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

Computational Toxicology Research

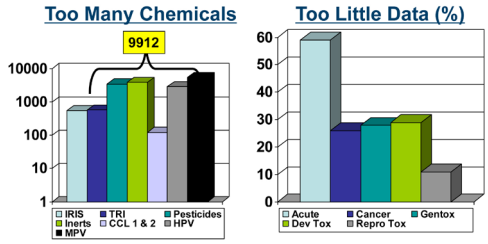
Fast, Automated Screening for Risk-Based Chemical Prioritization

Tens of 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 evaluated fully for potential human health effects.

Through its computational toxicology (CompTox) research, the U.S. Environmental Protection Agency (EPA) is working to figure out how to change the current approach used to evaluate the safety of chemicals. CompTox 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 CompTox, 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)

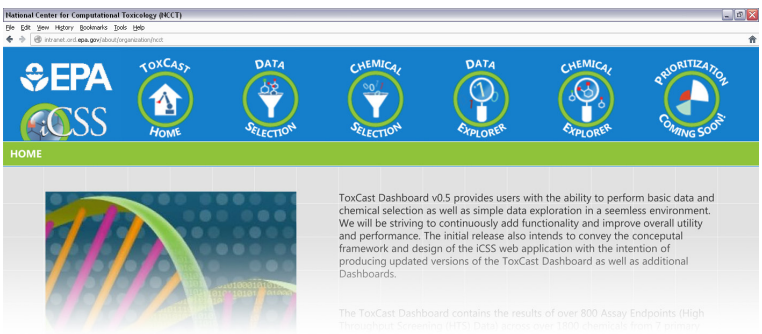


EPA's Need for Toxicity Data

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.

iCSS Dashboards
(interactive Chemical Safety for Sustainability Dashboards)

iCSS Dashboards (iCSS) are web-based applications that provide a portal to computational toxicology data. Currently, iCSS Dashboards provide a portal for users to search and query rapid, automated (high-throughput) screening data on thousands of chemicals. Advances in computational toxicology allow iCSS Dashboards to integrate these diverse sources of information and make it available to decision-makers and the public via an easy-to-use, interactive software application. Users can access iCSS Dashboards to search and interact with the data compiled by the CompTox program in order to better understand potential risks to human health and the environment.



Computational Toxicology Research Program

ToxRefDB
(Toxicity Reference Database)

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.

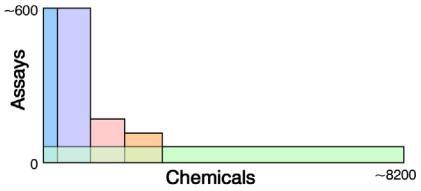
DSSTox
(Distributed Structure-Searchable Toxicity Database)

DSSTox provides scientists and decision-makers with high quality chemical structures and annotations in association with toxicity data. It helps to build a data foundation for improved structure-activity relationships and predictive toxicology. DSSTox publishes summarized chemical activity representations for structure-activity modeling and provides a structure browser. It also houses the chemical inventories for the ToxCast and Tox21 projects.

ToxCast™
(Toxicity Forecaster)

ToxCast & Tox21
Number of Chemicals and Assays

Set	Chemicals	Assays	Endpoints	Available
ToxCast Phase I	293	~600	~1100	Now
ToxCast Phase II	767	~600	~1100	12/2013
ToxCast Phase IIIa	1001	~100	~100	2014
E1K (endocrine)	880	~50	~120	12/2013
Tox21	8193	~25	~50	Ongoing



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 2,000 chemicals evaluated in over 700 high-throughput assays.

A large contributor to ToxCast is the Toxicity Testing in the 21st century (Tox21) Federal agency collaboration. Tox21 is using robotics technology to screen over 10,000 chemicals in a subset of the high-throughput assays. 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 iCSS dashboard. The iCSS dashboard provides access to chemicals, assays, genes, pathways and endpoints.

EPA is working with scientific review boards and external stakeholders to identify and evaluate applications of ToxCast data for informing chemical safety decisions. One potential application is to use ToxCast to help prioritize chemicals for EPA’s Endocrine Disruptor Screening Program. Using ToxCast, EPA researchers have evaluated almost 1,800 chemicals in approximately 50 endocrine-related high-throughput assays.

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 1,763 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

CompTox actively engages 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. CompTox has workshops, webinars, and training for partners and to ask for partner feedback about how to improve CompTox research. CompTox hosts monthly Communities of Practice webinars and anyone with an interest in CompTox research can participate. CompTox also partners with hundreds of outside organizations to collaborate on research and it funds academic centers working on various aspects of computational toxicology through EPA’s Science to Achieve Results (STAR) program. In addition, CompTox hosts visiting scientists, doctoral students and post-doctoral fellows collaborating on computational research.

For 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 (B-205-01)
Research Triangle Park, NC 27711

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