Computational Toxicology Research

United States Environmental Protection Agency

epa.gov/research

Innovative Science for a Sustainable Future

Fast, Automated Screening for Risk-Based Chemical Prioritization

Under different federal statutes, EPA makes a broad range of decisions to protect public health and the environment from unintended consequences of using chemicals. Decisions about chemicals are also made by other Federal Agencies, State Environmental and Health Agencies, International Governmental Agencies and Industry. As examples, there are specific federal laws for pesticides, drinking water contaminants, commercial and industrial chemicals, chemicals found on contaminated sites, and endocrine disrupting chemicals.

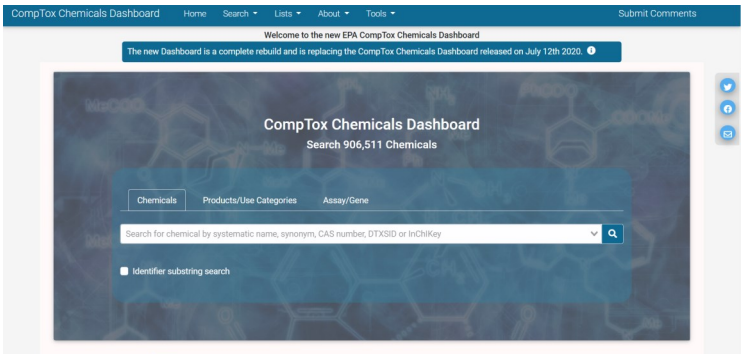
Through its computational toxicology research, the U.S. Environmental Protection Agency (EPA) is developing ground-breaking approaches to change how chemicals are evaluated for potential health effects. Computational toxicology research integrates advances in biology, biotechnology, chemistry, and computer science to identify important biological processes that may be disrupted by chemicals and to trace those biological disruptions to a related dose and human exposure. The combined information helps with prioritization of 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

CompTox Chemicals Dashboard

The Computational Toxicology (CompTox) Chemicals Dashboard provides easy access to chemistry, toxicity, and exposure information for over 900,000 chemicals. Data and models within the Dashboard also help with efforts to identify chemicals of most need of further testing and reduce the use of animals in chemical testing. The Dashboard can be searched by chemical identifiers (e.g. Name and CASRN), consumer product categories (i.e. view chemicals found in certain product types), and assays/genes associated with high-throughput screening data. Using high-throughput screening, living cells or proteins are exposed to chemicals and examined for subsequent changes that suggest potential biological responses.

These data are compiled from sources including the EPA's computational toxicology research databases, and public domain databases such as the National Center for Biotechnology Information's PubChem database and EPA's ECOTOX Knowledgebase.



ExpoCast *(Exposure Forecaster)*

EPA's ExpoCast effort is developing rapid, automated chemical exposure predictions for thousands of chemicals based on chemical structure, manufacture, use, and release information. EPA scientists developed ExpoCast to estimate exposures for over 470,000 chemicals using statistical methods that integrate structure and use information, predictions from many exposure models, and available biomonitoring data. 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.

Since indoor and consumer product use are large determinates of exposure, ExpoCast estimates are improved as this information is considered. Indoor and consumer use information come from the EPA Chemical and Products Database (CPDat), a database that maps more than 20,000 chemicals to a set of terms categorizing their use or function in commerce and in 60,000 consumer products (e.g., shampoo, soap, surface cleaners). This information comes from a wide variety of sources and is available online through the CompTox Chemicals Dashboard, with a full data release at https://doi.org/10.23645/epacomptox.5352997.

EPA researchers are also developing more precise methods for estimating chemical concentrations in humans following exposure. EPA scientists developed a method to make its high-throughput results more applicable to humans by replacing the traditional constant exposure rate with more realistic human exposure pathways.

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EPA researchers developed four toxicokinetic models within a R software package called high-throughput toxicokinetics to estimate chemical concentrations in humans. The package can currently use human high-throughput screening data to make predictions in humans, rats, mice, dogs, and rabbits for 391 chemicals, including 76 pharmaceuticals and 282 ToxCast chemicals.

ToxCast™

ToxCast is a multi-year, multi-million dollar effort that uses advanced scientific 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.

The strategies being developed to guide the implementation of the Toxic Substance Control Act's pre-prioritization and the use of new approach methods for chemical testing describe the use of ToxCast data. ToxCast has also been used to develop and evaluate new methods to test chemicals for potential health effects such as endocrine disruption. ToxCast chemical screening data is publicly available through the CompTox Chemicals Dashboard and through the CompTox downloadable data website.

ToxRefDB (Toxicity Reference Database)

The Toxicity Reference Database (ToxRefDB) contains in vivo study data from over 5000 in vivo toxicity studies. While employing a controlled vocabulary for enhanced data quality, this information includes study design, quantitative dose response, and endpoint testing status given guideline specifications. ToxRefDB allows scientists and the interested public to access thousands of animal toxicity testing results, which is a great resource for retrospective and predictive toxicology applications. There are over 1,000 chemicals in ToxRefDB, primarily pesticides, and curation is ongoing.

Virtual Tissues

Virtual Tissue Models map existing chemical research to dynamic computer simulated models of biological tissues. These computer models can 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.

For more information, visit: www.epa.gov/comptox
National Center for Computational Toxicology

CompTox Chemicals Dashboard:
https://comptox.epa.gov/dashboard

Downloadable CompTox Data: https://www.epa.gov/chemical-research/downloadable-computational-toxicology-data

Rusty Thomas Director
thomas.russell@epa.gov
Main Office: 919.541.4219
109 T.W. Alexander Drive
Mail code D143-02
Research Triangle Park, NC 27711

www.epa.gov/comptox