National Institute of Environmental Health Sciences
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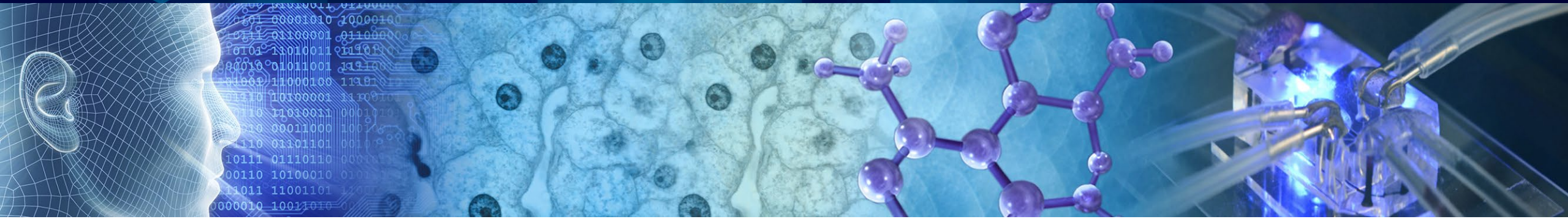

NICEATM tools: ICE and OPERA

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NIH/NIEHS/DTT/NICEATM, RTP, NC, USA

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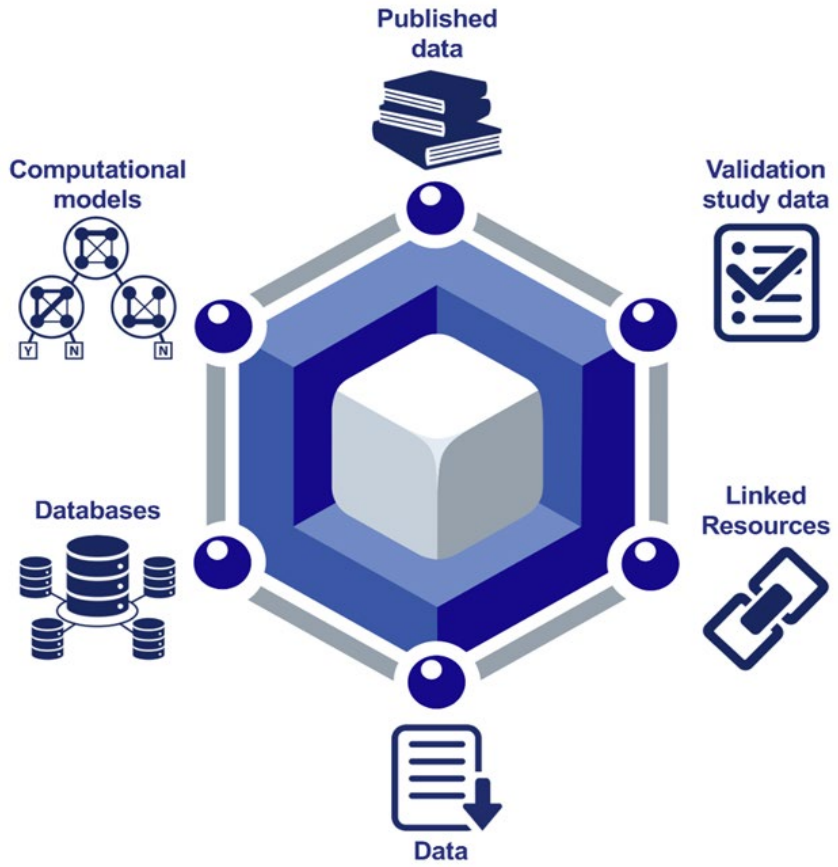
Integrated Chemical Environment (ICE)



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

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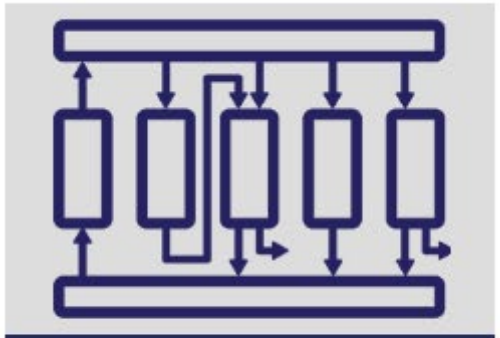
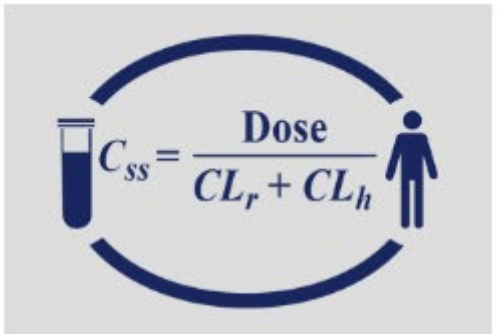
ICE Tools


Search ▸

Chemical Quest ▸


Curve Surfer ▸


PBPK ▸



IVIVE ▸

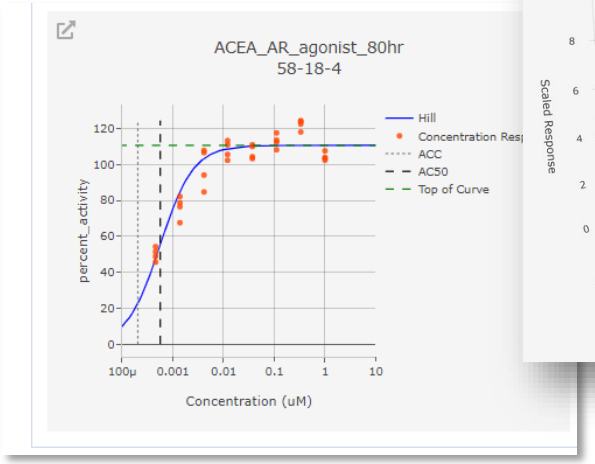

Chemical Characterization ▸

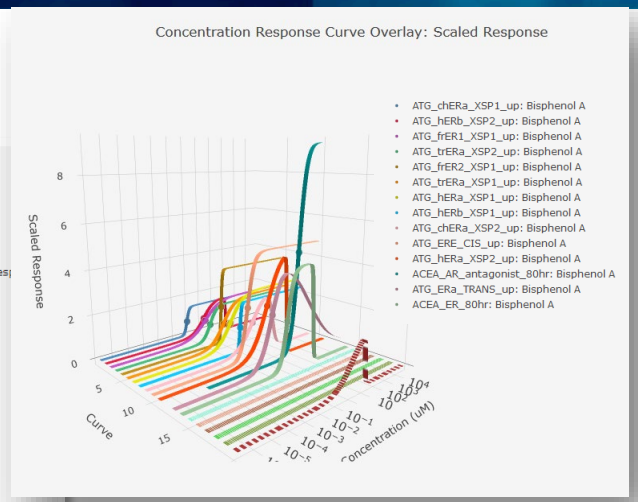

Data ▸

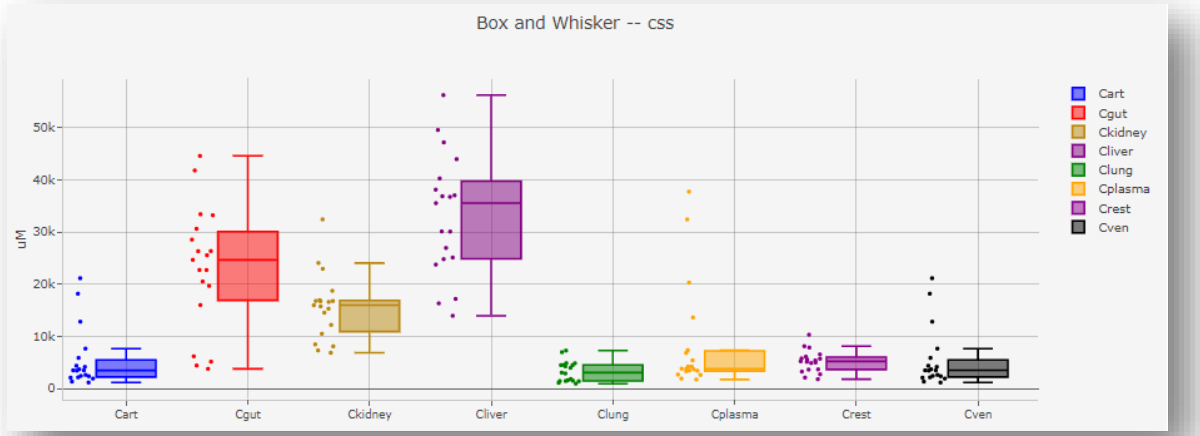

Help Videos ▸

ICE Tools

cHTS Data Exploration

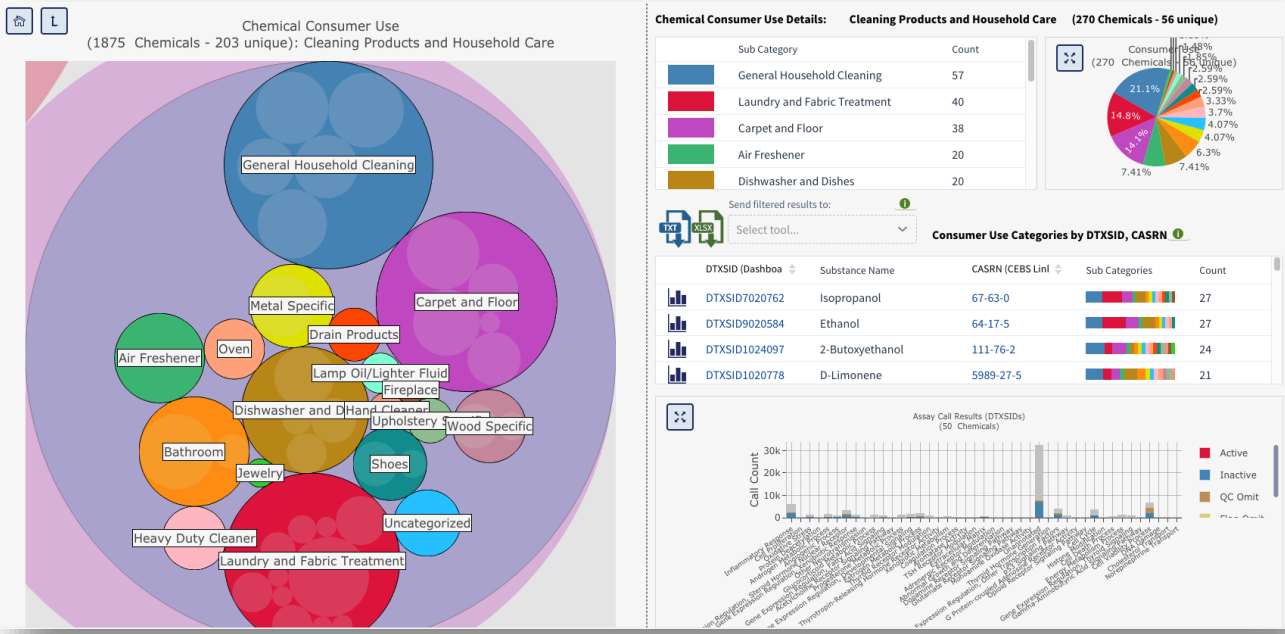






Predicting Tissue Concentration

Chemical Similarity



Chemical Exposure and Consumer Use

New Features in ICE 4.0

PBPK and IVIVE Tools Feature Enhancements:

- ICE PBPK and IVIVE tools now incorporate a gestational model from the U.S. Environmental Protection Agency (EPA)'s httk package (v2.2.2; released February 2023).
- Users modeling inhalation exposure now have the option of selecting a dose unit of ppmv rather than the existing option of µM.

Exposure Predictions:

- ICE tools integrate exposure predictions from the EPA's SEEM3 (Systematic Empirical Evaluation of Models) model (Ring et al. 2019).
- Exposure predictions can be accessed through a download file in the ICE Data Sets page and the ICE REST API. These predicted exposure data can also be compared to the equivalent administered doses (EADs) predicted by the IVIVE tool.

Search Results Redesign (BETA):

- A completely redesigned Search results interface features new summary interactive visualizations.

Chemical Name Input Option:

- ICE tools and the ICE REST API now accept chemical names and synonyms as input along with other pre-existing input options like CASRN, DTXSID, SMILES, and InChIKeys. This enhances comprehensive data retrieval to meet growing data needs in NAMs development.

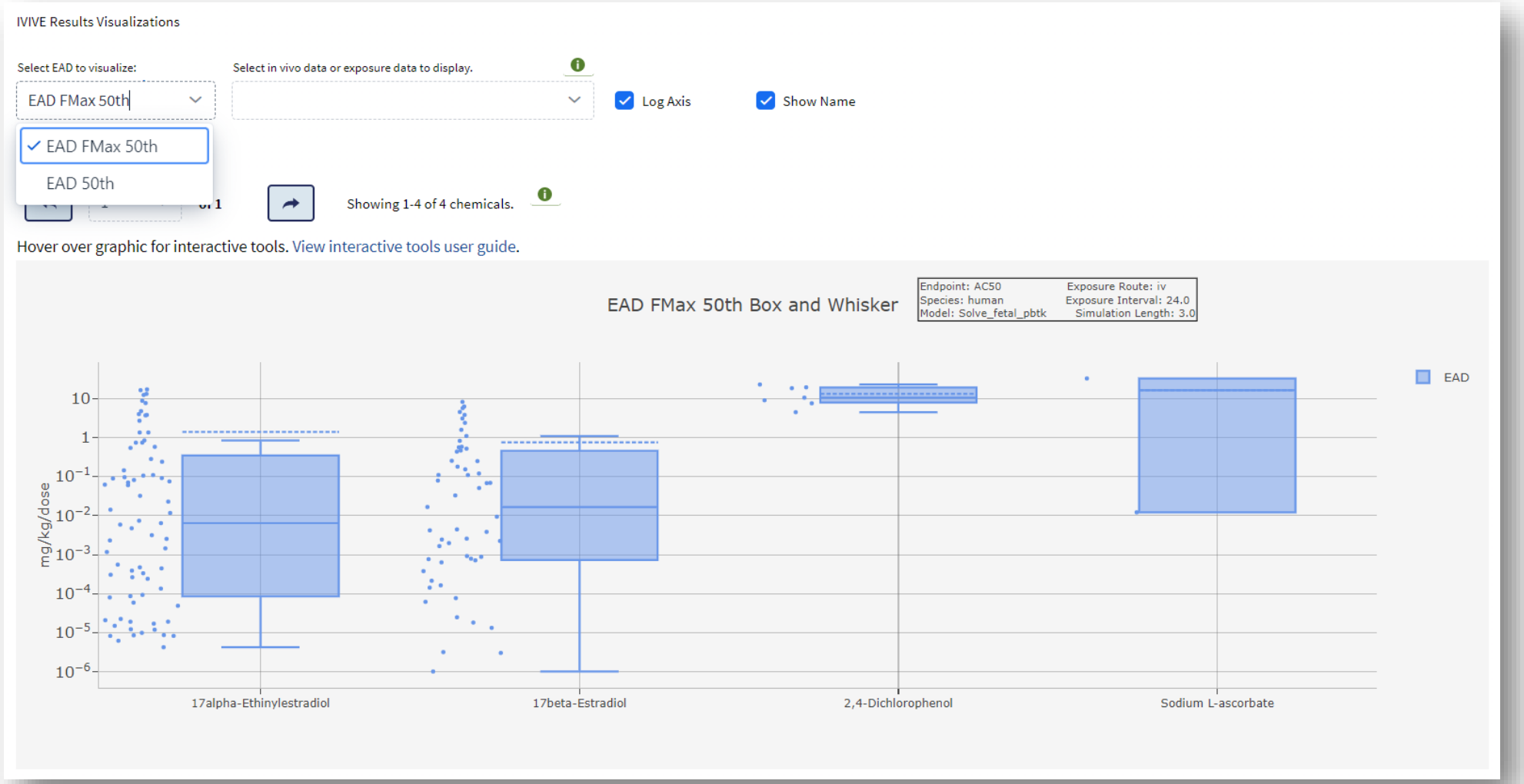
New Gestational Model in ICE PBPK Tool

- Human PBPK model yields concentration-time profiles in various maternal and fetal compartments (e.g., kidney, liver, plasma, thyroid, etc.)
- Users can provide gestation day when exposure starts (anywhere from 13 to 40 weeks)

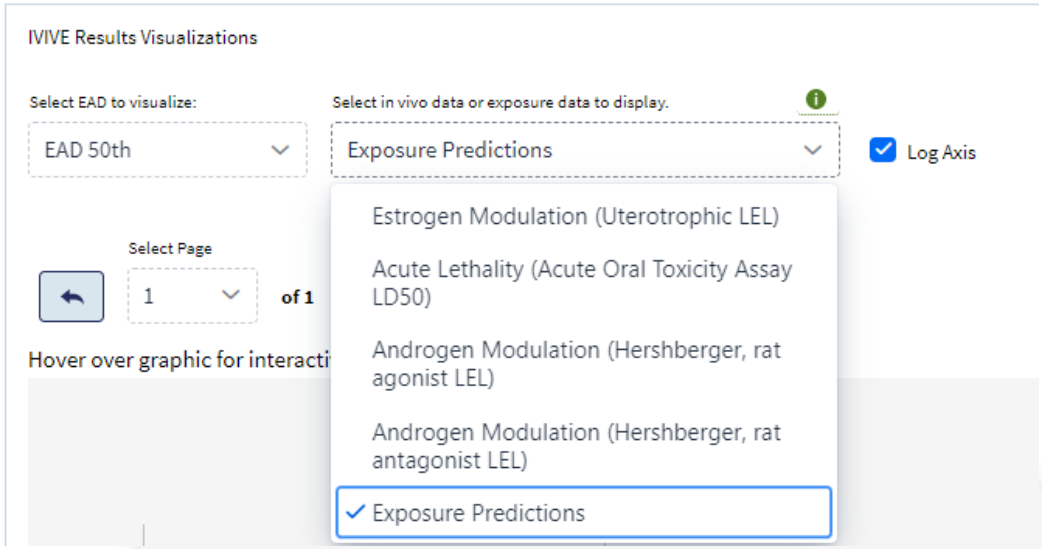
Results visualizations provides filtering options to select maternal and/or fetal compartments for plotting to facilitate comparisons

New Gestational Model in ICE IVIVE Tool

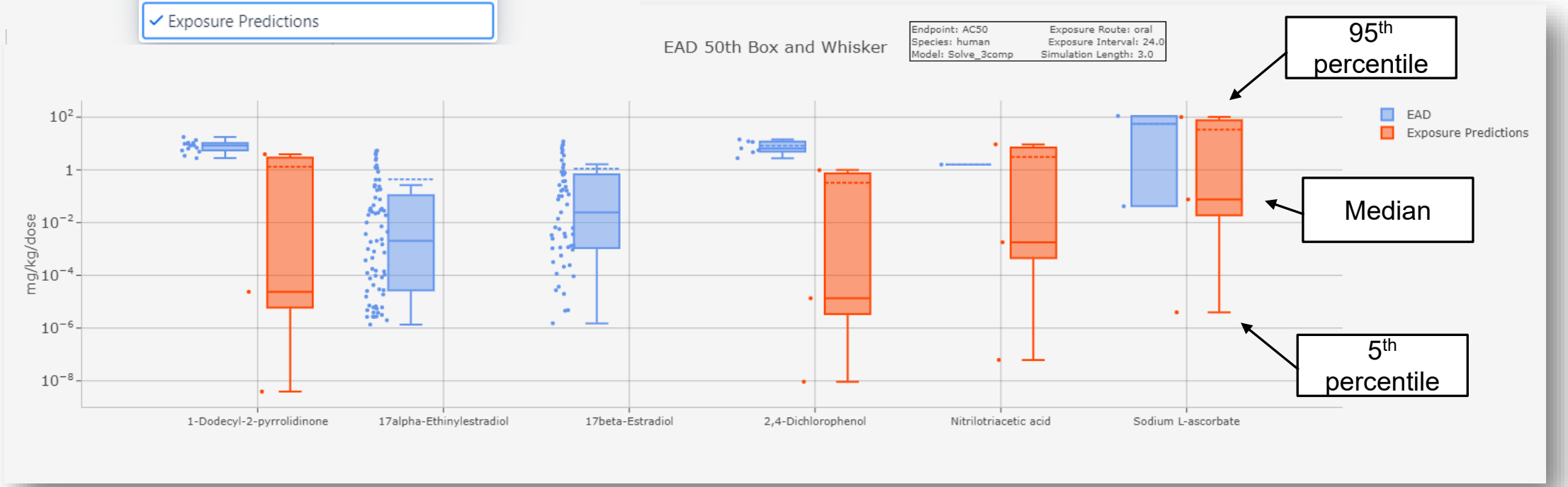
IVIVE tool can predict maternal and/or fetal EADs for multiple chemicals based on in vitro inputs (using ICE data or user-provided values)



Exposure Overlay in IVIVE Tool



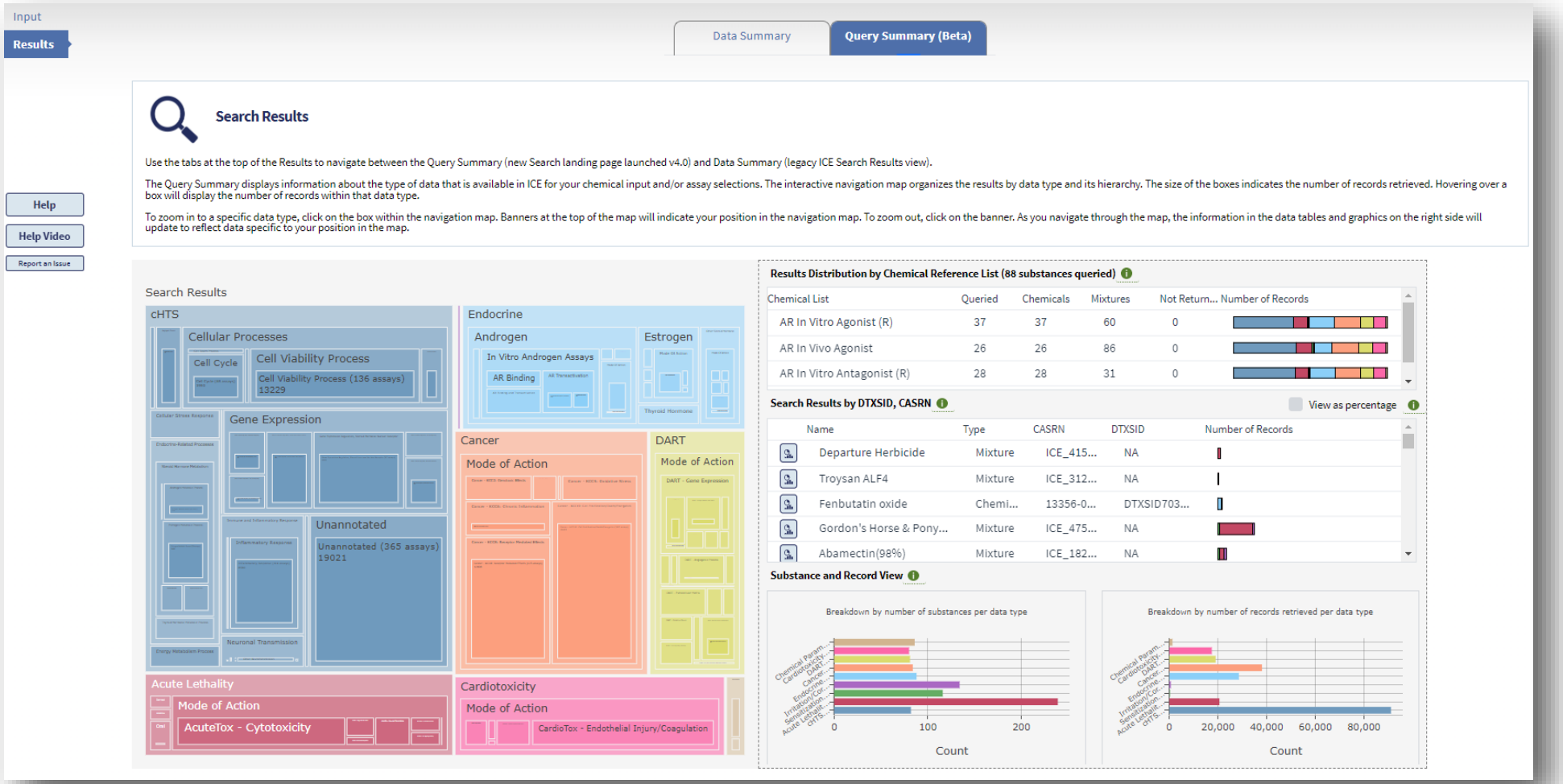
- There is now an overlay option for population-level exposure predictions derived from EPA's SEEM3
- It considers exposure from consumer, dietary, industrial, and pesticide pathways
- To ensure fair comparisons, IVIVE models should be run with 24-hour dosing interval since exposure predictions are in units of mg/kg/day



New Search “Query Summary”

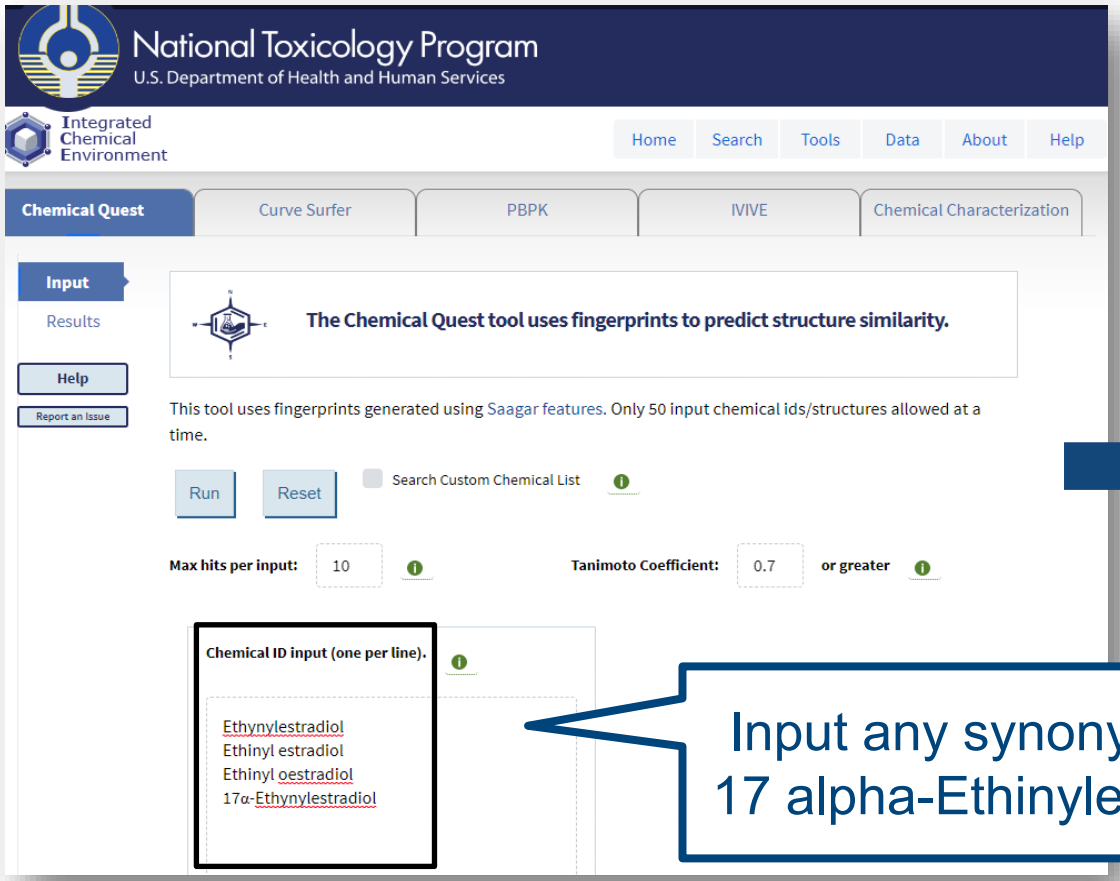
Interactive visualizations allow you to see the scope and breakdown of your query.

The Data Summary that used to appear for Search in previous versions of ICE is available in the “Data Summary” tab.

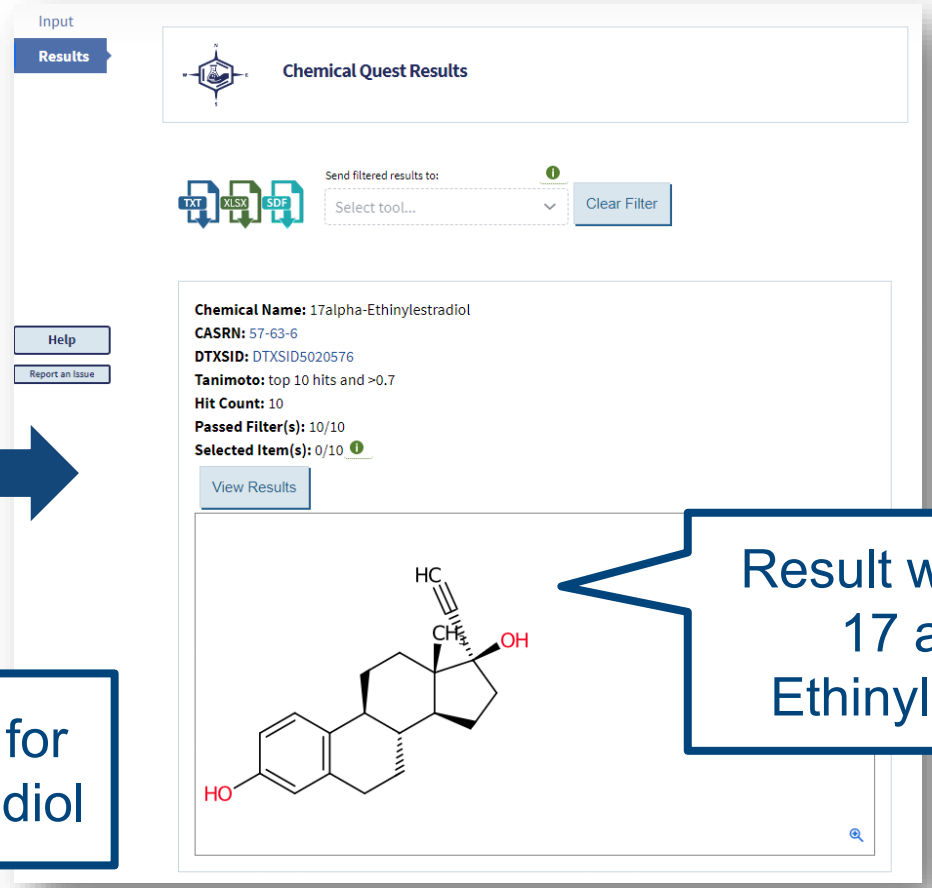


Chemical Name Searching

- ICE now offers a chemical name and synonym matching option in all its tools



Input any synonyms for 17 alpha-Ethinylestradiol

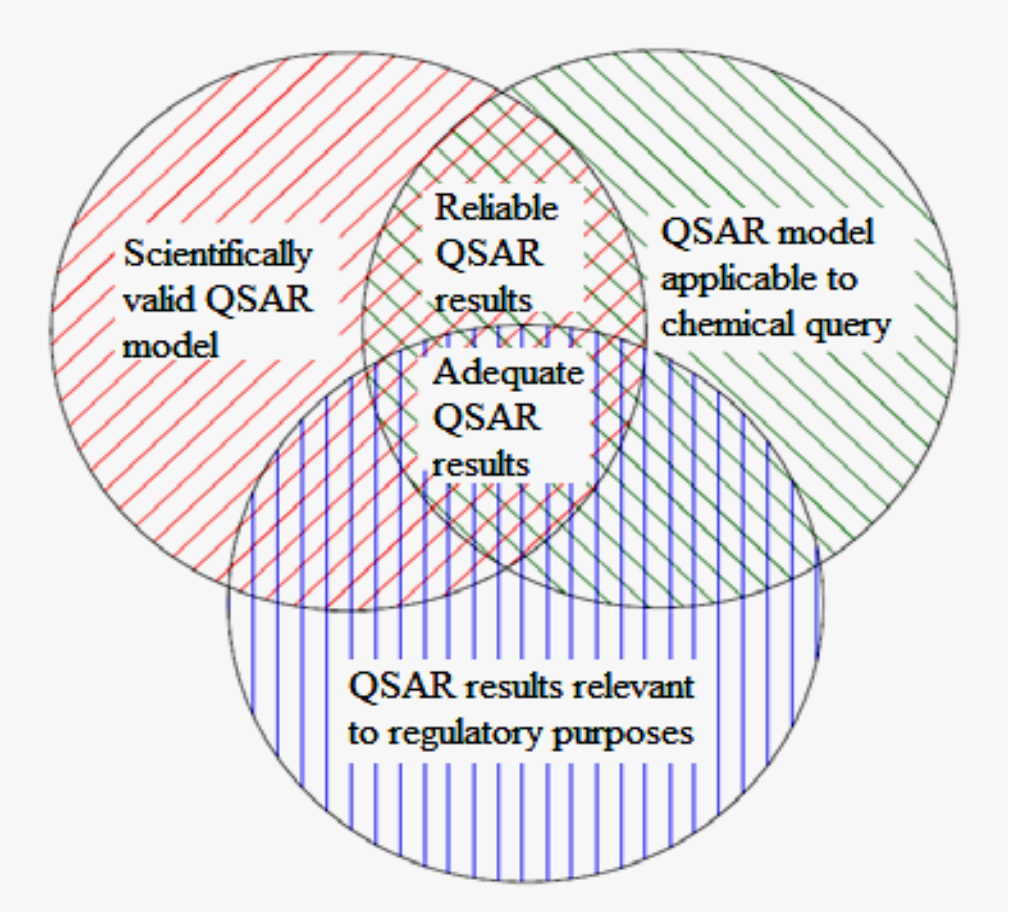


Result will display 17 alpha-Ethinylestradiol

OPERA

QSARs for regulatory purposes

The 5 OECD Principles
1) A defined endpoint
2) An unambiguous algorithm
3) A defined domain of applicability
4) Appropriate measures of goodness-of-fit, robustness and predictivity
5) Mechanistic interpretation, if possible



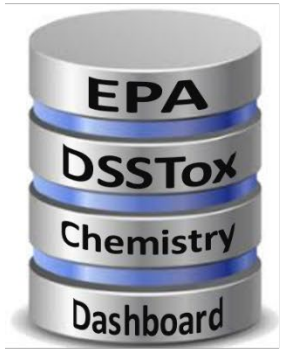
Journal of Cheminformatics
December 2018, 10:10 | Cite as

OPERA models for predicting physicochemical properties and environmental fate endpoints

OPERA
OPEn (q)saR App

OPERA approach

- Curated **open** access datasets (https://doi.org/10.1186/s13321-018-0263-1)
- **Open-source** code (github.com/NIEHS/OPERA)
- **Transparent** unambiguous algorithms (https://qsardb.jrc.ec.europa.eu/qmrf/)
- **Transparent** validated performances (https://doi.org/10.1080/1062936X.2016.1253611)
- **Defined** applicability domain and limitations of the models
- Predictions **available** through:
  - NICEATM's Integrated Chemical Environment (https://ice.ntp.niehs.nih.gov/)
  - The EPA's CompTox Dashboard (https://comptox.epa.gov/dashboard)
  - Free and open-source standalone application (github.com/NIEHS/OPERA)



Integrated Chemical Environment

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OPERA models (version 2.9)

Physchem properties		Chemicals	Version
BP	**Boiling Point**	**7860**	**2.9**
HL	**Henry's Law Constant**	**2233**	**2.9**
LogP	**Octanol-water Partition Coefficient**	**18154**	**2.9**
MP	**Melting Point**	**22554**	**2.9**
VP	**Vapor Pressure**	**6764**	**2.9**
WS	**Water Solubility**	**9943**	**2.9**
pKa	Acid Dissociation Constant	6503	2.6
KOA	Octanol/Air Partition Coefficient	270	2.6

Environmental fate		Chemicals	Version
AOH	Atmospheric Hydroxylation Rate	692	2.6
BCF	Bioconcentration Factor	626	2.6
BioHL	Biodegradation Half-life	150	2.6
RB	Ready Biodegradability	1603	2.6
KM	Fish Biotransformation Half-life	541	2.6
KOC	Soil Adsorption Coefficient	728	2.6

Toxicity endpoints		Chemicals	Version
ER	Estrogen Receptor Activity	32464	2.6
AR	Androgen Receptor Activity	47673	2.6
AcuteTox	Acute Oral Systemic Toxicity	50660	2.6

ADME properties		Chemicals	Version
FUB	**Fraction unbound**	**3229**	**2.8**
Clint	**Intrinsic clearance**	**1346**	**2.8**
CACO2	**Caco-2 permeability**	**4601**	**2.8**

New/updated since 2021

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PFAS in OPERA models

	Models	PFAS/Total
BP	Boiling Point	346/7860
LogP	Octanol-water Partition Coef.	97/18154
MP	Melting Point	409/22554
VP	Vapor Pressure	178/6764
WS	Water Solubility	105/9943

VP Vapor Pressure

Deviation of log$_{10}$*p* (*Pa*) estimates from experimental measurements at 25 °C

	COSMOtherm	EPI Suite	NICEATM	ACD/Labs	TEST	OPERA
MAE	1.22	1.08	1.46	1.53	1.31	0.95
RMSE	1.48	1.48	2.06	1.99	1.91	1.26

LogP Octanol-water Coef

Deviation of octanol–water partition ratio (log K_{OW}) estimates from experimental measurements at 25 °C

	COSMOtherm	EPI Suite	NICEATM	ACD/Labs	OPERA	LSER
MAE	0.41	0.25	0.68	0.61	0.21	0.33
RMSE	0.50	0.29	1.13	0.70	0.28	0.36

WS Water solubility

Deviation of water solubility (log *S*; mg/L) estimates from experimental measurements at 25 °C

	COSMOtherm	EPI Suite	NICEATM	TEST[a]	OPERA
MAE	0.35	1.82	2.38	0.95	0.23
RMSE	0.41	2.20	2.55	1.36	0.36

Environmental Chemistry

Property Estimation of Per- and Polyfluoroalkyl Substances: A Comparative Assessment of Estimation Methods

Alina Lampic and J. Mark Parnis*

Chemical Properties Research Group (Canadian Environmental Modelling Centre), Department of Chemistry, Trent University, Peterborough, Ontario, Canada

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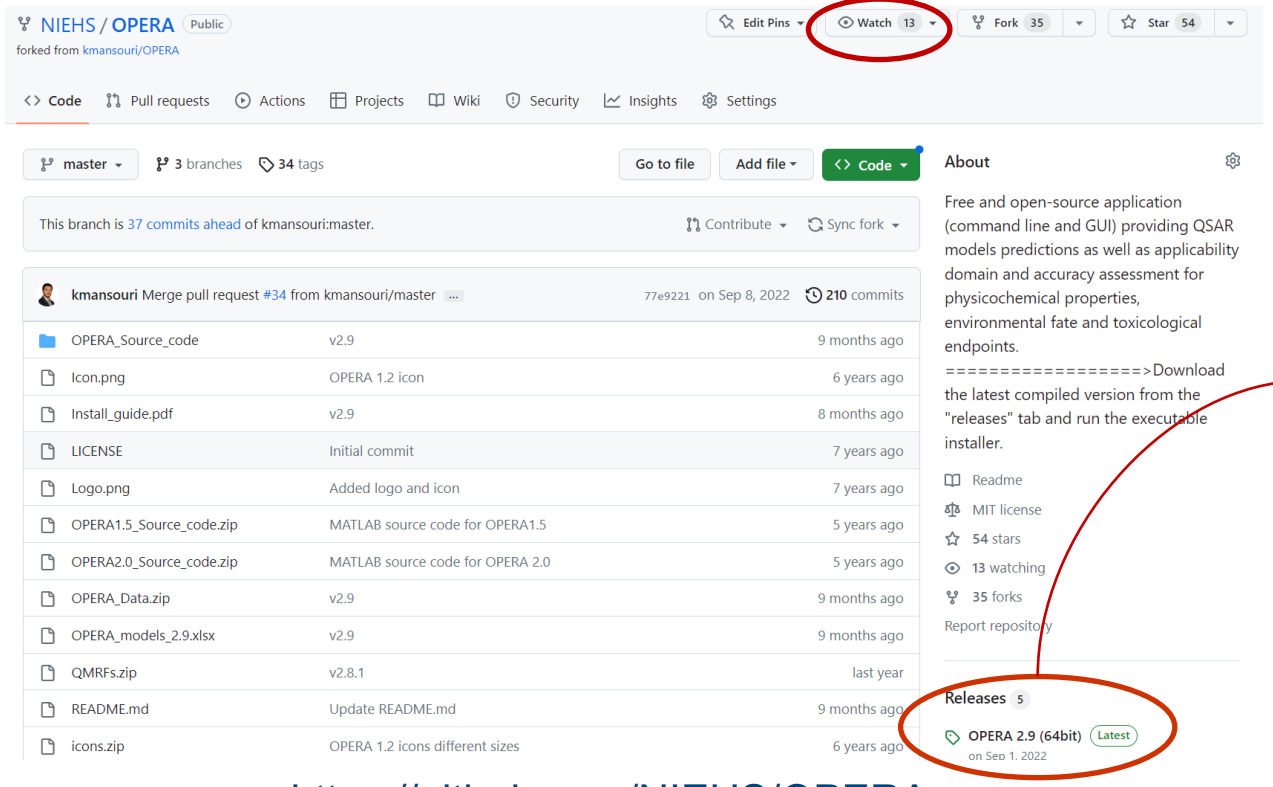
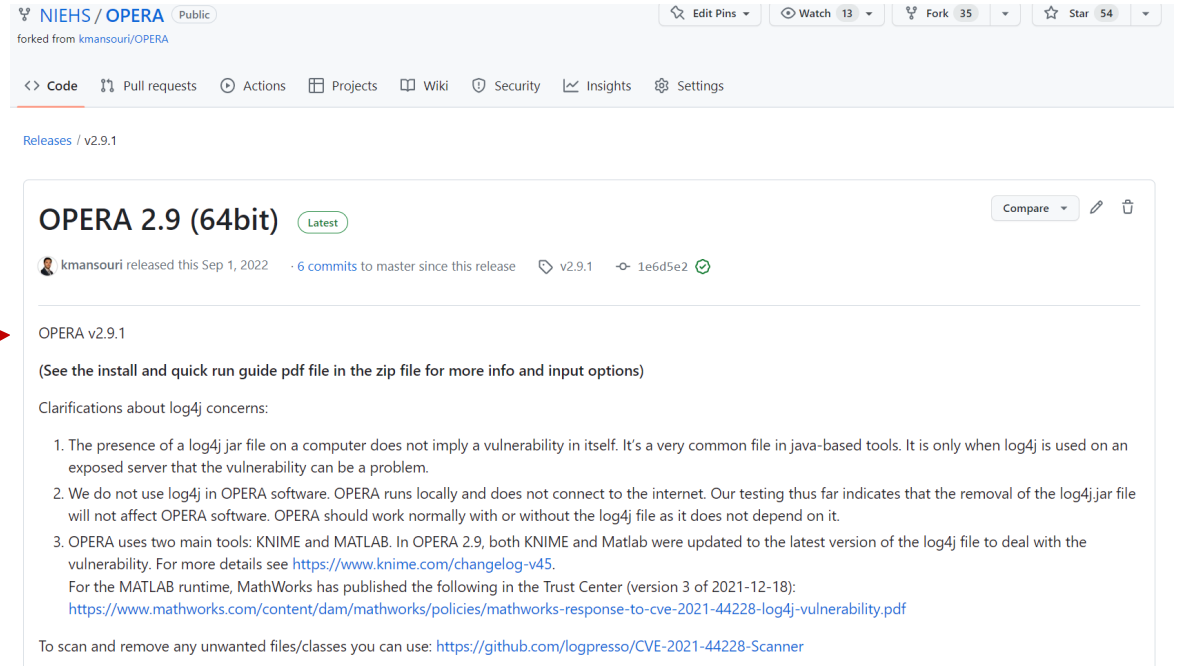
OPERA on GitHub

Source code

Packaged installers

Updates notifications





https://github.com/NIEHS/OPERA

https://github.com/NIEHS/OPERA/releases

Over 5000 downloads

(https://tooomm.github.io/github-release-stats/)

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OPERA as a standalone desktop application

OPERA standalone application:

- Free, opensource & open-data
- Single chemical and batch mode
- Multiple platforms (Windows and Linux)
- Embeddable libraries (java, C, C++, Python)
- **Command line & Graphical user interface**

OPERA models:

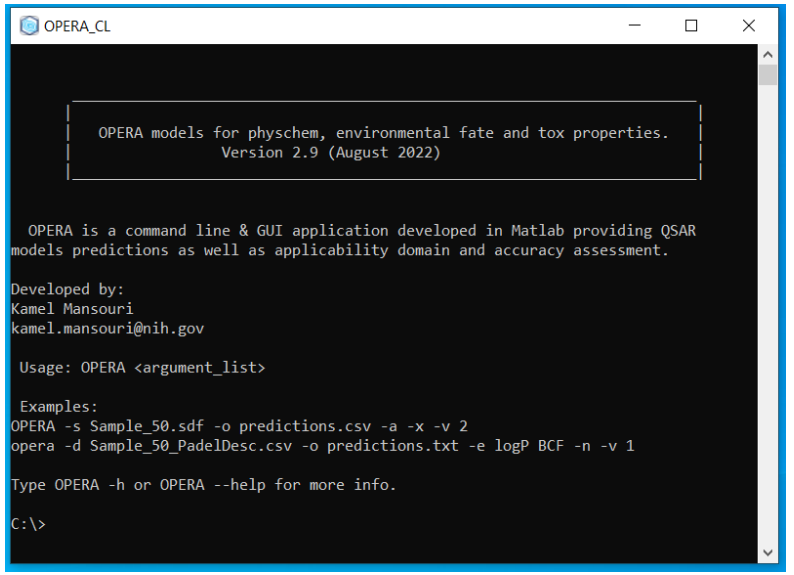
- Physicochemical properties
- Environmental fate
- ADME properties
- Toxicity endpoints

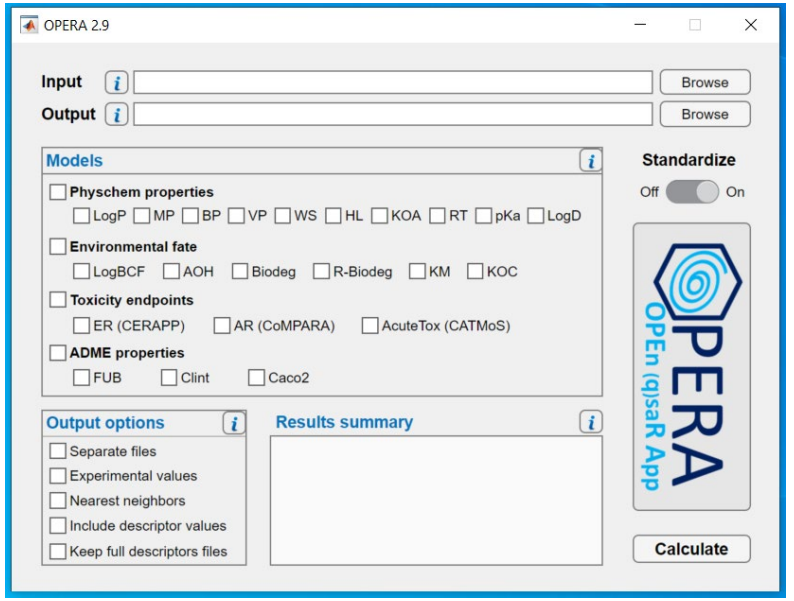
Input options:

- Structure IDs (CAS, DTXSID, InChIKey)
- Structure files (SMILES, SDF, Mol)

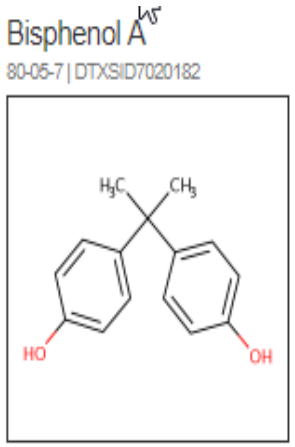
Links:

https://github.com/NIEHS/OPERA
https://ntp.niehs.nih.gov/go/opera
https://jcheminf.biomedcentral.com/articles/10.1186/s13321-018-0263-1

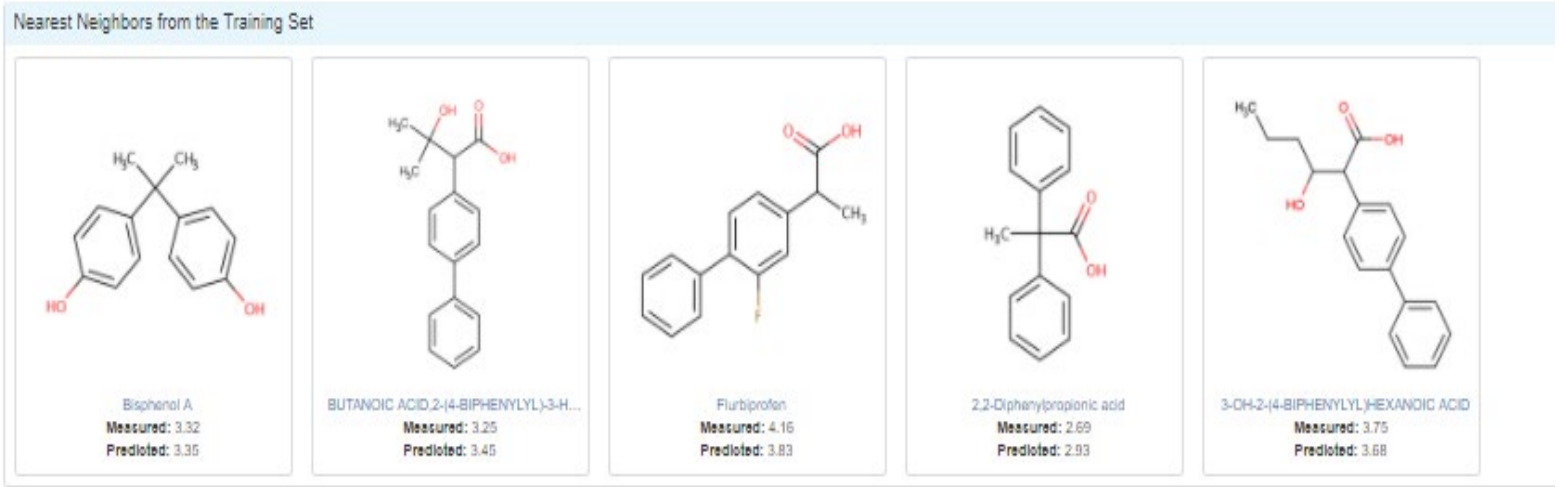




OPERA output



- Predicted value
- Experimental value, if available
- Global applicability domain
- Local applicability domain index [0:1]
- Accuracy index [0:1]
- Confidence interval [min:max]
- 5 nearest neighbors:
  - Identifiers (CAS, DTXSID, InChiKey)
  - Experimental values
  - Predicted values
- Molecular descriptors values



	MoleculeID	DTXSID7020182
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	LogP_pred	3.32
	LogP_predRange	[3.27:3.37]
	AD_LogP	1
	AD_index_LogP	1
	Conf_index_LogP	0.948
	LogP_CAS_neighbor_1	80-05-7
	LogP_CAS_neighbor_2	93371-55-2
0	LogP_CAS_neighbor_3	85-27-8
1	LogP_CAS_neighbor_4	5104-49-4
2	LogP_CAS_neighbor_5	5558-66-7
3	LogP_InChiKey_neighbor_1	IISBACLAFKSPIT-U
4	LogP_InChiKey_neighbor_2	ZNPAJPOVURPJFI
5	LogP_InChiKey_neighbor_3	PQSXNIMHIHYFE
5	LogP_InChiKey_neighbor_4	SYTBZMRGLBWN
7	LogP_InChiKey_neighbor_5	ODELFXJUOVNEF
8	LogP_DTXSID_neighbor_1	DTXSID7020182
9	LogP_DTXSID_neighbor_2	DTXSID5087493C
0	LogP_DTXSID_neighbor_3	DTXSID50100531
1	LogP_DTXSID_neighbor_4	DTXSID0037231
2	LogP_DTXSID_neighbor_5	DTXSID4020412E
3	LogP_Exp_neighbor_1	3.32
4	LogP_Exp_neighbor_2	3.25
5	LogP_Exp_neighbor_3	2.11
5	LogP_Exp_neighbor_4	4.16
7	LogP_Exp_neighbor_5	2.69
8	LogP_pred_neighbor_1	3.18
9	LogP_pred_neighbor_2	3.66
0	LogP_pred_neighbor_3	3.5
1	LogP_pred_neighbor_4	3.05
2	LogP_pred_neighbor_5	3.44

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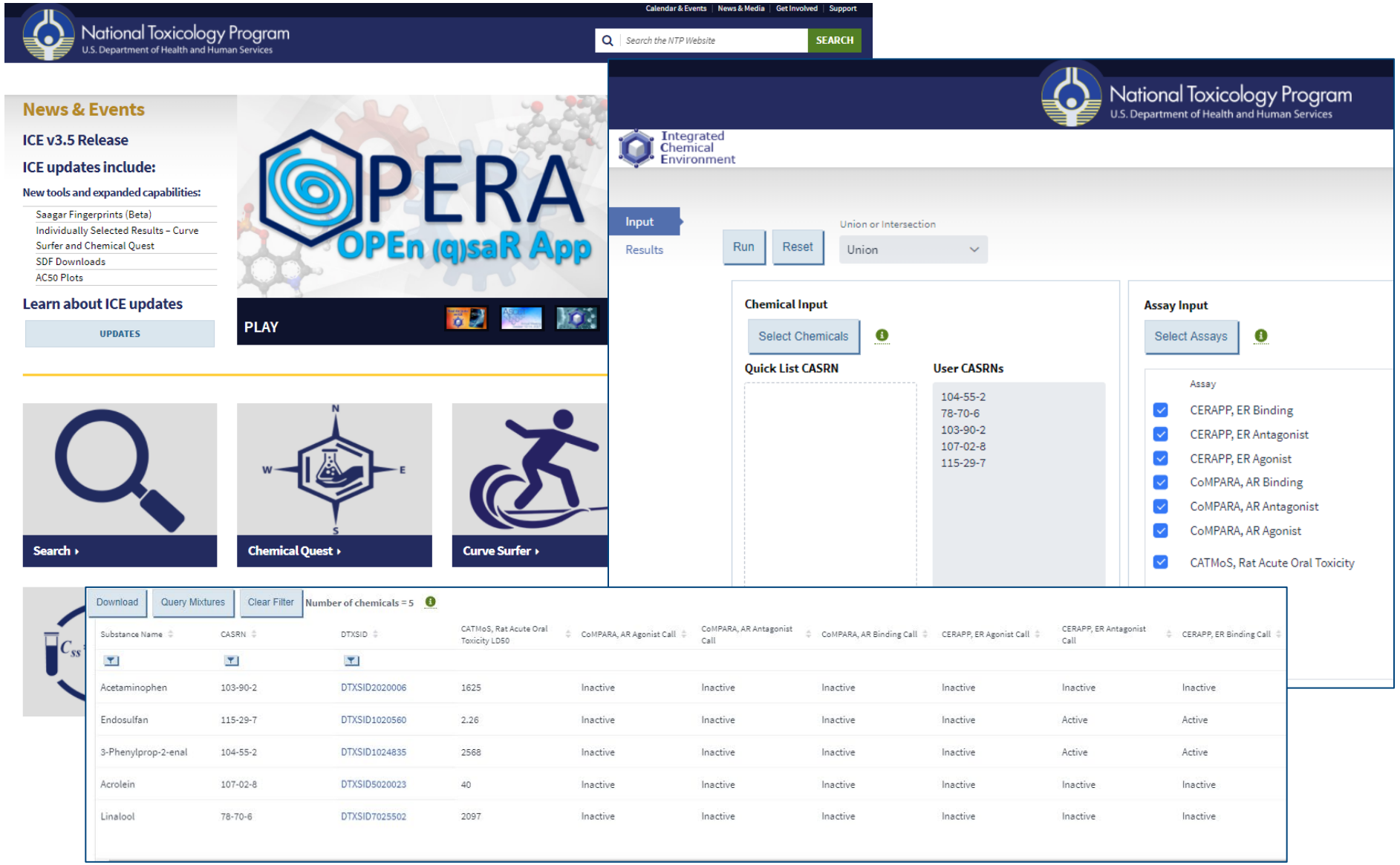
Predictions on NICEATM's ICE



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

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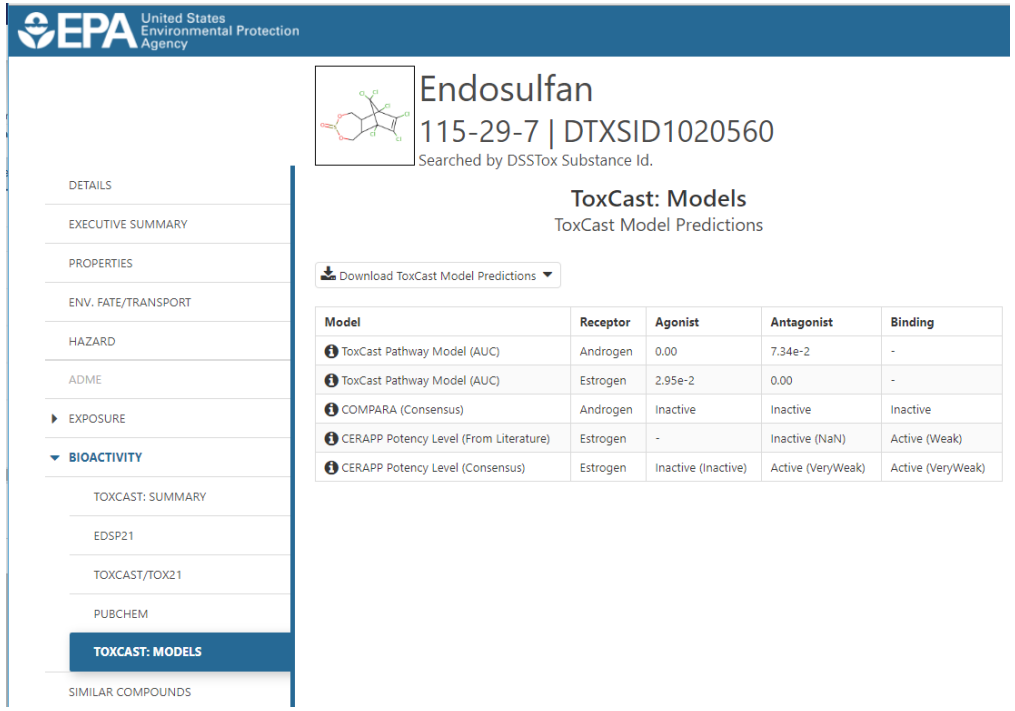
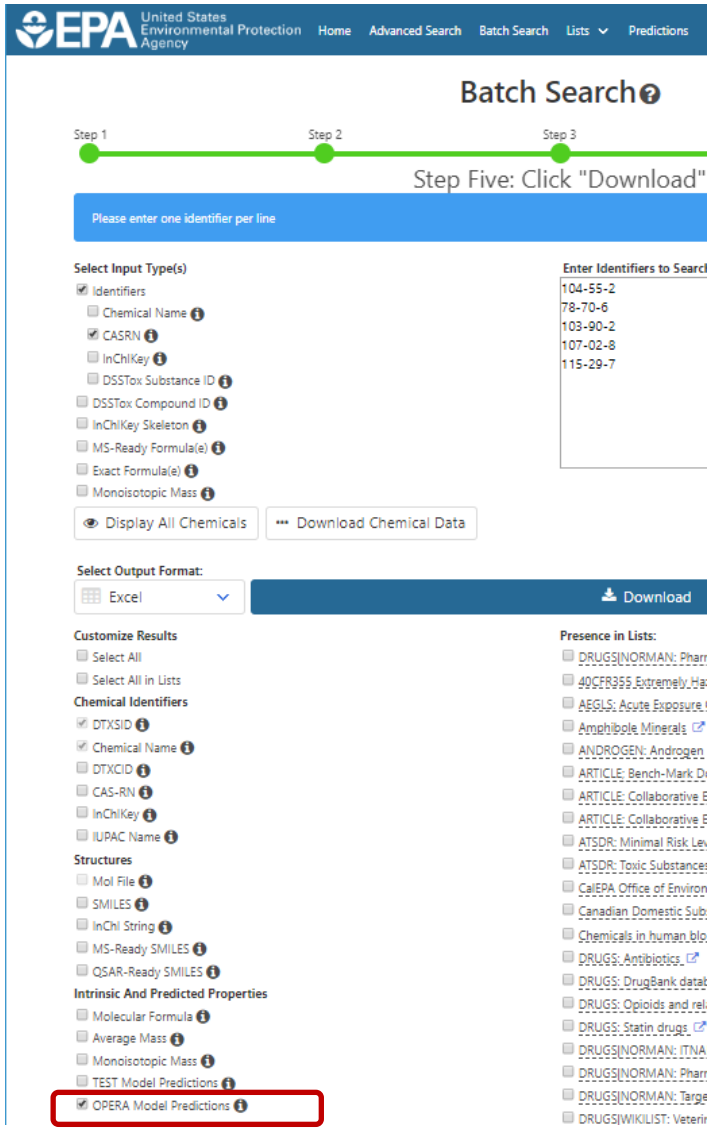
Predictions on the EPA Dashboard

Single chemical



https://comptox.epa.gov/dashboard/dsstoxdb/results?search=DTXSID1020560#bioactivity-toxcast-models

Batch search



https://comptox.epa.gov/dashboard/dsstoxdb/batch_search

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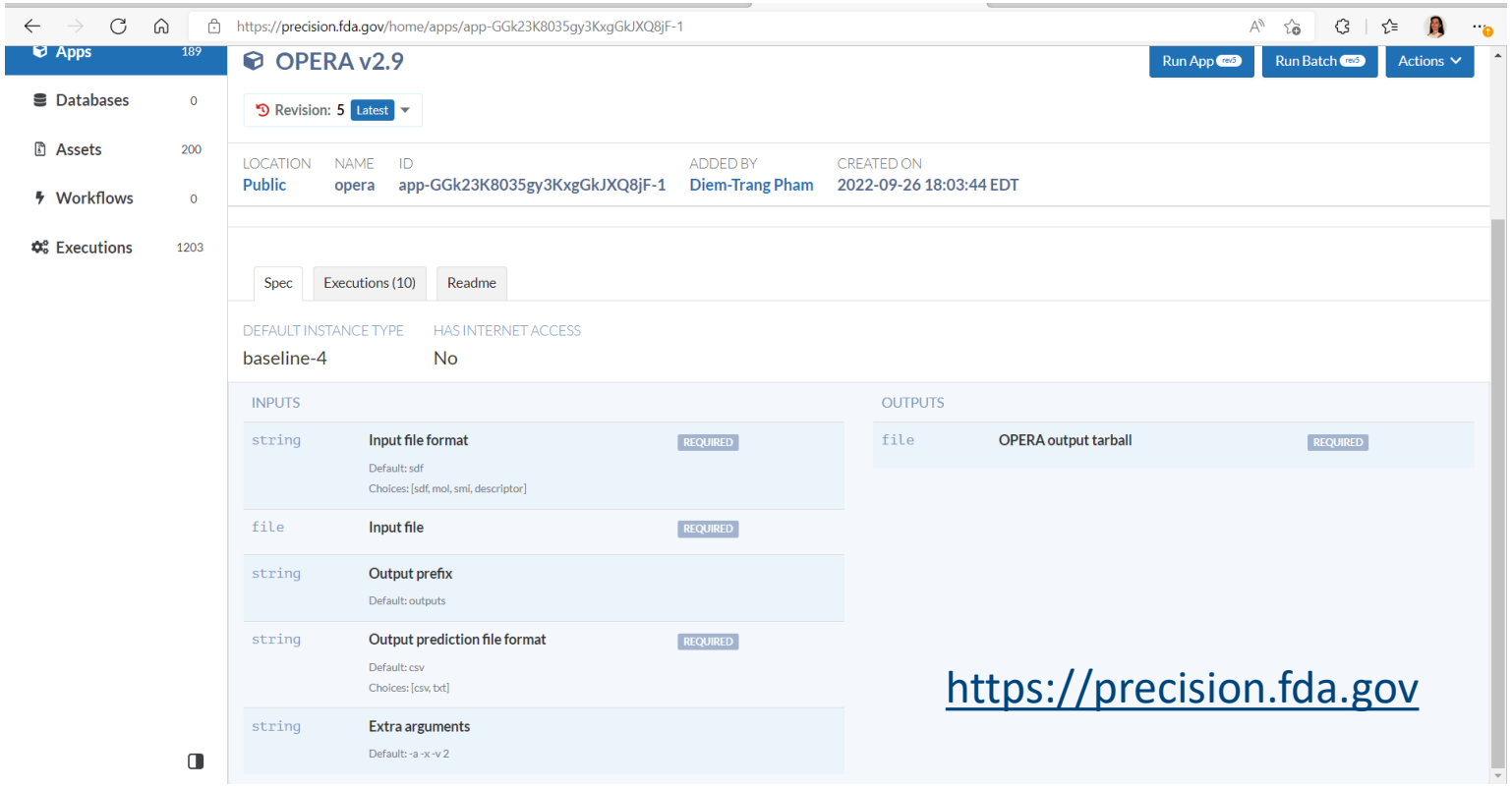
Predictions on FDA's precision platform

precisionFDA

A secure, collaborative, high-performance computing platform that builds a community of experts around the analysis of biological datasets in order to advance precision medicine.



https://precision.fda.gov

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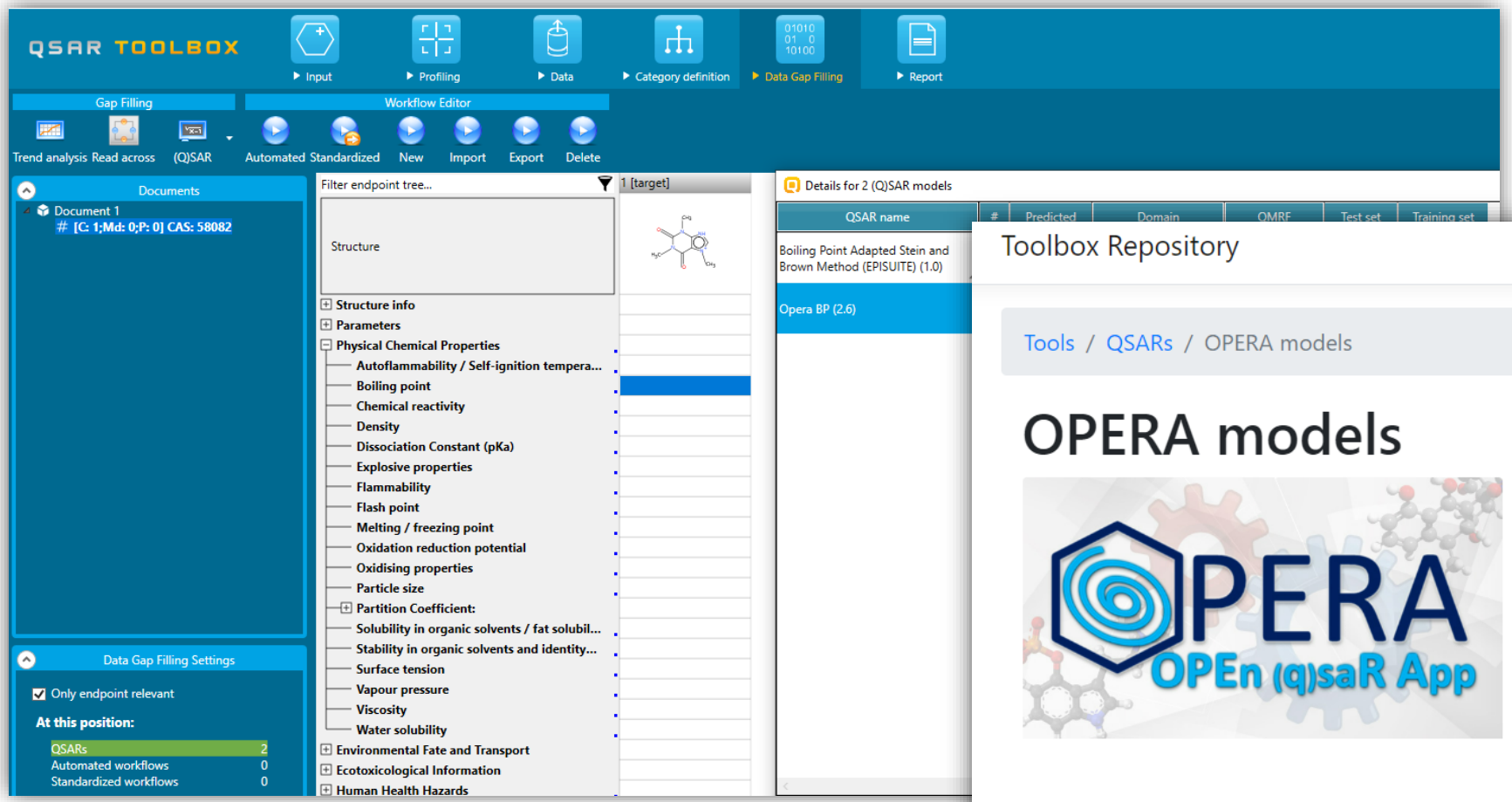
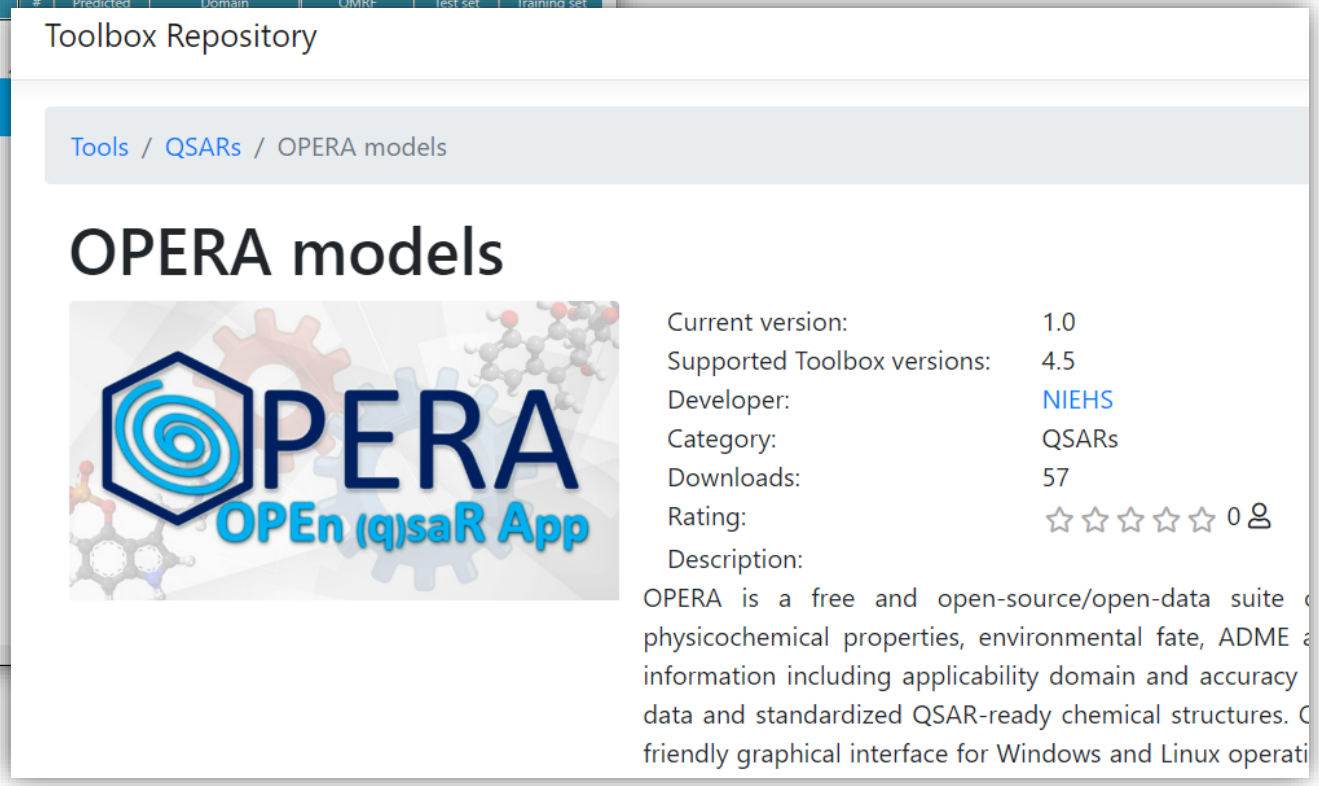
OPERA in the OECD Toolbox





https://repository.qsartoolbox.org/

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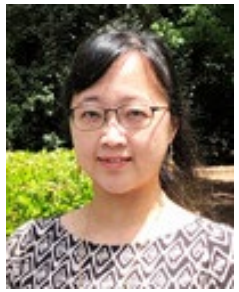
Acknowledgments



The NICEATM Group

Integrated Chemical Environment

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

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