

# The Integrated Chemical Environment

## Tools and data to support toxicity assessments



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*Disclaimer: ILS staff provide technical support for NICEATM, but do not represent NIEHS, NTP, or the official positions of any federal agency.*

# Acknowledgements

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<https://ntp.niehs.nih.gov/go/niceatm>

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**Integrated  
Chemical  
Environment**

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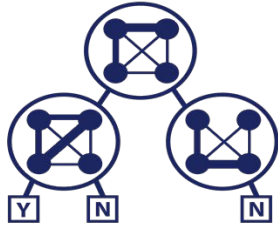
# Integrated Chemical Environment

- Resource access point designed for NICEATM stakeholders
  - U.S. Federal agencies and agencies within government that use or generate toxicological data
  - Researchers and Institutional Animal Care and Use Committee (IACUC) members in companies or research institutions that perform toxicological testing
  - Companies that develop toxicological tests
  - Animal welfare organizations
  - Consumer protection organizations
  - The public
- User-friendly access to high-confidence data and reference chemical lists
- Easy-to-use resources supporting prioritization and exploration
  - Search
    - Designed for ease of use; assays organized on regulatory endpoints
  - Tools
    - Web-based for easy use and exploration

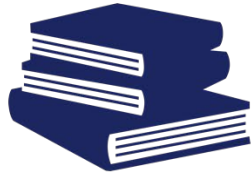


# What is ICE?

Computational models



Published data



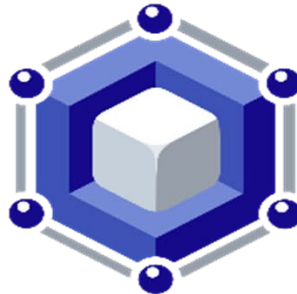
Databases



Validation studies



Download reference lists



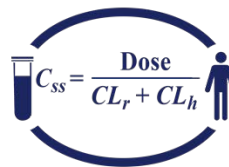
Export queries and results



Search



Data



IVIVE



Chemical characterization



# Data in ICE

Toxicity endpoint	Assays	# of chemicals*
Acute Oral Toxicity	<i>In vivo</i> acute oral toxicity	10,335**
Skin Sensitization	DPRA, hCLAT, KeratinoSens, LLNA, human potency, etc.	578
Skin Irritation	<i>In vivo</i> acute skin irritation/corrosion, 4h HPT; <i>In vitro</i> irritation/corrosion (e.g., EpiSkin, TER)	819
Eye Irritation	<i>In vivo</i> acute eye irritation/corrosion (e.g., Draize eye), Vitrigel	796
Endocrine	AR/ER Pathway Models, Uterotrophic, Hershberger, AR/ER transactivation	280**
cHTS	Curated ToxCast and Tox21 assays	9,213
OPERA predictions	BP, HLC, KOA, BCF, LogP, MP, MW, VP, WS, COMPARA, CERAPP, CATMoS, intrinsic clearance, fraction unbound	838,911
Formulation data	Six-pack	297 (747 formulations)
Experimental ADME	Intrinsic clearance and fraction unbound data generated from experimental studies	1,603

\*Values from July 2020

\*\*Does not include in silico predictions from OPERA or MOA-linked assays



# New Developments and Future Plans

- An NTP advisory group formed
  - Providing additional guidance on tool development
  - Leveraging domain expertise as ICE expands its increased curation and toxicological context of assays
- Integration with other resources
  - Send chemical list to bulk query on EPA's Chemical Dashboard
  - Links to NTP's Chemical Effects in Biological Systems (CEBS) planned for fall
- Increased visualizations and interactions under development

Calendar & Events | News & Media | Get Involved | Support

National Toxicology Program  
U.S. Department of Health and Human Services

Integrated Chemical Environment

HOME | SEARCH | TOOLS | DATA | ABOUT | HELP

### News & Events

#### ICE v3.1 Release

ICE updates include:

- Search has metadata added to Excel result downloads and assay selection dialog
- Chemical Characterization tool has PCA plots for data visualization
- Users can send Search query results to

- ▶ EPA CompTox Chemicals Dashboard

Learn about ICE updates

UPDATES

## OPERA

OPEn (q)saR App

### ICE includes QSAR predictions generated by OPERA

Learn more about OPERA

PAUSE

SEARCH

DATA

CHEMICAL CHARACTERIZATION

MVE

$$C_{ss} = \frac{\text{Dose}}{CL_r + CL_h}$$


# ICE Search



Input  
Results

Run Reset Union or Intersection  
Union

### Chemical Input

Select Chemicals

#### Quick List CASRNs

[Empty dashed box for Quick List CASRNs]

#### User CASRNs

[Empty dashed box for User CASRNs]

Add chemicals with identical QSAR structures

### Assay Input

Select Assays

Assay	Description	Assay Type





# ICE Search

National Toxicology Program  
U.S. Department of Health and Human Services

Search the NTP Website **SEARCH**

Integrated Chemical Environment

Input  
Results

HELP

### Select Assays

- cHTS
- Acute Lethality
- Sensitization
- Irritation/Corrosion
- Endocrine
- Cancer
- DART
- Chemical Parameters

- cHTS
  - Cellular Processes
  - Signal Transduction
  - Host Defense Mechanism
  - Steroid Metabolic Process
    - Endocrine System
      - in vitro
      - Androgen Metabolic Process in vitro
      - Estrogen Metabolic Process in vitro
      - Thyroid Hormone Metabolic Process in vitro
      - Progesterone Metabolic Process in vitro
      - Glucocorticoid Metabolic Process in vitro
      - Vitamin D Metabolic Process in vitro
    - Developmental Process
    - 40 assays relating to cellular developmental processes in vitro
    - Unannotated in vitro

Finished



# ICE Search

The screenshot displays the ICE Search web application interface. At the top left is the logo for 'Integrated Chemical Environment'. The top navigation bar includes 'HOME', 'SEARCH', 'TOOLS', 'DATA', 'ABOUT', and 'HELP'. Below this, there are tabs for 'Chemicals' and 'Mixtures'. On the left side, there are buttons for 'Input' and 'Results'. The main content area features a 'Select Assays' dialog box with a close button (X) in the top right corner. The dialog box has several tabs: 'cHTS', 'Acute Lethality' (which is selected), 'Sensitization', 'Irritation/Corrosion', 'Endocrine', 'Cancer', 'DART', and 'Chemical Parameters'. Under the 'Acute Lethality' tab, there is a tree view of assay categories: 'Acute Lethality' (expanded), 'Oral' (expanded), 'In Vivo Acute Oral Toxicity Assays', 'In Silico Acute Oral Toxicity Predictions', and 'Mode of Action' (expanded). The 'Mode of Action' category is currently selected and highlighted. Below it, a list of specific assays is shown, each with a checkbox, an information icon (i), the assay name, and the assay type (all are 'in vitro').

Assay Name	Assay Type
Acute Lethality	
Oral	
In Vivo Acute Oral Toxicity Assays	
In Silico Acute Oral Toxicity Predictions	
Mode of Action	
Cell Senescence/Death	in vitro
DNA Disruption	in vitro
Energy Disruption	in vitro
Immune System Disruption	in vitro
Neurotransmission Disruption	in vitro
Oxidative Stress	in vitro
p53 Activation	in vitro

Finished



# ICE Search

**National Toxicology Program**  
U.S. Department of Health and Human Services

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Search the NTP Website **SEARCH**

HOME SEARCH TOOLS DATA ABOUT HELP

**Input**  
Results

Union or Intersection  
Union

**Chemical Input**  
Select Chemicals 3 chemical quick lists selected.

**Quick List CASRNs**  
57-63-6  
84-16-2  
56-53-1  
50-28-2  
57-91-0  
53-16-7  
140-66-9  
446-72-0  
77-40-7  
80-05-7  
486-66-8  
521-18-6  
789-02-6  
599-64-4  
143-50-0

**User CASRNs**

Add chemicals with identical QSAR structures

**Select one or more chemical quick lists.**

Select All Deselect All

- Tox21
- AR In Vitro Agonist (R)
- AR In Vitro Antagonist (R)
- AR In Vivo Agonist
- AR In Vivo Antagonist
- EPA Active Ingredients
- EPA IRIS Carcinogenicity Classifications
- EPA Inert Ingredients Food and Nonfood Use
- ER In Vitro (R)
- ER In Vivo (R)
- Eye Irritation Corrodents
- IARC Classifications
- NTP Cancer Bioassay Chemicals
- RoC Classifications
- Skin Corrosion (R)
- Steroidogenesis - Androgen
- Steroidogenesis - Estrogen
- Thyroid

Finished

43 chemicals with estrogenic activity characterized in guideline-like rodent uterotrophic assays. Click for more information.

Description	Assay Type
Cancer	in vitro
Cancer	in vitro
Cancer	in vitro
Cancer	in vitro
Cancer	in vitro
Cancer	in vitro
Cancer	in vitro
Cancer	in vitro
Irritation/...	in vivo
Irritation/...	in vivo
cHTS	in vitro


BACK TO TOP

Web page last updated on Feb. 21, 2020



# ICE Search

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 **National Toxicology Program**  
U.S. Department of Health and Human Services

Search the NTP Website **SEARCH**

HOME SEARCH TOOLS DATA ABOUT HELP

Chemicals Mixtures

Input Results Run Reset Union or Intersection Union

### Chemical Input

Select Chemicals 3 chemical quick lists selected.

Quick List CASRNs	User CASRNs
57-63-6	50-50-0
84-16-2	
56-53-1	
50-28-2	
57-91-0	
53-16-7	
140-66-9	
446-72-0	
77-40-7	
80-05-7	
486-66-8	
521-18-6	
789-02-6	
599-64.4	
143-50-0	
58-18-4	

Add chemicals with identical QSAR structures

### Assay Input

Select Assays

Assay	Description	Assay Type
<input checked="" type="checkbox"/> KCC10: Cell Proliferation/Death/Energetics	Cancer	in vitro
<input checked="" type="checkbox"/> KCC8: Receptor Mediated Effects	Cancer	in vitro
<input checked="" type="checkbox"/> KCC6: Chronic Inflammation	Cancer	in vitro
<input checked="" type="checkbox"/> KCC5: Oxidative Stress	Cancer	in vitro
<input checked="" type="checkbox"/> KCC4: Epigenetic Alterations	Cancer	in vitro
<input checked="" type="checkbox"/> KCC3: Alteration of DNA Repair/Genomic Stability	Cancer	in vitro
<input checked="" type="checkbox"/> KCC2: Genotoxic Effects	Cancer	in vitro
<input checked="" type="checkbox"/> KCC1: Electrophilic/Metabolically Activated	Cancer	in vitro
<input checked="" type="checkbox"/> Four-hour Human Patch Test	Irritation/...	in vivo
<input checked="" type="checkbox"/> Rabbit Draize Skin Irritation/Corrosion Test	Irritation/...	in vivo
<input checked="" type="checkbox"/> Angiogenic Process	cHTS	in vitro



# ICE Search



Chemicals Mixtures

Input

Results

Details

> Selected Chemical Quick Lists (3)

∨ Selected Assays (15)

Coagulation Process, Inflammatory Response, Immune System Process, Neuronal Development, Angiogenic Process, KCC1: Electrophilic/Metabolically Activated, KCC2: Genotoxic Effects, KCC3: Alteration of DNA Repair/Genomic Stability, KCC4: Epigenetic Alterations, KCC5: Oxidative Stress, KCC6: Chronic Inflammation, KCC8: Receptor Mediated Effects, KCC10: Cell Proliferation/Death/Energetics, Rabbit Draize Skin Irritation/Corrosion Test, Four-hour Human Patch Test

Download

Query Mixtures

EPA Search

Clear Filter

Number of chemicals = 83

Substance Name	CASRN	DTXSID	Qsar Ready ID	Coagulation Process Cell (# Assays=17)	Inflammation Response Cell (# Assays=1...)	Immune System Process Cell (# Assays=1)	Neuronal Development Cell (# Assays=11)	Angiogenic Process Cell (# Assays=29)	KCC1: Electrophilic/Metabolically Activated Cell (# Assays=31)	KCC2: Genotoxic Effects Cell (# Assays=27)	KCC3: Alteration of DNA Repair/Genomic Stability Cell (# Assays=3)	KCC4: Epigenetic Alterations Cell (# Assays=9)	KCC5: Oxidative Stress Cell (# Assays=2)
Linuron	330-55-2	DTXSID20...	XKJMBINC... UHFFFAOY... N	Inactive(N=...)	Active(N=4...) Omit(N=2...) Tested(N=...)		Active(N=1...) Omit(N=1...) Tested(N=9)	Active(N=2...) Tested(N=5)	Active(N=2...) Omit(N=2...) Tested(N=...)	Active(N=1...) Omit(N=1...) Tested(N=8)	Active(N=1...) Omit(N=1...) Tested(N=6)	Active(N=1...) Omit(N=1...) Tested(N=6)	Active(N=1...) Omit(N=1...) Tested(N=6)
4-tert-Butylphenol	98-54-4	DTXSID10...	QHQPWRB... UHFFFAOY... N	Inactive(N=...)	Active(N=3...) Omit(N=2...) Tested(N=...)			Active(N=1...) Tested(N=5)	Inactive(N=...) Tested(N=...)	QC-Omit(N=1...) Tested(N=...)	QC-Omit(N=3)	Active(N=2...) Tested(N=6)	Active(N=1...) Omit(N=1...) Tested(N=6)
...	...	...	KLSJWNV... UHFFFAOY...	Inactive(N=...)	Omit(N=2...)			Inactive(N=...)	Inactive(N=...) Omit(N=1...)	Inactive(N=...) Omit(N=7)	QC-	Inactive(N=...) Omit(N=1...)	Inactive(N=...) Omit(N=1...)



# ICE Search

Integrated Chemical Environment

HOME SEARCH TOOLS DATA ABOUT HELP

Chemicals Mixtures

Input

Results

Details

> Selected Chemical Quick Lists (3)

Selected Assays (15)

Coagulation Process, Inflammatory Response, Immune System Process, Neuronal Development, Angiogenic Process, KCC1: Electrophilic/Metabolically Activated, KCC2: Genotoxic Effects, KCC3: Alteration of DNA Repair/Genomic Stability, KCC4: Epigenetic Alteration of DNA, KCC5: Oxidative Stress, KCC6: Chronic Inflammation, KCC7: Cell Death, KCC8: Receptor Mediated Effects, KCC10: Cell Proliferation, Irritation/Corrosion Test, Four-hour Human Patch Test

Download Query Mixtures EPA Search Clear Filter

Substance Name	CASRN	DTXSID	Qsar Ready ID	Coagulation Process Cell (#) Assays=1
Linuron	330-55-2	DTXSID20...	XKJMBINC... UHFFFAOY... N	Inactive(N=1)
4-tert-Butylphenol	98-54-4	DTXSID10...	QHQPWRB... UHFFFAOY... N	Inactive(N=1)
...	...	...	KLSJWNV... UHFFFAOY...	Inactive(N=1)

### Download Results

Summary Data

Wide Format Data

Long Format Data

Note: For "Wide Format" downloads (when available), cHTS assay data only includes AC50 values for assays with an "Active" chemical. Call values are returned for assays with no active chemicals.

KCC1: Electrop... Activated Cell (#) Assays=31	KCC2: Genotoxic Effects Cell (#) Assays=27	KCC3: Alteration of DNA Repair/G... Stability Cell (#) Assays=3	KCC4: Epigenetic Alterations Cell (#) Assays=9	KCC5: Oxidativ... Stress Ce... Cell (#) Assays=2
Active(N=2... Omit(N=2)... Tested(N=...	Active(N=1... Omit(N=1)... Tested(N=6)	Active(N=1... Omit(N=1)...	Active(N=1... Tested(N=6)	Active(N=1... Tested(N=6)
Inactive(N... Tested(N=...	QC- Omit(N=1... Tested(N=...	QC- Omit(N=3)	Active(N=2... Tested(N=6)	Active(N=1... Omit(N=1... Tested(N=6)
Inactive(N... Omit(N=1)...	Inactive(N... Omit(N=7)	QC-	Inactive(N... Omit(N=1)	Inactive(N... Omit(N=1)



# ICE Tool: IVIVE

- Calculates the **equivalent administered dose (EAD)** that would be needed to achieve the concentration that yielded the in vitro response
- Compares relationships between EADs resulting from different in vitro assays
- Overlays different in vivo endpoints on to EAD plot
- Informs on the predictability of the in vitro assay for the given endpoint
- Characterizes the probability of a biological effect given the likely in vivo exposure
  - [https://github.com/NIEHS/ICE\\_IVIVEpipeline](https://github.com/NIEHS/ICE_IVIVEpipeline)



# ICE TOOL: IVIVE

- Choose from:
  - **1C**: One-compartment pharmacokinetic (1C PK) model including population simulation
  - **Solve\_3comp**: Three-compartment physiologically based pharmacokinetic (PBPK) models using EPA's htk package (Version 1.9.2)
  - **Solve\_pbtk**: Multi-compartment physiologically based pharmacokinetic (PBPK) models using EPA's htk package (Version 1.9.2)
- New for 2020:
  - Uploading of user-supplied in vitro data for use in modeling
  - Improved assay selection using the cHTS mechanistic target mapping
  - Selection from Mode of Action is assay selection





# ICE Tool: IVIVE

**IVIVE** Chemical Characterization

Input

The IVIVE tool uses pharmacokinetic models to predict the equivalent administered dose (EAD) from the activity concentration of selected assays.

Run Reset

Endpoint: AC50, Species: human, Model: Solve\_pbtck, Exposure Route: iv, Exposure Interval: 24 Hours, Exposure Length: NA, Simulation Length: 3 Days

In Vitro Endpoint: AC50

Species: human

Model: Solve\_pbtck

Exposure Route: iv

Exposure Interval, Hours: 24

Exposure Length, Hours: NA

Simulation Length, Days: 3

These models come from the US EPA htkk 1.9.2 package. For details see Userguide

**Chemical Input**

Select Chemicals

Quick List CASRNs

User CASRNs

**Data Input**

Select Assays

Upload File... Drop file here

Assay	Description	Assay Type
-------	-------------	------------



# ICE Tool: IVIVE

The screenshot displays the IVIVE tool interface. At the top, the National Toxicology Program logo and name are visible, along with navigation links for Calendar & Events, News & Media, Get Involved, and Support. A search bar is present with the text "Search the NTP Website" and a "SEARCH" button. Below the header, the "Integrated Chemical Environment" logo is on the left, and navigation buttons for HOME, SEARCH, TOOLS, DATA, ABOUT, and HELP are on the right. The main content area is titled "IVIVE" and "Chemical Characterization". A descriptive text states: "The IVIVE tool uses pharmacokinetic models to predict the equivalent administered dose (EAD) from the activity concentration of selected assays." Below this, there are "Run" and "Reset" buttons. A summary line reads: "Endpoint: AC50, Species: human, Model: Solve\_pbtck, Exposure Route: iv, Exposure Interval: 24 Hours, Exposure Length: NA, Simulation Length: 3 Days". The "In Vitro Endpoint" dropdown is set to "AC50", "Exposure Route" to "iv", "Species" to "human", and "Model" to "Solve\_pbtck". A note below the model dropdown says: "These models come from the US EPA httk 1.9 Userguide". A "Data Input Info" modal window is open, containing the following text: "Click the 'Select Assays' button to choose cHTS assays to use in your model.", "Click 'Upload File' to load assay data to use in your model. Click the template sample links below to view format of upload file.", "File types supported: Text (.txt), Excel (.xlsx)", "Template Assay File for IVIVE (Text)", "Template Assay File for IVIVE (Excel)", and a "Close" button. At the bottom left, there are sections for "Chemical Input" with a "Select Chemicals" button, and "Quick List CASRNs" and "User CASRNs" input areas. On the right, there is a "Drop file here" area and a table with columns for "Description" and "Assay Type".

# ICE Tool: IVIVE

The screenshot shows a Microsoft Excel spreadsheet with the following data:

	A	B	C	D	E	F	G	H	I
1	casrn	user assay1	user assay2	user assay3	user assay4				
2	115-32-2	1.2	1.3	1.5	1.7				
3	117-81-7	2.2	2.3	2.5	2.7				
4	120-47-8	3.6	3.7	3.8	3.9				
5	13311-84-7	4.1	4.2	4.3	4.4				
6	140-66-9	5.1	5.2	5.3	5.4				
7									
8									
9									
10									
11									
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22									

# ICE Tool: IVIVE

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**Select Assays** ⓘ

**cHTS** | Mode of Action

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Cellular Processes						
	Signal Transduction						
	Host Defense Mechanism						
	Steroid Metabolic Process						
	Developmental Process						
	Xenobiotic Metabolism					in vitro	
	Unannotated					in vitro	

**Finished**

# ICE Tool: IVIVE

**Input**

The IVIVE tool uses pharmacokinetic models to predict the equivalent administered dose (EAD) from the activity concentration of selected assays.

Results

Endpoint: AC50, Species: human, Model: 1C, Exposure Route: NA, Exposure Interval: NA, Exposure Length: NA, Simulation Length: NA

ⓘ

ⓘ

ⓘ

ⓘ

ⓘ

ⓘ

ⓘ

The 1C model predicts the steady state plasma concentration from a single daily bolus dose without differentiation between i.v. and oral exposure

**Chemical Input**

Select Chemicals

2 chemical quick lists selected.

**Quick List CASRNs**

- 103-90-2
- 107-02-8
- 61-82-5
- 84-65-1
- 1912-24-9
- 86-50-0
- 65-85-0
- 82657-04-3
- 10043-35-3
- 133-06-2
- 63-25-2
- 1563-66-2
- 999-81-5
- 76-06-2
- 1897-45-6
- 56-77-4

**User CASRNs**

Empty input field for User CASRNs.

**Data Input**

Select Assays

Upload File... Drop file here

Assay	Description	Assay Type
<input checked="" type="checkbox"/> Cancer (KCC10: Cell Proliferation/Death/Energetics)	MOA	in vitro
<input checked="" type="checkbox"/> Cancer (KCC8: Receptor Mediated Effects)	MOA	in vitro
<input checked="" type="checkbox"/> Cancer (KCC6: Chronic Inflammation)	MOA	in vitro
<input checked="" type="checkbox"/> Cancer (KCC5: Oxidative Stress)	MOA	in vitro
<input checked="" type="checkbox"/> Cancer (KCC4: Epigenetic Alterations)	MOA	in vitro
<input checked="" type="checkbox"/> Cancer (KCC3: Alteration of DNA Repair/Genomic Stability)	MOA	in vitro
<input checked="" type="checkbox"/> Cancer (KCC2: Genotoxic Effects)	MOA	in vitro
<input checked="" type="checkbox"/> Cancer (KCC1: Electrophilic/Metabolically Activated)	MOA	in vitro
<input checked="" type="checkbox"/> Vitamin D Metabolic Process	cHTS	in vitro
<input checked="" type="checkbox"/> Glucocorticoid Metabolic Process	cHTS	in vitro
<input checked="" type="checkbox"/> Progesterone Metabolic Process	cHTS	in vitro

# ICE Tool: IVIVE

The screenshot displays the IVIVE tool interface. At the top, the National Toxicology Program logo and name are visible, along with navigation links for Calendar & Events, News & Media, Get Involved, and Support. A search bar is present with the text "Search the NTP Website" and a "SEARCH" button. Below the header, a navigation menu includes "HOME", "SEARCH", "TOOLS", "DATA", "ABOUT", and "HELP". The main content area is titled "IVIVE" and "Chemical Characterization". On the left, a sidebar shows "Input" and "Results" tabs, with "Results" selected. The main content area is titled "IVIVE workflow results" and contains a section for "Download IVIVE Files" with an information icon. Below this, three items are listed:

- Physicochemical and ADME inputs for chemicals used in the IVIVE modeling.**  
[Download Chemical Parameters Input](#)
- A table of in vitro assay data used to run the IVIVE calculations.**  
[Download in vitro Assay Input](#)
- A table of calculated EADs from the analysis.**  
[Download IVIVE Results](#)

At the bottom of the main content area, there is a link: [> IVIVE Results](#)

# ICE Tool: IVIVE

Input

Results

## IVIVE workflow results

> Download IVIVE Files

IVIVE Results



Clear Filter

Number of rows = 2118

> CASRNs Not Returned By Query

Chemical	CASRN	DTXSID	Assay	Mode of Action	Mechanis... Targets	AC50 uM	EAD 50th Percentile (mg/kg/d...	LogP	Clint	Fraction Unbound	pKa Donor	pKa Accept	HI
Diethylstil...	56-53-1	DTXSID30...	BSK_hDFC...	System Disruption	Response,...	10.0	0.0859	5.067	1.607	0.0	10.542	NA	-9
Diethylstil...	56-53-1	DTXSID30...	BSK_LPS_...	Vascular Disruption... System Disruption	Inflammat... Response,...	10.0	0.0859	5.067	1.607	0.0	10.542	NA	-9

Users can filter using the annotations for in vitro mode of action or mechanistic target

# ICE Tool: IVIVE

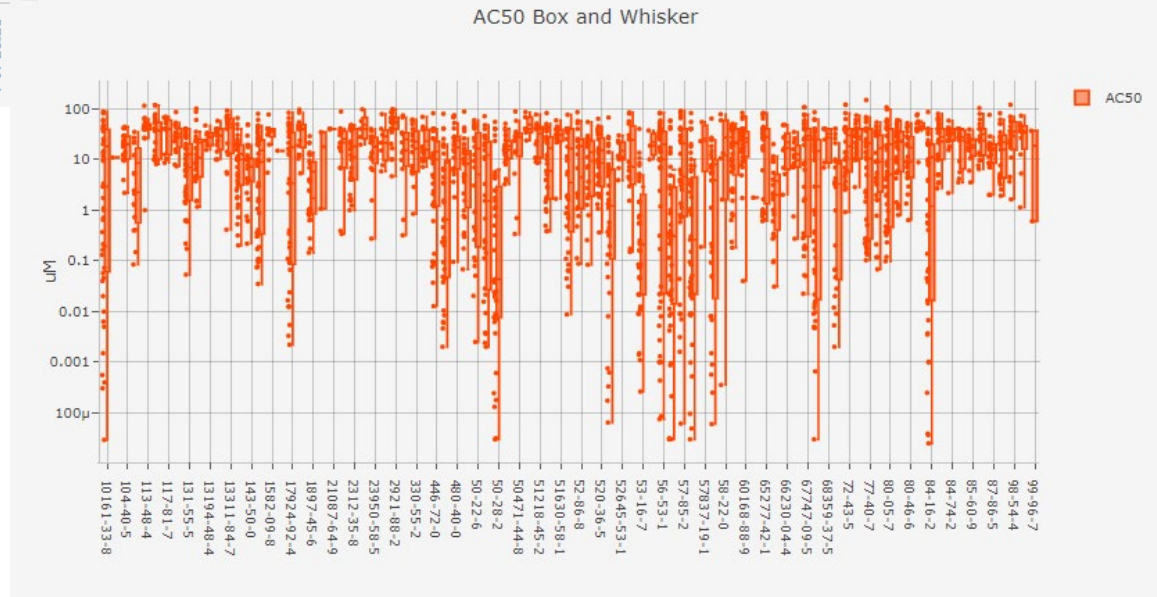
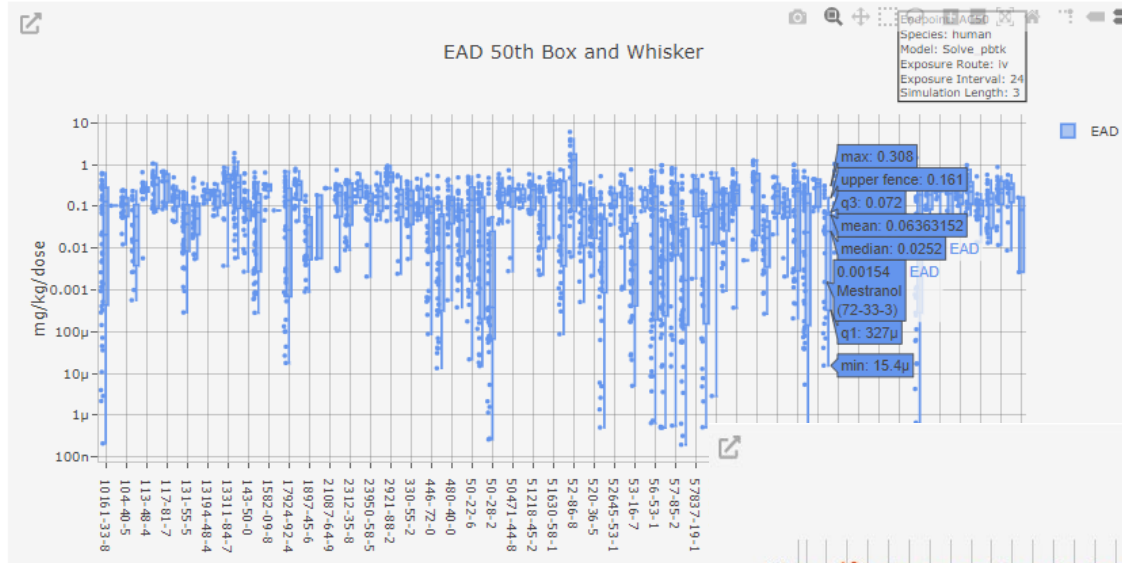
Select EAD to visualize:

EAD 50th

Select in vivo data to display.

Log  
Axis

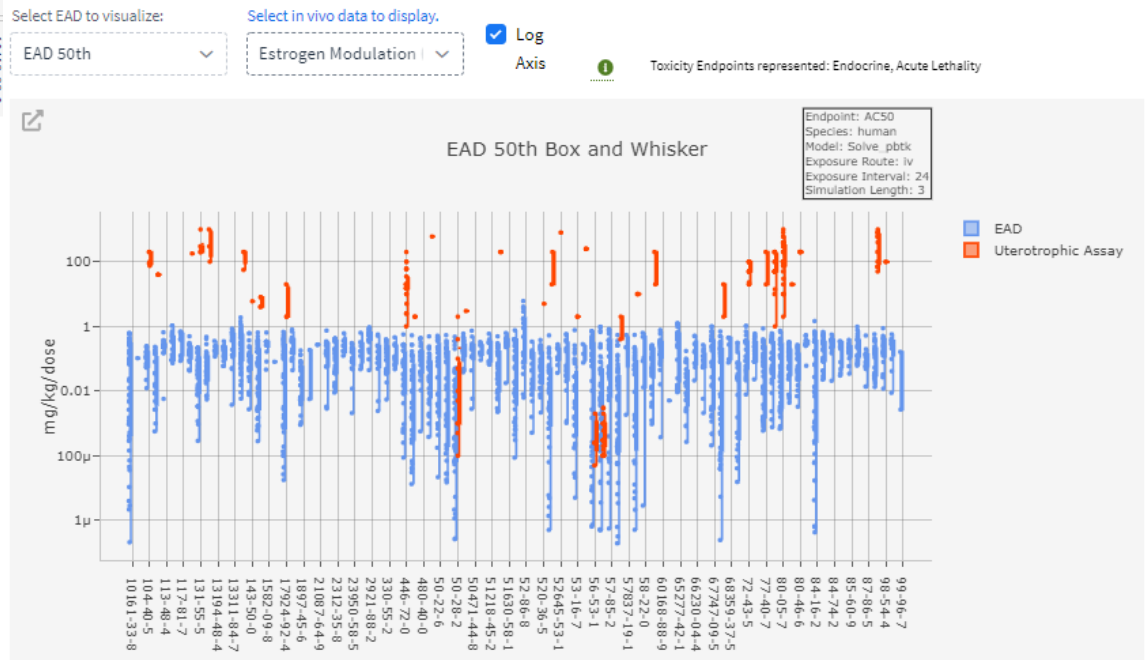
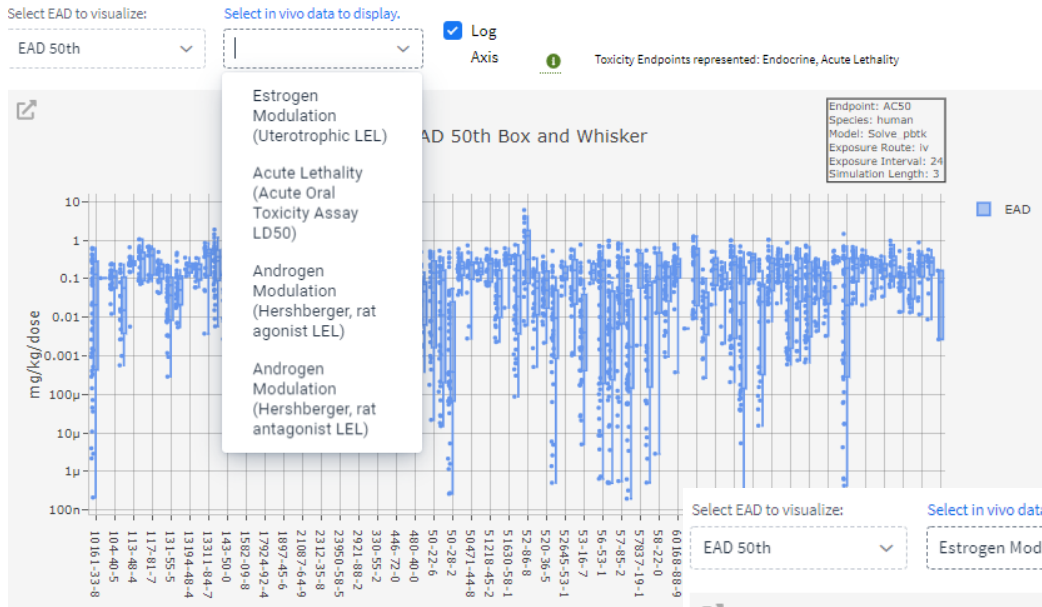
Toxicity Endpoints represented: Endocrine, Acute Lethality



- The graphs are rescaled
- The x-axis only shows the CASRN



# ICE Tool: IVIVE



- The graphs are rescaled
- The x-axis only shows the CASRN

# ICE Tool: IVIVE



Clear Filter

Number of rows = 730/2118

> CASRNs Not Returned By Query

Chemical	CASRN	DTXSID	Assay	Mode of Action	Mechanis... Targets	AC50 uM	EAD 50th Percentile (mg/kg/d...	LogP	Clint	Fraction Unbound	pKa Donor	pKa Accept	H
meso-Hexestrol	84-16-2	DTXSID20...	NVS_NR_h...	Estrogen	Estrogen Modulation...		6.23E-7	4.274	0.109	0.035	9.754	NA	-€

Select EAD to visualize:

EAD 50th

Select in vivo data to display:

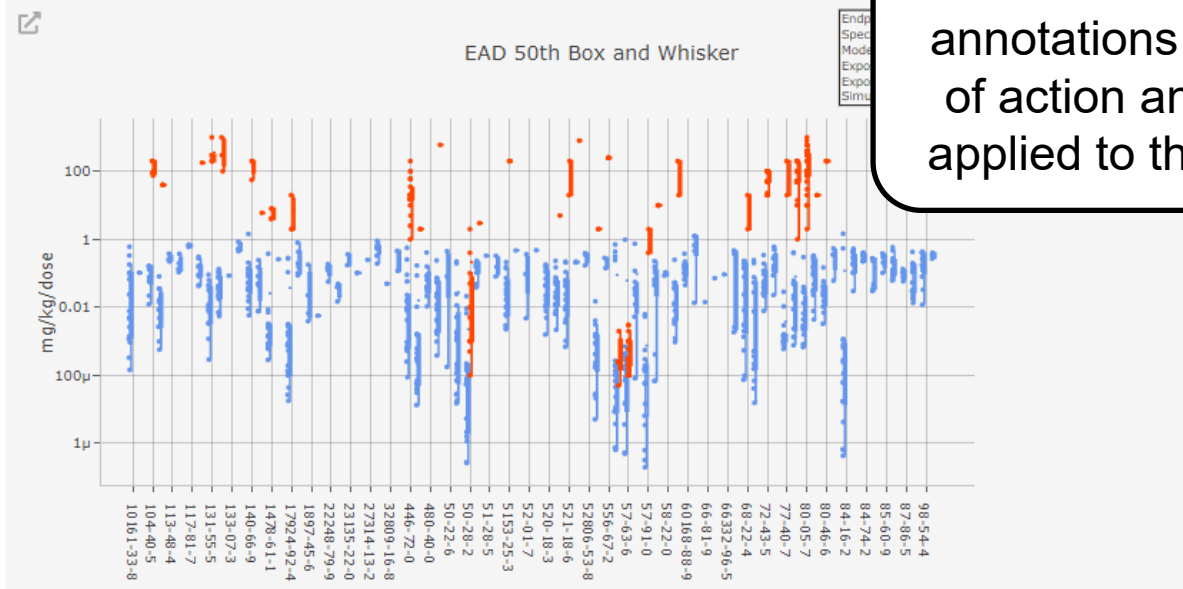
Estrogen Modulation



Log

Axis

Toxicity Endpoints represented:



Users can filter using the annotations for in vitro mode of action and have the filter applied to the interactive plot

# ICE Tool: Chemical Characterization

- Comparison tool that allows user to look at the property distribution between one or two lists of chemicals
- Chemical characterization tool is aimed at:
  - Allowing users to explore property distributions relationships
  - Look at what properties may be driving differences in performance of chemicals in assays
  - Characterize the differences between lists to identify possible redundancy or define the range of property coverage in preparation for testing
- New for 2020:
  - Enable the user to rename the list
  - Addition of PCA plots to enable visual comparisons of properties of user's chemical lists to Tox21 and ICE chemicals

# ICE Tool: Chemical Characterization

Input

Results

This tool allows you to view and compare up to two chemical lists based on their physicochemical properties. Comparisons are available in tabular format along with PCA plots of list against subsets of the ICE chemical innovatory.

Run Reset

List Name Chemical Input List 1 (required)

Select Chemicals 1 chemical quick list selected.

Quick List CASRNs

427-51-0  
63612-50-0  
13311-84-7  
330-55-2  
50471-44-8  
67747-09-5  
80-05-7  
122-34-9  
16752-77-5  
1912-24-9  
486-66-8  
52918-63-5  
58-18-4  
58-22-0  
63-05-8

User CASRNs

List Name Chemical Input List 2 (optional)

Select Chemicals 1 chemical quick list selected.

Quick List CASRNs

1608-10-7  
100-41-4  
100-44-7  
10049-04-4  
101-55-3  
101-61-1  
101-68-8  
1024-57-3  
103-23-1  
103-33-3  
10595-95-6  
10599-90-3  
106-44-5  
106-89-8  
106-93-4

User CASRNs

# ICE Tool: Chemical Characterization

The screenshot displays the National Toxicology Program (NTP) website interface. At the top, the NTP logo and name are visible, along with the text "U.S. Department of Health and Human Services". A search bar is present with the placeholder text "Search the NTP Website" and a "SEARCH" button. The main navigation menu includes "HOME", "SEARCH", "TOOLS", "DATA", "ABOUT", and "HELP". The "Integrated Chemical Environment" logo is also present. The "Chemical Characterization" tool is selected, showing a sub-menu with "IVIVE" and "Chemical Characterization". The "Chemical Characterization Results" section is active, displaying a list of results with expandable arrows and a count of 40 for each item. The results are:

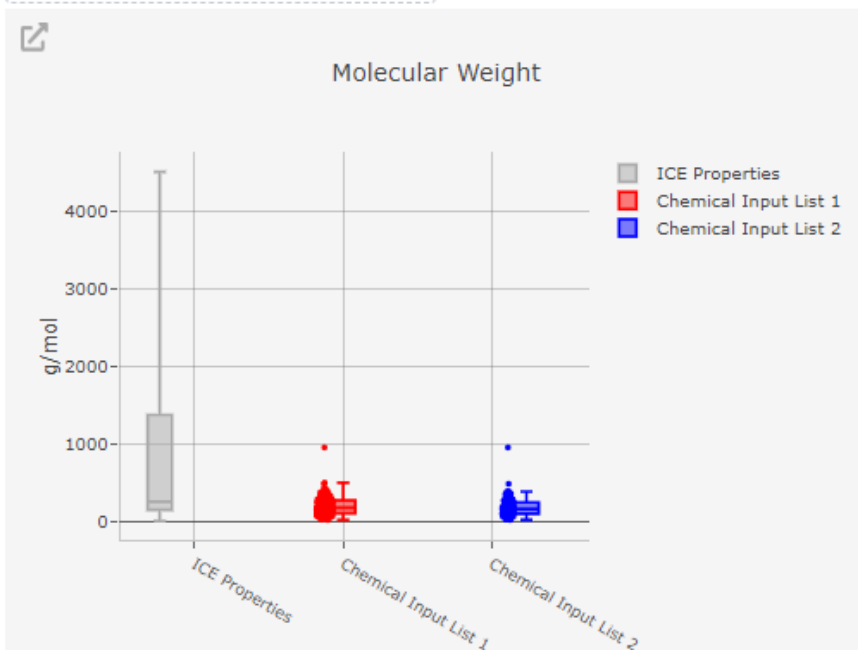
- > All CASRNs Not Returned by Query (40)
- > CASRNs in Chemical Input List 1 Not Returned by Query (40)
- > CASRNs in Chemical Input List 2 Not Returned by Query (40)
- > Chemical Properties Summary 1
- > Visualization of Chemical Properties 1
- > PCA 1

# ICE Tool: Chemical Characterization

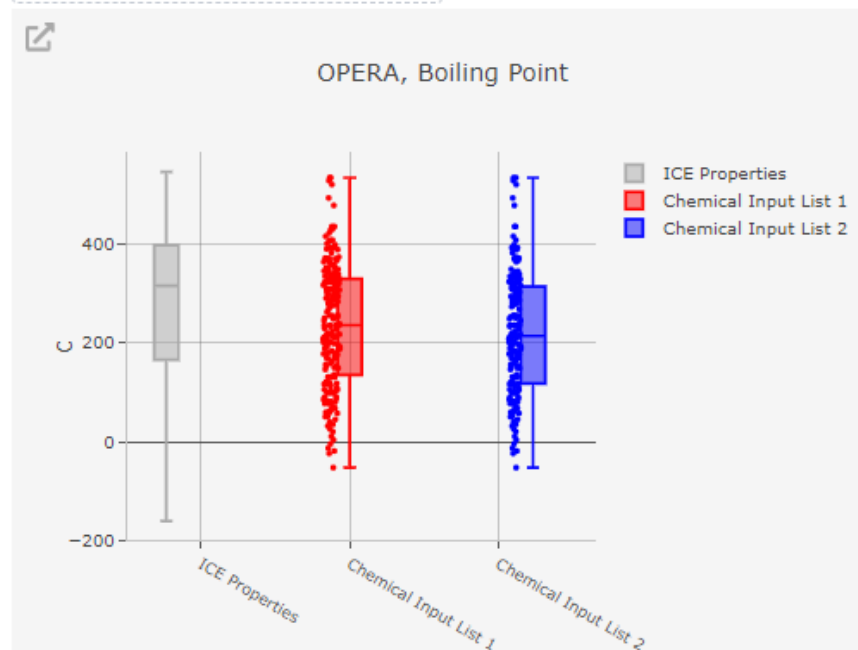
Visualization of Chemical Properties ?

## Visualization of Chemical Property Data

Molecular Weight ?



OPERA, Boiling Point ?



# ICE Tool: Chemical Characterization

Use the drop down to choose either Tox21 or OPERA for the background

PCA ⓘ

## Plot of returned CASRN PCA data shown with various PCA data backgrounds

Principal Component Analysis (PCA) plots show the dimensionally reduced scatter plot rendering of chemicals based on their physicochemical predictions. Two different backgrounds (OPERA and Tox21) and two different coordinate generations (Chemical Properties and Molecular Descriptors) are available to increase the users ability to visually compare predicted properties.

Selected background:

Tox21

Coordinate Type:

Chemical Properties

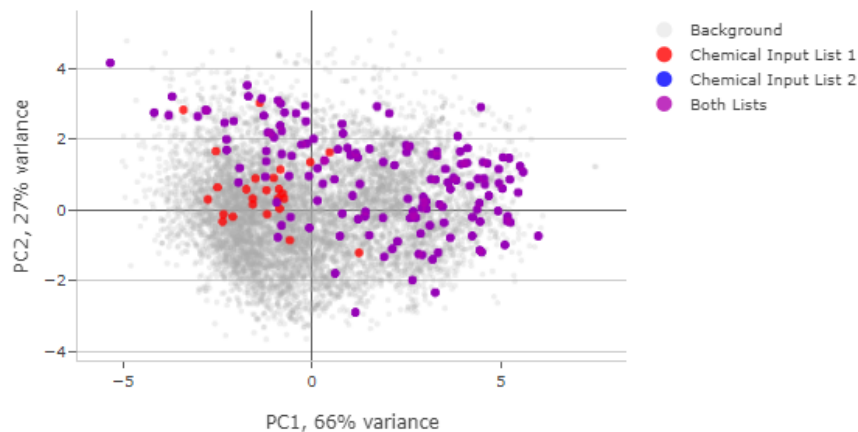
Tox21: displays user chemical lists against the background of over 9000 chemicals tested in Tox21.

Chemical Properties: eight or more properties that describe the characteristics of the chemical substance during a reaction or a chemical change. These properties include but are not limited to boiling point, KOA, and molecular weight.

Use the drop down to choose either Chemical Properties or Molecular Descriptors for coordinate Type



Returned CASRN PCA Data (Chemical Properties), Background: Tox21



# Resources

- OPERA <https://github.com/NIEHS/OPERA>
- QSAR ready KNIME workflow:  
<https://github.com/kmansouri/QSAR-ready>
- ICE:<https://ice.ntp.niehs.nih.gov/>
- ICE IVIVE workflow notebook:  
[https://github.com/NIEHS/ICE\\_IVIVEpipeline](https://github.com/NIEHS/ICE_IVIVEpipeline)
- NICEATM computational toxicology:  
<https://ntp.niehs.nih.gov/go/niceatm-comptox>