

# Providing Context to In Vitro High-throughput Screening Data via Annotation and Visualization Tools

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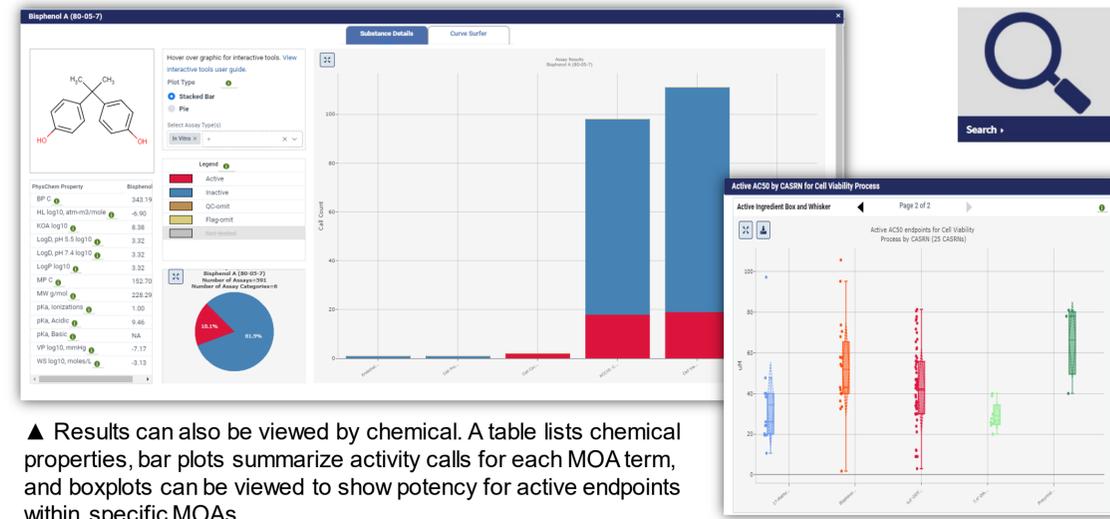
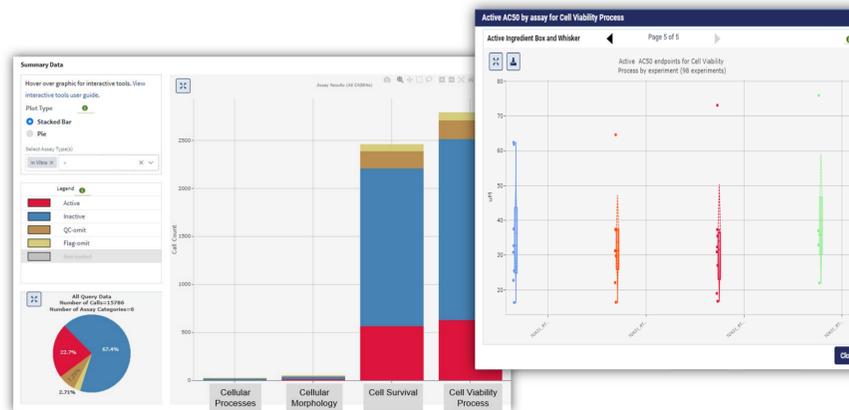
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## Introduction

- Building confidence in new approach methodologies (NAMs) for chemical evaluation requires access to reliable and relevant data that are openly accessible, and to interpretable tools easily used by all stakeholders.
- To address these needs, 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 NAMs.
- ICE data are processed to help leverage high-throughput screening (HTS) data, including data from Tox21 and ToxCast assays:
  - Curation helps users identify the most robust data.
  - Assays are annotated by experts using controlled terminology.
  - ICE tools integrate multiple data streams.
  - ICE visualizations allow quick summaries and data evaluation.
- This presentation describes how the ICE Search and Curve Surfer tools can make HTS data more accessible and transparent for all users.

## Visualizing Search Results

Searching by MOA “cytotoxicity” yields bar plots summarizing activity calls for all annotation terms related to “cytotoxicity”. Boxplots can be viewed to evaluate all chemical AC50 values per assay within a specific annotation term (in this example, “cell viability process”).



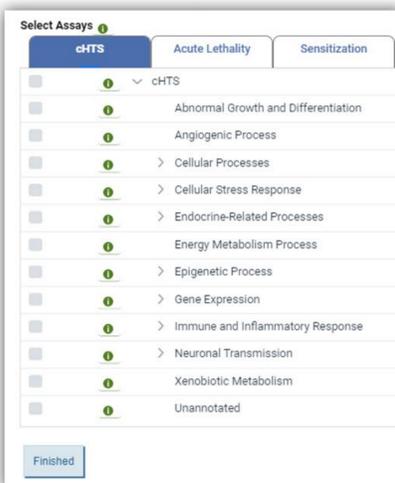
Results can also be viewed by chemical. A table lists chemical properties, bar plots summarize activity calls for each MOA term, and boxplots can be viewed to show potency for active endpoints within specific MOAs.

## Searching for cHTS Data in ICE

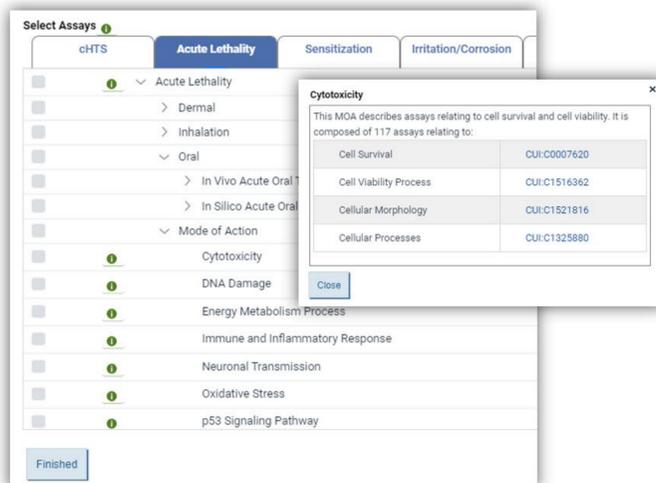


- In the ICE Search tool, users can easily find curated HTS (cHTS) data via the Assay Selection feature.
- Assays are grouped by controlled vocabulary terminology to facilitate retrieval of orthologous or complementary assays:
  - Mechanistic Target** terms organize assays based on biological processes to facilitate assay interpretation.
  - Mode of Action (MOA)** terms organize assays based on pathways relevant to toxicological outcomes of regulatory concern.

### Mechanistic Target-Based Search



### Mode of Action-Based Search

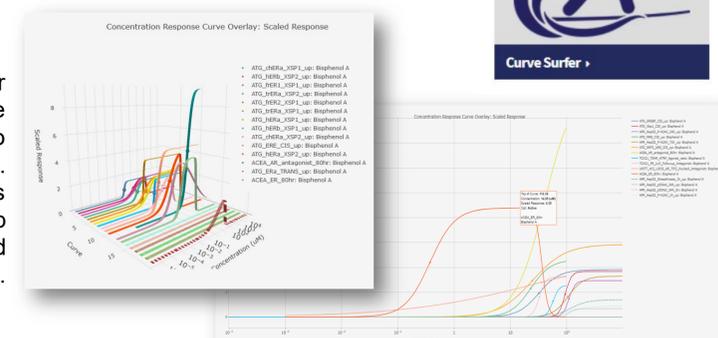


## Visualizing Concentration-Response Details for cHTS Assays



Every concentration-response data series from cHTS assays can be viewed using the ICE Curve Surfer tool. Results include details for chemical and assay, including Mechanistic Target terms associated with the assay to aid interpretation.

Concentration-response curves for multiple chemical/assay combinations can be viewed using the curve overlay tool to facilitate comparisons. The 3D view clearly shows relationships between curves and dashed lines help review how inactive or curation-omitted responses compare to active responses.



## Summary

- Mode of Action groupings in ICE Search provide context to interpret assays for potential toxicological relevance, allowing users to retrieve assay data for relevant biological pathways.
  - Results are grouped based on toxicological endpoints of regulatory significance.
  - Users can easily compare orthologous or complementary assays.
  - Outputs help review data in support of building weight-of-evidence evaluations.
  - Search results can help identify data gaps.
- ICE visualization tools help users interpret query results by grouping per assays or chemical.
  - Using ICE Curve Surfer to view individual concentration-response curves can help build confidence and improve understanding of assay results and provide context to activity calls.

## More Information

This project was funded with federal funds from the National Institute of Environmental Health Sciences, National Institutes of Health, under Contract No. HHSN273201500010C.

Learn more about NICEATM and ICE tools at SOT:

- Rooney et al. Abstract 4000 / Poster P698
- Abedini et al. Abstract 4004 / Poster P702
- Mumtaz et al. Abstract 5042 / Poster P146

Visit ICE at <https://ice.ntp.niehs.nih.gov/>

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