



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

NAMs Training Workshop

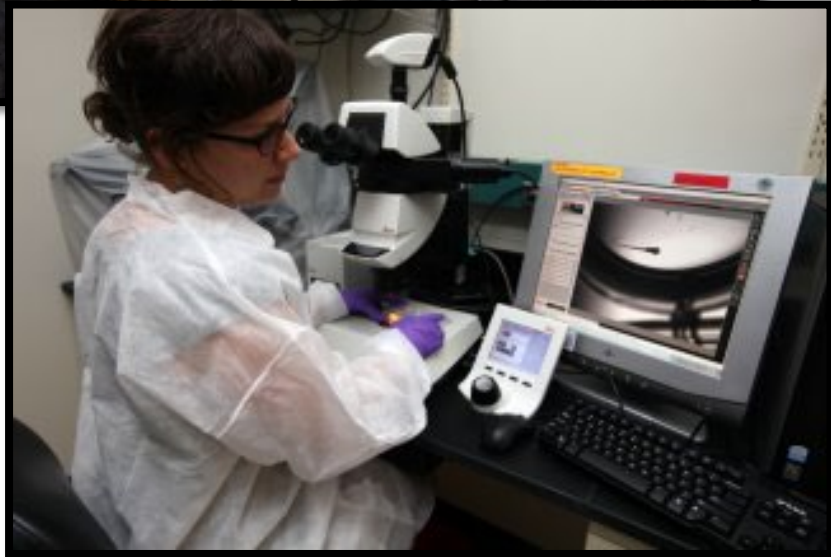
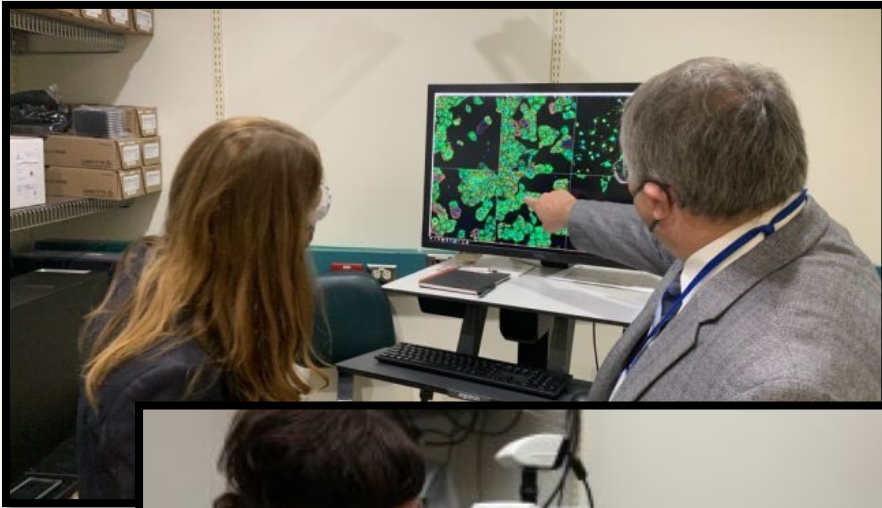
RTP, NC

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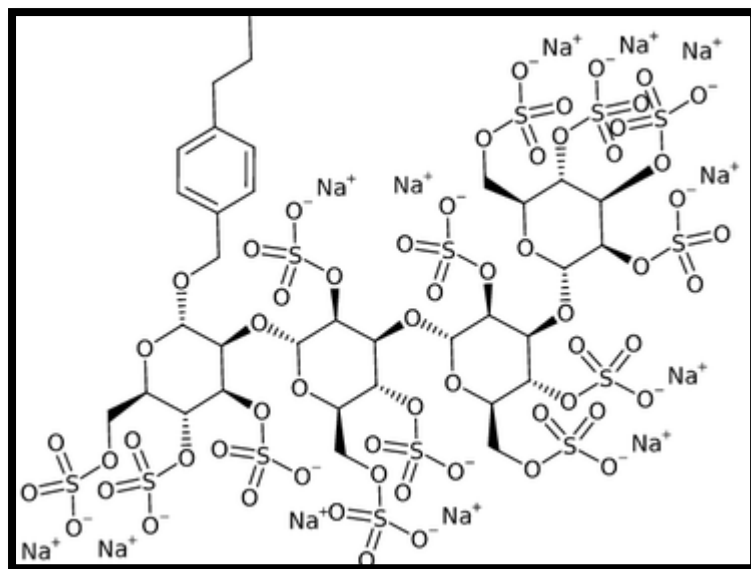


Purpose of TEST



- 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.

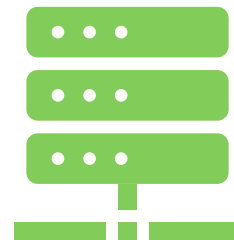
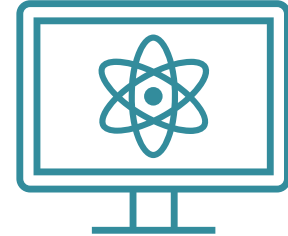
Data and Connections



- 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

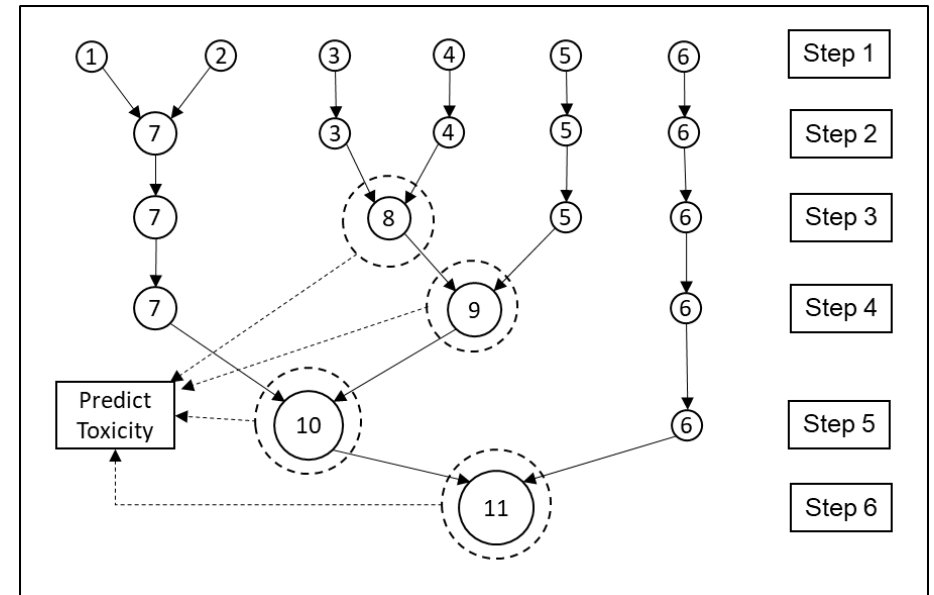
QSAR Methodologies

- 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

The screenshot displays the T.E.S.T. software interface, which is divided into several functional areas:

- Search Section:** Located at the top left, it includes a text input field for entering a CAS, SMILES, Name, InChi, InChiKey, or DTXSID, a 'Search' button, and fields for 'Molecule ID' (containing '91-20-3') and 'Name' (containing 'Naphthalene').
- Calculation Options:** This section allows users to configure the toxicity estimation process. It features dropdown menus for 'Endpoint' (set to 'Fathead minnow LC50 (96 hr)') and 'Method' (set to 'Consensus'). There are also checkboxes for 'Relax fragment constraint' and 'Run CTS' (set to 'Hydrolysis'). A 'Select output folder' field is present with a 'Browse...' button, and a 'View results' button is located at the bottom right of this section.
- Draw Chemical:** This is a chemical sketcher window on the right side of the interface. It has a menu bar with 'Edit', 'View', 'Atom', 'Bond', and 'Tools'. The drawing area contains a skeletal structure of naphthalene. A toolbar on the left and right sides of the drawing area provides various drawing tools. At the bottom of the drawing area, there is a row of element buttons: C, H, O, N, P, S, F, Cl, Br, I, R, and a 'Calculate!' button.

At the bottom right of the main window, there are two buttons: 'Switch to Batch Mode' and 'Calculate!'.

Example of Tool/Data Use

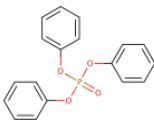
- Estimation of aquatic toxicity of triphenyl phosphate (TPP):

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

^aNote: 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	<chem>O=P(OC1=CC=CC1)(OC2=CC=CC2)OC3=CC=CC3</chem>		5.54	5.93	0.93	0.39
Product of 115-86-6, Accumulation = 50.0	<chem>O=P(O)(OC1=CC=CC1)OC2=CC=CC2</chem>		N/A	5.65	N/A	0.56
Product of 115-86-6, Accumulation = 50.0	<chem>OC1=CC=CC1</chem>		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



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