National Institute of Environmental Health Sciences
Division of the National Toxicology Program

ICE Tools to Support Chemical Evaluations

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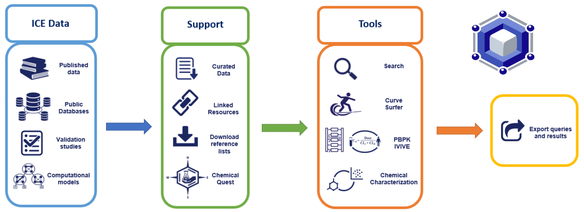
Abstract 4004/P702

Learn more about NICEATM and ICE tools at SOT:
- Rooney et al. Abs 4000 / P698
- Karmaus et al. Abs 4005 / P703
- Krishna et al. Abs 4683 / P729
- Mumtaz et al. Abs 5042 / P146

Case Study Introduction

The National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) developed the user-friendly Integrated Chemical Environment (ICE). ICE provides data and computational tools to aid in finding, analyzing, and contextualizing new approach methodologies (NAMs).

- ICE tools provide data to users in a computationally friendly format, and tools are accessible to non-subject matter experts.
- Extensive data curation ensures that users can retrieve, integrate, and analyze data that are trustworthy and ready to use.



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

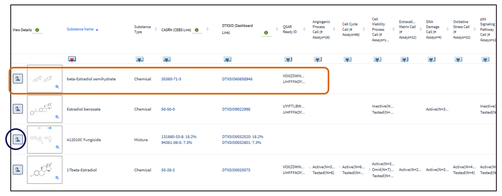
Read about ICE:
doi.org/10.1016/j.comtox.2021.100184

The case study presented herein demonstrates how ICE can be used to query and contextualize NAM data as well as identify data gaps and overcome data sparsity for chemical evaluations.

STEP 1: Search

The ICE **Search** tool enables selecting and merging data sets to query lists of chemicals and mixtures. Search results provide summaries that allow users to review available information for curated reference data and assays grouped by modes of action relevant to toxicity endpoints of regulatory significance.

Identify data-poor chemicals



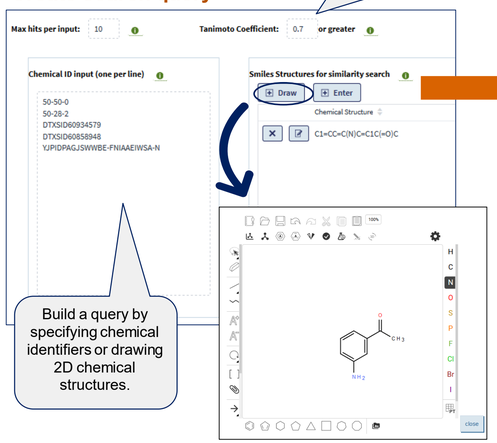
Detail View for chemicals and mixtures shows the structure and physicochemical properties for each substance and active ingredient, their activity in cHTS assays, and AC50/LD50 values for mixture active ingredients.

STEP 2: Expand Query and Characterize Chemicals

The ICE **Chemical Quest** tool allows users to query ICE for chemicals that are structurally similar to a target chemical. Similar chemicals are identified based on fingerprints generated from Saagar molecular descriptors (described in doi.org/10.1021/acs.chemrestox.0c00464).

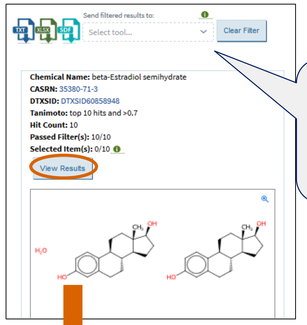
Create search query

Specify similarity stringency.



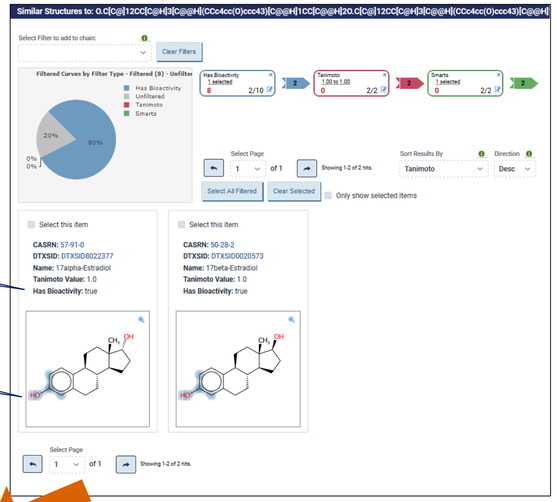
Build a query by specifying chemical identifiers or drawing 2D chemical structures.

Review identified analogs



Structural analogs can be examined and individually selected for export or sent to other ICE tools for further analysis.

Refine and select analogs

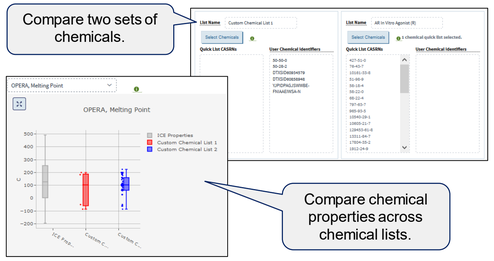


"has bioactivity" filtering limits results based on the presence of bioactivity data in ICE.

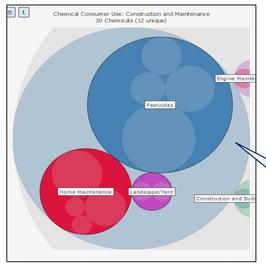
"SMARTS" strings filtering reduces results and highlights desired structural features on the chemical structure renderings.

The ICE **Chemical Characterization** tool provides context on chemical properties and chemical uses.

Compare two sets of chemicals.



Compare chemical properties across chemical lists.



View product use categories from the EPA Chemical and Products Database.

Compare chemicals and gain insight into chemical properties and uses

STEP 3: Contextualize NAM Data

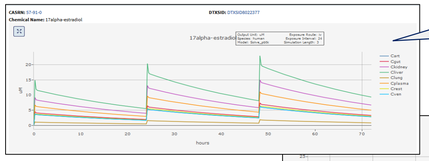
The ICE **In Vitro to In Vivo Extrapolation (IVIVE)** tool relates in vitro bioactivity concentrations to an in vivo dose exposure.

Relate in vitro concentration to in vivo dose

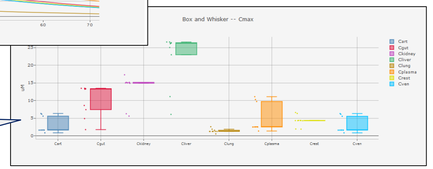
Output graphs allow users to compare extrapolations from in vitro data to relevant in vivo data sets.

The ICE **Physiologically Based Pharmacokinetics (PBPK)** tool generates predictions of tissue-specific chemical concentration profiles using models from the U.S. Environmental Protection Agency's httk package.

Relate external exposure to tissue biological response



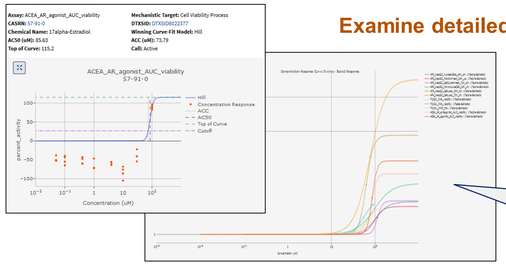
Curves show concentration of chemical over time after each dosing event.



Points in the box plot correspond to the compartment Cmax for each chemical.

The ICE **Curve Surfer** tool allows users to explore concentration–response relationships for curated high-throughput screening assays.

Examine detailed assay outputs



Overlay multiple curves to compare results from different assays or chemicals.

Acknowledgements

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