T.E.S.T. (Toxicity Estimation Software Tool)

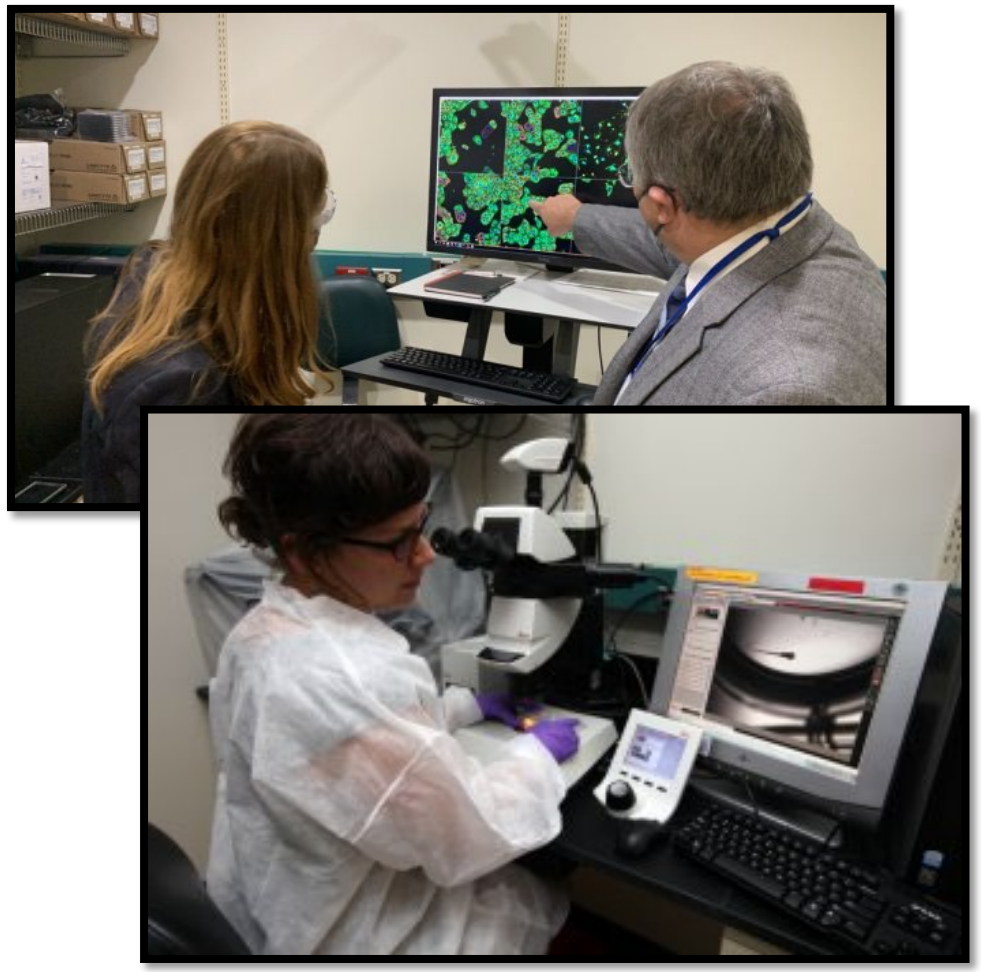
NAMs Training Workshop

RTP, NC

April 24– 25, 2024

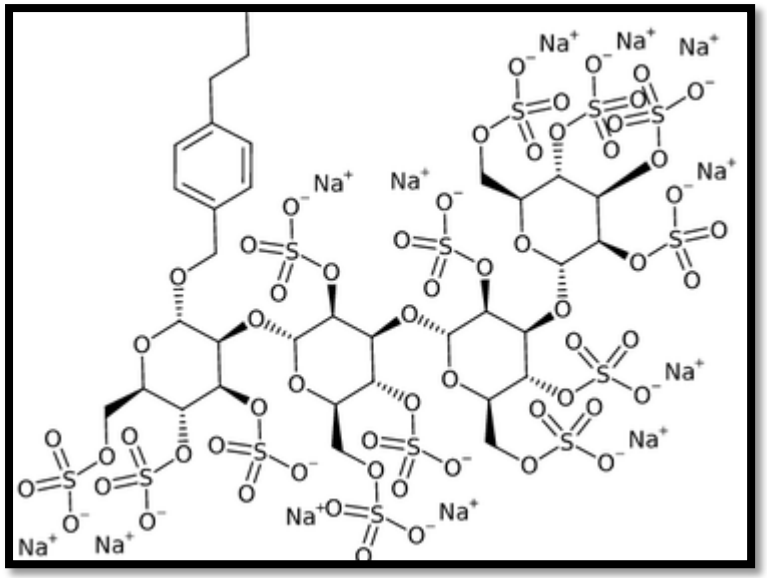
Dr. Todd Martin

Purpose of TEST



- Hazardous chemicals present in the environment create a need for understanding the risk of exposure to living things.
- EPA's Office of Research and Development is creating tools that make toxicity estimation accessible.
- TEST uses New Approach Methods for toxicity estimation.

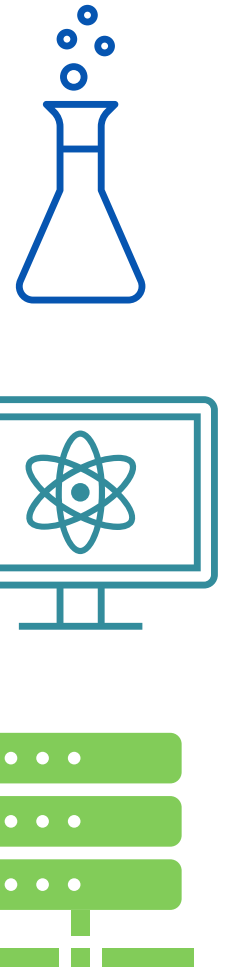
Data and Connections



- TEST is based on The Chemistry Development Kit , an open-source Java library for computational chemistry.
- The Chemistry Development Kit can:
  - Read and write chemical data formats
  - Render chemical structures
  - Algorithms for chemical graph theory
  - QSAR descriptors

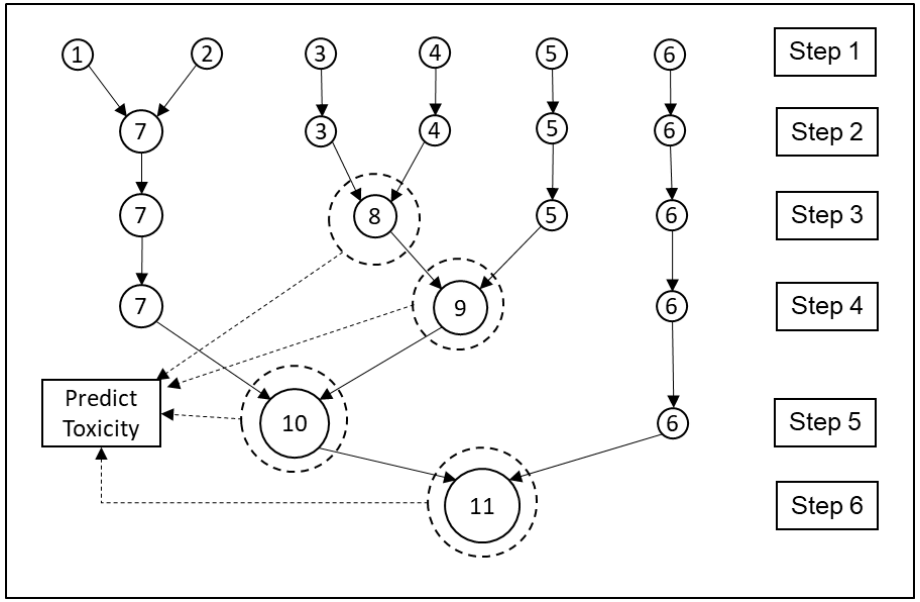
QSAR Methodologies

- TEST provides QSAR (Quantitative structure-activity relationship) models to estimate chemical safety relevant endpoints for data-poor chemicals
- QSAR models predict toxicity from the molecular structure via structural features known as descriptors
- TEST can predict toxicity endpoints such as acute aquatic toxicity and physicochemical properties such as water solubility



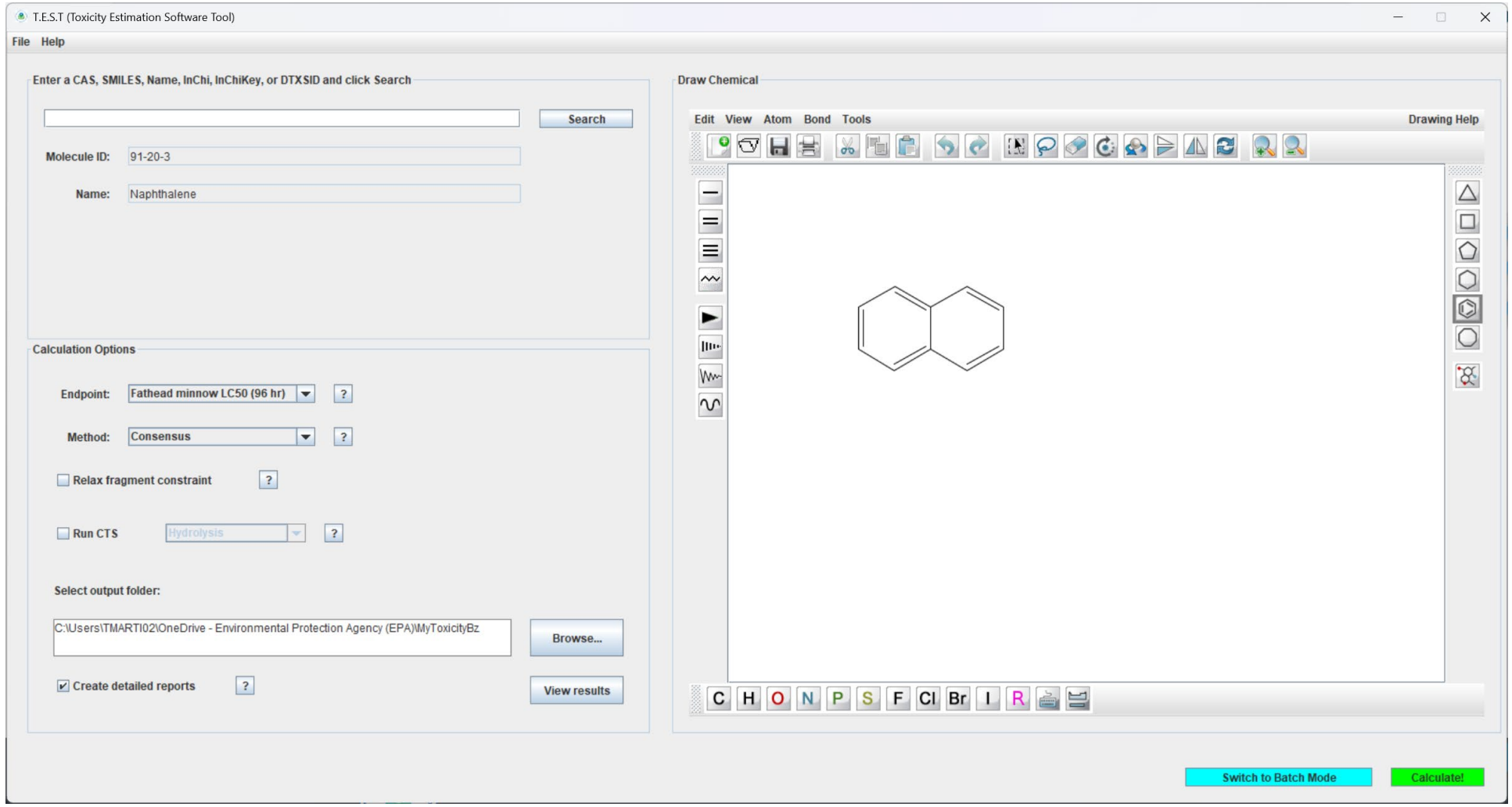
QSAR Methodologies

- T.E.S.T. uses using several different methodologies:
  - Hierarchical method
  - Single-model method
  - Group contribution method
  - Nearest neighbor method
  - Consensus method
  - Mode of action method



Using T.E.S.T.

- Users input a chemical to evaluate by drawing it in an included chemical sketcher window, entering a structure text file, or importing it from an included database of structures.
- Once entered, the toxicity is estimated using the selected QSAR methodology



Example of Tool/Data Use

- Estimation of aquatic toxicity of triphenyl phosphate (TPP):

Predicted Fathead minnow LC50 (96 hr) for DTXSID1021952 (115-86-6) from Consensus method

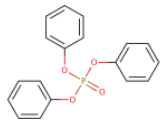
Prediction results

Endpoint	Experimental value (CAS= 115-86-6) Source: ECOTOX	Predicted value[a]
Fathead minnow LC_{50} (96 hr) -Log10(mol/L)	5.54	5.93
Fathead minnow LC_{50} (96 hr) mg/L	0.93	0.39

[a]Note: the test chemical was present in the external test set.

Individual Predictions

Method	Predicted value -Log10(mol/L)
Hierarchical clustering	6.42
Single model	6.05
Group contribution	N/A
Nearest neighbor	5.30



Descriptor values for test chemical

- Estimation of aquatic toxicity of TPP and its breakdown products:

Query	SmilesRan	Error	Exp_Value: -Log10(mol/L)	Pred_Value: -Log10(mol/L)	Exp_Value: mg/L	Pred_Value: mg/L
triphenyl phosphate	O=P(OC=1C=CC=CC1)(OC=2C=CC=CC2)OC=3C=CC=CC3		5.54	5.93	0.93	0.39
Product of 115-86-6, Accumulation = 50.0	O=P(O)(OC=1C=CC=CC1)OC=2C=CC=CC2		N/A	5.65	N/A	0.56
Product of 115-86-6, Accumulation = 50.0	OC=1C=CC=CC1		3.50	3.39	30.11	38.69

Limitations/Considerations

- T.E.S.T. can only make predictions for organic molecules that are not salts or mixtures.
- T.E.S.T. can only make accurate predictions for compounds that are similar to training set compounds
  - In the next generation of T.E.S.T., the data sets for physicochemical properties were expanded using publicly available data

Accessing TEST

- https://www.epa.gov/comptox-tools/toxicity-estimation-software-tool-test

TEST Point of Contact

Todd Martin
martin.todd@epa.gov