An Integrated Chemical Environment to Support 21st Century Toxicology

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**Integrated Chemical Environment**

*What is ICE?*

ICE is the Integrated Chemical Environment, which houses:

- High quality, curated in vivo, in vitro and in silico data from the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) and partners
- Reference chemical lists (chemicals that can be used as a reference for a given assay or endpoint) and associated data
- Computational tools and workflows (Summer 2017)

**What need does ICE fill?**

NICEATM developed ICE to:

- Provide a central location for computer-friendly versions of NICEATM data and computational models
- Facilitate data use by NICEATM stakeholders
**What can ICE do?**

Currently ICE supports:

- Data integration: bringing together data from different endpoints and experiments for comparison
- Results exploration: dynamic, graphical exploration of query results with capability to refine within query results
- Data accession: obtaining reference chemical lists and supporting data

Resources available soon (Summer 2017):

- Data analysis: downloadable computational tools and workflows to support test method development

**Search by Chemical and Integrate Data from Multiple Assays**

**Querying ICE**

ICE data are searchable by chemical and/or assay:

**Select chemicals**

- Input user-defined CASRNs
- or
- Select reference chemical lists to combine with your custom list or use on their own
- or
- Search selected datasets for all chemicals in ICE by leaving the input chemical field blank
- Chemicals not found in the results will be listed in a separate download file
Select assay data

- Data Integrator allows users to combine selected data streams of interest.
- Assay Selection field enables organization of data either by endpoints of regulatory interest or by data type (e.g., in vitro and in silico data)
- Queries are joined using “or” logic (e.g., ocular irritation or dermal irritation) by default
- Explore view allows users to dynamically refine queries
**What Data Are in ICE?**

**Available data**

- High quality, curated data from scientific literature sources
- Data used to support the reference chemical lists
- High-throughput screening Tox21/ToxCast data, curated by chemical QC results
- Computational predictions useful in developing models of health impacts or chemical characterization
- Other data useful in developing/evaluating new approaches or chemical safety

| Data Types                  | Availability        | Type     | Endpoint Examples                                      |
|-----------------------------|---------------------|----------|--------------------------------------------------------|
| Acute dermal toxicity       | October 2017 (tentative) | in vivo  | Rodent LD50                                            |
| Acute inhalation toxicity   | October 2017 (tentative) | in vivo  | Rodent LC50                                            |
| Acute oral toxicity         | March 2017           | in vivo  | Rodent LD50                                            |
| Acute oral toxicity         | March 2017           | in vitro | Basal cytotoxicity IC50                                |
| Androgenic activity         | March 2017           | in vitro | Androgen receptor binding and transactivation (agonist and antagonist activity) |
| Androgenic activity         | July 2017 (tentative) | in vivo  | Lowest effect level in the rodent Hershberger assay    |
| Androgenic activity         | July 2017 (tentative) | in silico| Androgen receptor pathway model scores                  |
| Curated HTS                 | March 2017           | in vitro | Assay ACC, AC50                                        |
| Dermal irritation           | March 2017           | in vivo  | Skin irritation/corrosion classification categories     |
| Dermal sensitization        | March 2017           | in vivo  | Mouse LLNA EC3 and human patch test lowest effect level |
| Dermal sensitization        | March 2017           | in vitro | KeratinoSens, DPRA, hCLAT results                      |
| Dermal sensitization        | July 2017 (tentative) | in silico| Binary sensitizer/nonsensitizer call                    |
| Estrogenic activity         | March 2017           | in vivo  | Lowest effect level in the rodent uterotrophic assay   |
| Estrogenic activity         | July 2017 (tentative) | in silico| Estrogen receptor pathway model scores                  |
| Ocular irritation           | March 2017           | in vivo  | Eye irritation/corrosion classification categories      |
| Physicochemical property predictions | March 2017 | in silico | LogP, logVP, logBCF, logS, melting point, boiling point |

AC50, concentration that increases activity by 50%; ACC, activity concentration at cut-off, a measure of the activity threshold for an assay response based on curve-fitting models; BCF, bioconcentration factor; DPRA,
direct peptide reactivity assay; EC3, in the LLNA, a test chemical concentration that produces a stimulation index of 3; hCLAT, human cell line activation test; HTS, high throughput screening; IC50, concentration that inhibits activity (in this context, decreases cell viability) by 50%; LC50, inhalation concentration expected to produce lethality in 50% of animals tested; LD50, dose expected to produce lethality in 50% of animals tested; LLNA, local lymph node assay; logP, octanol-water partition coefficient; logVP, vapor pressure, logBCF, bioconcentration factor; logS, water solubility

*In vitro basal cytotoxicity assays proposed for setting starting doses for in vivo acute oral toxicity studies.

**Explore Query Results**

*Interactive data exploration*

- ICE displays results graphically with real-time updated exportable graphics
- User can filter search results to further refine results based on assay and/or chemicals
- User can dynamically explore results or export them to Excel or tab delimited files
**Analyze and Export Your Query**

**Get data for your analysis**

- Quick view of full query results prior to exporting
- Export data in Excel and tab delimited files
- See which chemicals were not found
- Query parameters are documented in export screen to ensure queries can be replicated, supporting reproducibility
Workflows (Launching July 2017)

- Physicochemical property predictions
- Physiologically based pharmacokinetic and toxicokinetic models

Current Timeline

| 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)       | October 2017                 | Data updates                                           |
| Update (v1.3)       | January 2018                 | Data updates                                           |
| Update (v1.4)       | April 2018                   | Interactive workflows                                  |
|                     |                               | Data updates                                           |

Quarterly updates will be conducted with notification and details of updates on the ICE webpage and announced through NICEATM News.

Contact Us

Access ICE

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Read more about ICE!

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