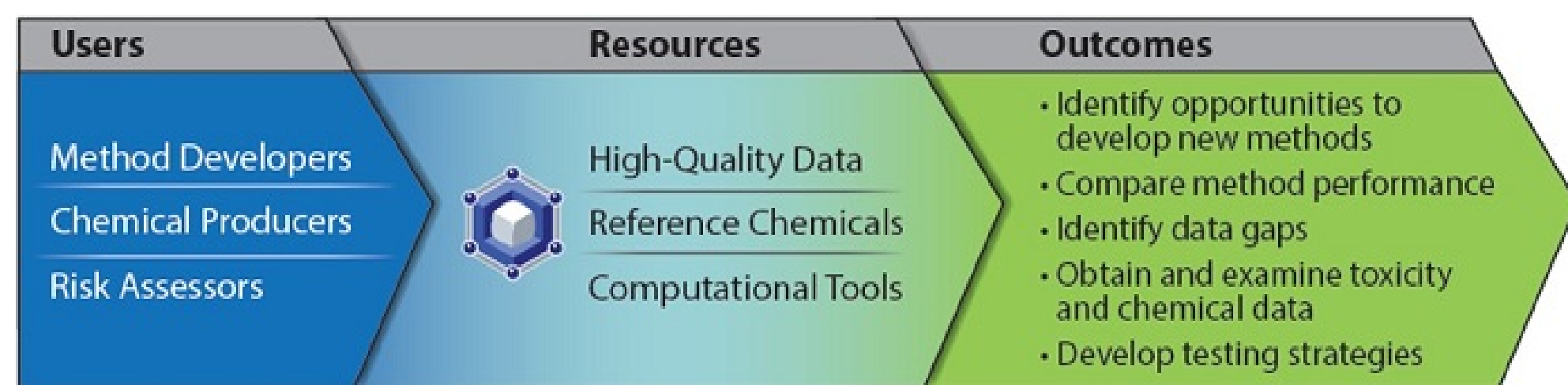


User-friendly Toxicology Tools from ICE Workflows

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The Integrated Chemical Environment



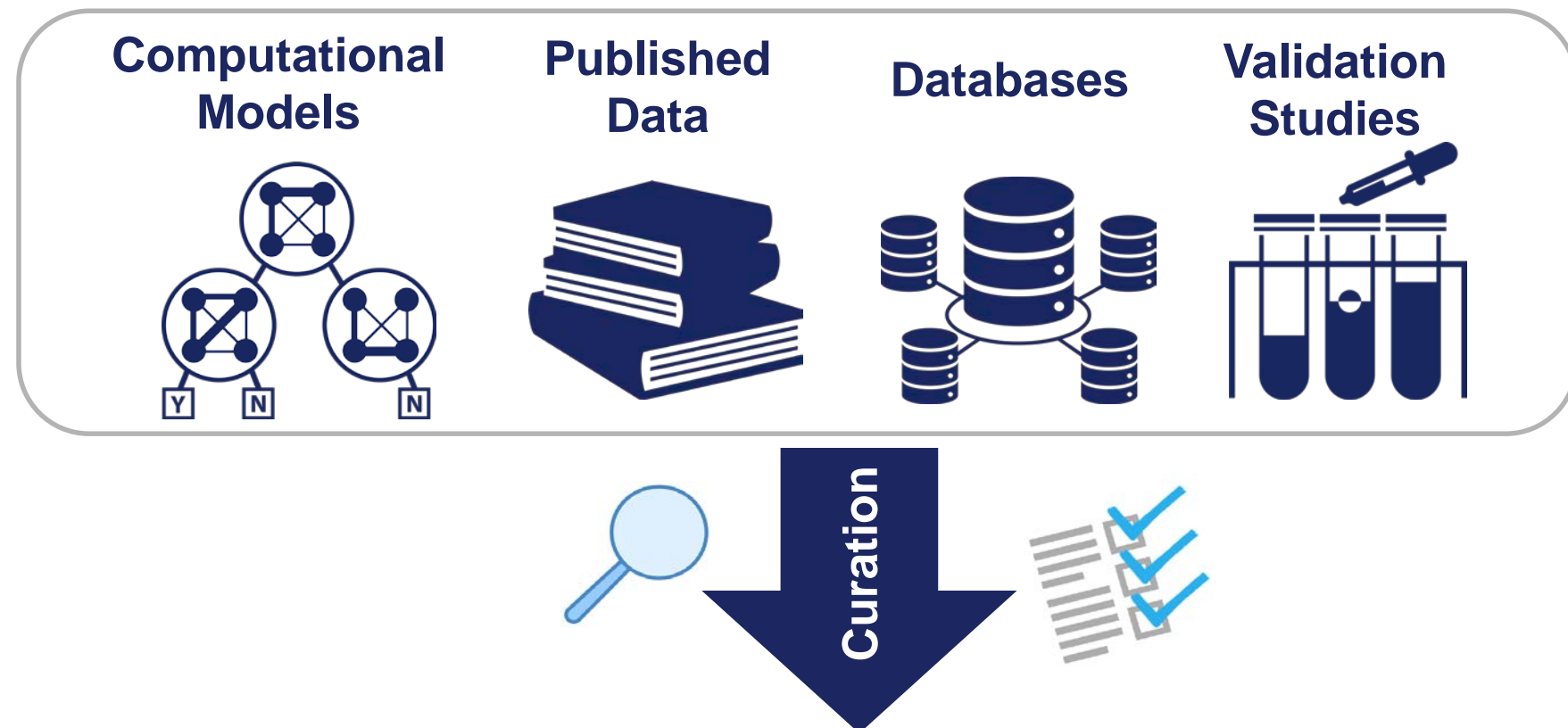
ICE provides free online access to:

- Curated in vivo and in vitro test data
- In silico toxicity predictions and chemical property data
- Reference chemical lists
- Computational tools and workflows related to chemical characterization and predicting toxicity

ICE supports:

- Data integration:** brings together available data, including data on formulations
- Results exploration:** enables dynamic, graphical exploration with publication-quality graphics
- Data analysis:** allows characterization of data using online workflows
- FAIR data access**

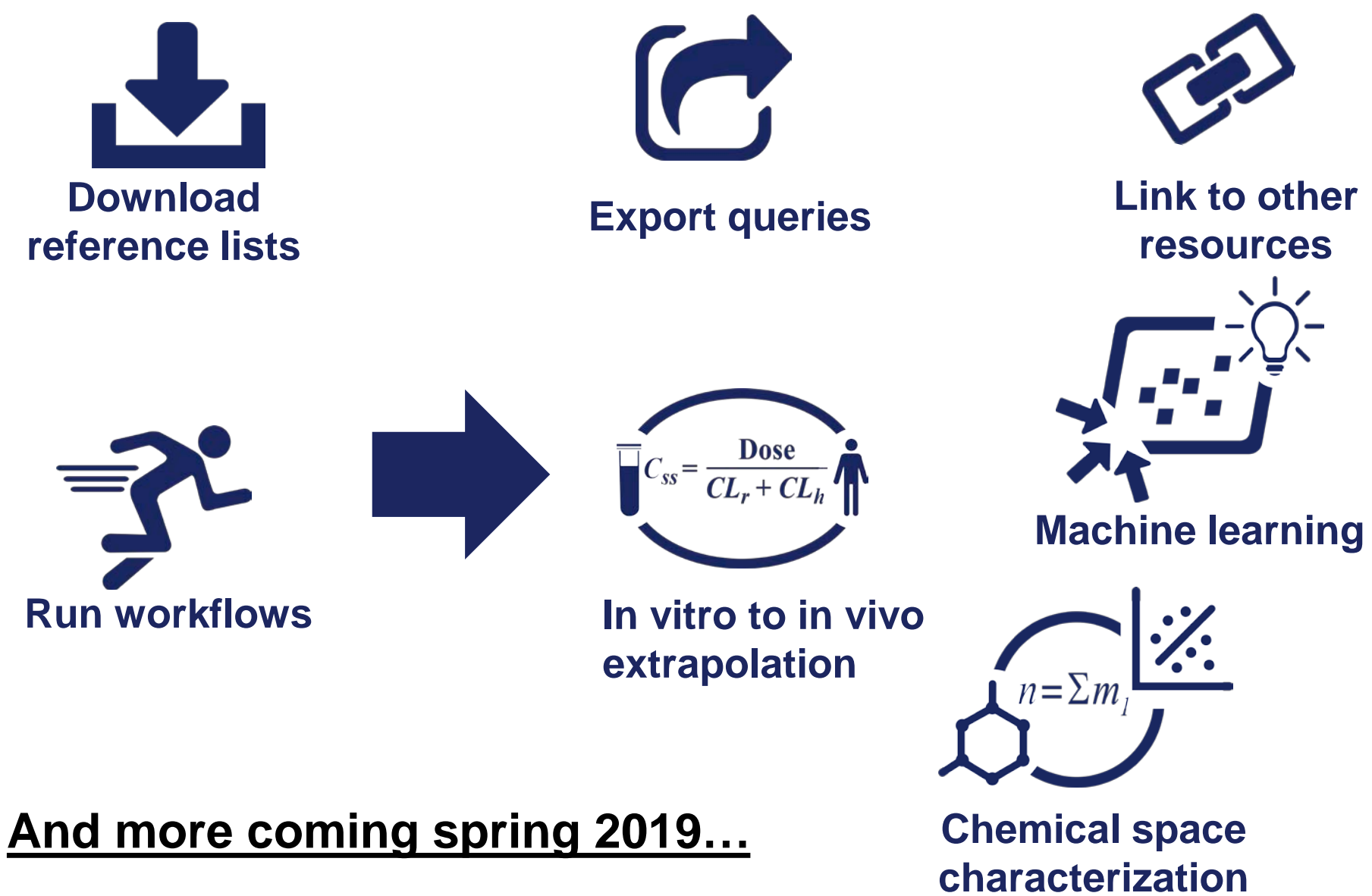
What Goes into ICE?



Chemical Breakdown

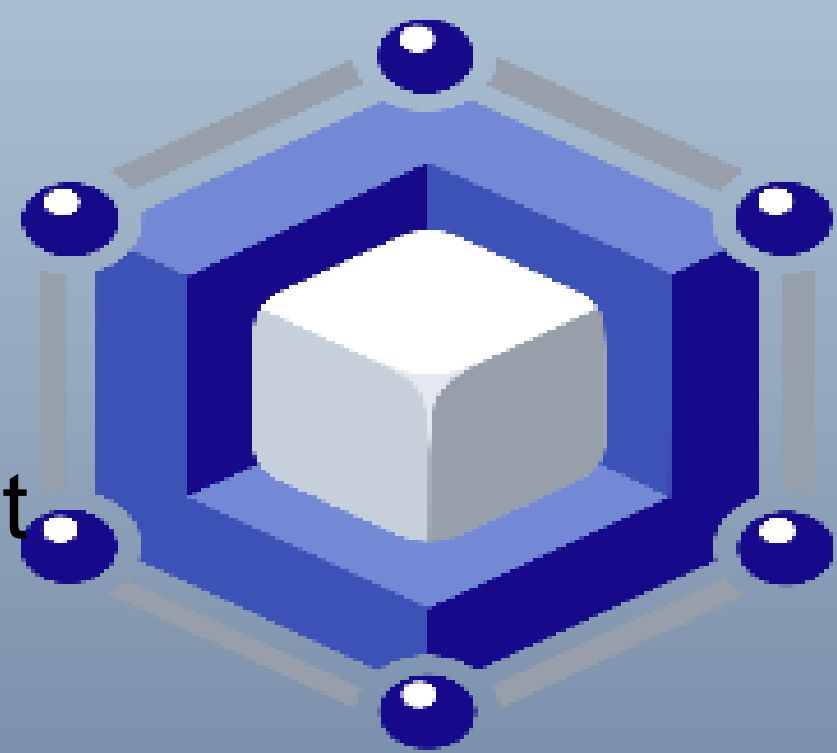
Assay	In silico	In silico+in vitro	In silico+in vitro+in vivo	In vitro+in vivo	In vivo
Acute Oral Toxicity	84	35	49	16	61
Skin Sensitization	16	10	10	10	10
Eye Irritation	112	42	23	111	109
Endocrine	111	111	111	111	111
Chemicals	111	111	111	111	111

Making Data and Tools Available



And more coming spring 2019...

Integrated Chemical Environment



Findable
Accessible
Interoperable
Reusable

Machine Learning

Use the machine learning tool for hypothesis generation and to explore different machine learning approaches using ICE data. Selected endpoints (for classification and regression modeling) and algorithms are available through ICE to facilitate the ease of use by those with limited background in computational toxicology

Endpoints for prediction

- LLNA: call
- Uterotrophic: call, LEL
- Human Potency: call, NOEL/LOEL

Machine learning methods available

- rf: random forest
- rpart: recursive partitioning
- knn: k-nearest neighbor
- svmRadial: support vector machine with a radial kernel
- pls: partial least squares regression

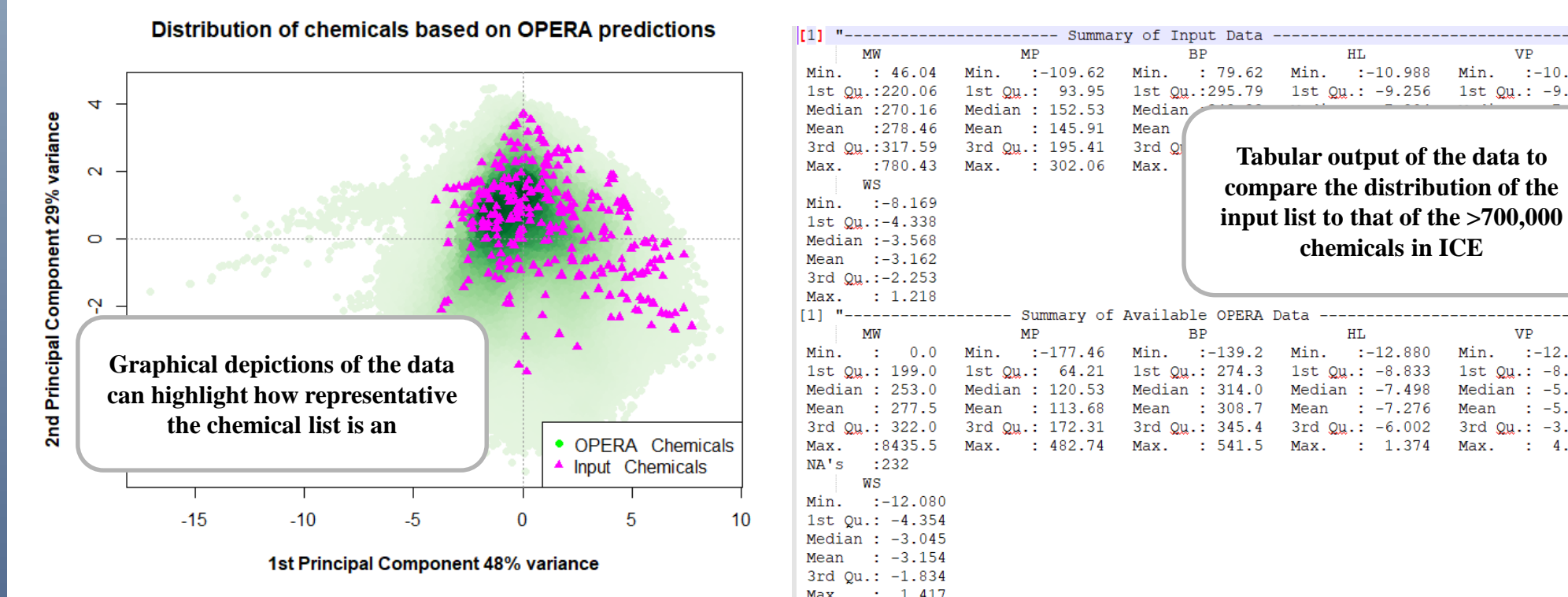
Models: knn, rf
Metrics: ROC, Sens, Spec
Number of differences: 1
p-value adjustment: bonferroni
[1] Machine Learning
Confusion Matrix at
Reference
Prediction Active
Active 61
Inactive 4
Accuracy : 0.9744
No Information Rate : 0.625
P-value [Acc > NIR] : 4.602e-15
Kappa : 0.899
McNemar's Test P-Value : 0.3711
Sensitivity : 0.9385
Specificity : 0.9744
Pos Pred Value : 0.9839
Neg Pred Value : 0.9048
Prevalence : 0.6250
Detection Rate : 0.5865
Detection Prevalence : 0.5962
Balanced Accuracy : 0.9564
'Positive' Class : Active

	A	B	C	D	E
1	CASRN	knn	svmRadial	toPredict	PhysChem
2	95-70-5	Active	Active	Active	0.355
3	26172-55-	Active	Active	Active	1.826
4	81406-37-	Active	Active	Active	0.675
5	119-96-8	Inactive	Inactive	Inactive	0.929
6	87-86-5	Active	Active	Active	-0.816
7	862892-90	Active	Active	Active	1.826
8	531-95-3	Active	Active	Inactive	0.675
9	66422-95-	Active	Active	Active	4.99
10	122-57-6	Active	Active	Active	0.929
11	150114-71	Inactive	Inactive	Inactive	0.675
12	1154-59-2	Active	Active	Active	4.99
13	89-25-8	Active	Active	Active	0.929

Imputation capabilities to allow missing data in the pipeline for spring

Chemical Characterization

Leverage ICE models to characterize a chemical list, getting information on the chemical space covered (or not covered) based on different physchem properties.



In Vitro to In Vivo Extrapolation

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

Use high-throughput in vitro data available from ICE to estimate external dose via a one-compartment model

IIVE tools planned for future releases:

- Three-compartment physiologically based pharmacokinetic model
- Glucuronidation and sulfation predictions
- Comparison with in vivo data (example: NTP/CEBS, EPA/ToxRefDB)
- Calculations with user-provided data on ICE platform

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