reference chemical lists used in ICE with the supporting information for the specified biological effect are available here for quick download.
Under Development: Formulations

Download full data
Under Development: Formulations

Send the CASRNs to the Integrator
Interoperability Across Systems

Consistent & compatible web-APIs

CEBS
ICE
Data Commons
Others...
NIEHS Data Systems

Consistent data set access & retrieval

CSS Dashboard
PubChem
Many others...
TOXNET
External Data Systems
Current timeline

Initial launch (V1.0) March 2017, SOT annual meeting
- Launch of web resource highlighting the data integrator

Update (V1.1) July 2017
- Launch of tools/workflows section
- Data updates

Update (V1.2) January 2018
- Data updates

Update (V1.3) March 2018
- Data updates
- Interactive workflows
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For any comments please contact:
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https://ice.ntp.niehs.nih.gov/