EPA
www.epa.gov/research
science in ACTION
INNOVATIVE RESEARCH FOR A SUSTAINABLE FUTURE

Computational Toxicology Research

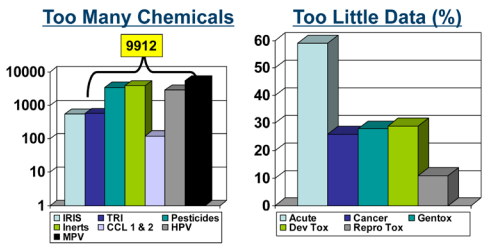
Fast, Automated Screening for Risk-Based Chemical Prioritization

Thousands of chemicals are currently in use, and hundreds more are introduced every year. Because current chemical testing is expensive and time consuming, only a small fraction of chemicals have been thoroughly evaluated for potential human health effects.

Through its computational toxicology research, the U.S. Environmental Protection Agency (EPA) is developing ground-breaking approaches to change how chemicals are evaluated for potential health effects. Computational toxicology research integrates advances in biology, biotechnology, chemistry, and computer science to identify important biological processes that may be disrupted by the chemicals and trace those biological disruptions to a related dose and human exposure. The combined information helps prioritize chemicals based on potential human health risks. Using this research, thousands of chemicals can be evaluated for potential risk at a small cost in a very short amount of time.

CompTox Tools and Resources

ACToR
(Aggregated Computational Toxicology Resource)



EPA's Need for Toxicity Data

ACToR enables scientists and the interested public to search and download thousands of toxicity testing results on thousands of chemicals. ACToR aggregates data from more than 1,000 public sources on over 500,000 chemicals. It can be used to query a specific chemical and find all publicly available hazard, exposure and risk assessment data.

ToxCast™
(Toxicity Forecaster)

ToxCast is a multiyear, multimillion dollar effort that uses advanced science tools to help understand how human biology is impacted by exposure to chemicals and to determine which exposures may lead to adverse health effects. ToxCast uses automated chemical screening technologies, called "high-throughput screening assays", to expose living cells or isolated proteins to chemicals. The cells or proteins are then screened for changes in biological activity that may suggest potential toxic effects. ToxCast has generated data on over 1,800 chemicals evaluated in over 1,000 high-throughput assay endpoint components.

ToxCast & Tox21
Number of Chemicals and Assays

Set	Chemicals	Assay Endpoint Components	Date Data Available
ToxCast Data Available	~1800	Over 1,000	Now
Phase I	~300		
Phase II	~700		
Endocrine Related	800	Over 30	
Future ToxCast Data			
Phase III	~2000	A subset of the ToxCast assays	2016
Tox21 Data	~9,000	Over 100	Now

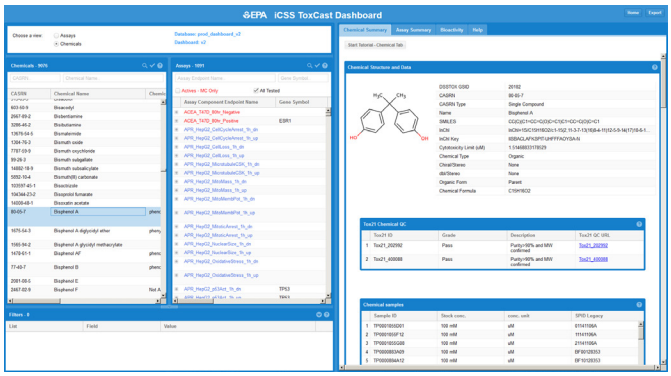
A large contributor to ToxCast is the Toxicity Testing in the 21st century (Tox21) Federal agency collaboration. Tox21 has screened over 9,000 chemicals in a subset of more than 100 high-throughput assay endpoint components. The Tox21 collaboration pools resources from the National Toxicology Program at the National Institute of Environmental Health Science, the National Institutes of Health's National Center for Advancing Translational Sciences, and the Food and Drug Administration. All ToxCast chemical screening data is publicly available through the Dashboard.

ToxCast Dashboard

The ToxCast Dashboard helps users examine high-throughput assay data to inform chemical safety decisions. To date, the ToxCast Dashboard has data on over 9,000 chemicals and information from more than 1,000 high-throughput assay endpoint components. Users of the ToxCast Dashboard can explore the data from a chemical or an assay viewpoint. Once the user selects the chemicals and assays of interest, they can then explore the biological activity for the chemical-assay combinations. Results from the selections are shown with tables, graphs and charts that can be downloaded by the user.

Continued on back

Computational Toxicology Research Program



Chemistry Dashboard

The Chemistry Dashboard provides access to chemistry data for hundreds of thousands of chemicals. Within the Chemistry Dashboard, users can access chemical structures, experimental and predicted physicochemical and toxicity data, and additional links to relevant websites and applications. It maps curated physicochemical property data associated with chemical substances to their corresponding chemical structures. These data are valuable information for analytical scientists involved in structure identification and can support targeted and non-targeted screening identification of environmental chemicals.

ToxRefDB
(Toxicity Reference Animal Data)

ToxRefDB contains approximately 30 years and $2 billion worth of animal studies. ToxRefDB allows scientists and the interested public to search and download thousands of animal toxicity testing results for hundreds of chemicals that were previously found only in paper documents. Currently, there are 474 chemicals in ToxRefDB, primarily the data rich pesticide active ingredients, but the number will continue to expand.

ExpoCast
(Exposure Forecaster)

EPA's ExpoCast effort is developing rapid, automated chemical exposure predictions for thousands of chemicals based on manufacture and use information. EPA scientists developed the ExpoCast model to predict exposures for almost 8,000 chemicals using production volume, environmental fate and transport models, and a simple indicator of consumer product use. The ExpoCast approach can be used to make high-throughput exposure predictions for human exposures to chemicals and to understand where additional information is required to improve these estimates. The ExpoCast model is being improved by adding more refined indoor and consumer use information since these are also large determinants of exposure.

Virtual Tissues

Virtual Tissue Models map existing chemical research to dynamic computer simulated models of biological tissues. These computer models are able to virtually simulate how chemicals interact with important biological processes or signaling pathways and how those interactions lead to potential adverse effects in human tissues. The computer models are constructed using an adverse outcome pathway (AOP) approach. The research is currently focusing on developing advanced computer simulated models of biological processes critical for normal development and function. An example includes the Virtual Embryo (v-Embryo™) model for predicting a chemical's potential to lead to developmental toxicity due to disruption of blood vessel development in embryos. Ultimately, the suite of v-Embryo models will help predict what chemical-biological interactions might lead to developmental toxicity and birth defects.

Collaboration Opportunities

EPA's computational toxicology research efforts actively engage a wide-range of partners including EPA regions and program offices, industry, academia, trade associations, other federal agencies, state and local government agencies and non-governmental organizations to help make this new chemical information more understandable and useable. EPA's computational toxicology stakeholder outreach includes workshops, webinars and training for partners as well as opportunities for stakeholders to provide suggestions for enhancing the research activities. Monthly Communities of Practice webinars are held and anyone with an interest in computational toxicology research can participate. EPA's computational toxicology researchers also partner with hundreds of outside organizations to collaborate on research. EPA provides funding to academic centers working on various aspects of computational toxicology through EPA's Science to Achieve Results (STAR) program.

More information,go to:
www.epa.gov/comptox

National Center for Computational Toxicology

Rusty Thomas
Director
thomas.russell@epa.gov

Monica Linnenbrink
Communications Director
linnenbrink.monica@epa.gov

Main Office: 919·541·4219
www.epa.gov/comptox
109 T.W. Alexander Drive
Mailcode D143-02
Research Triangle Park, NC 27711

Recycled/Recyclable
Printed on paper that contains a minimum of 50% postconsumer fiber content processed chlorine free