

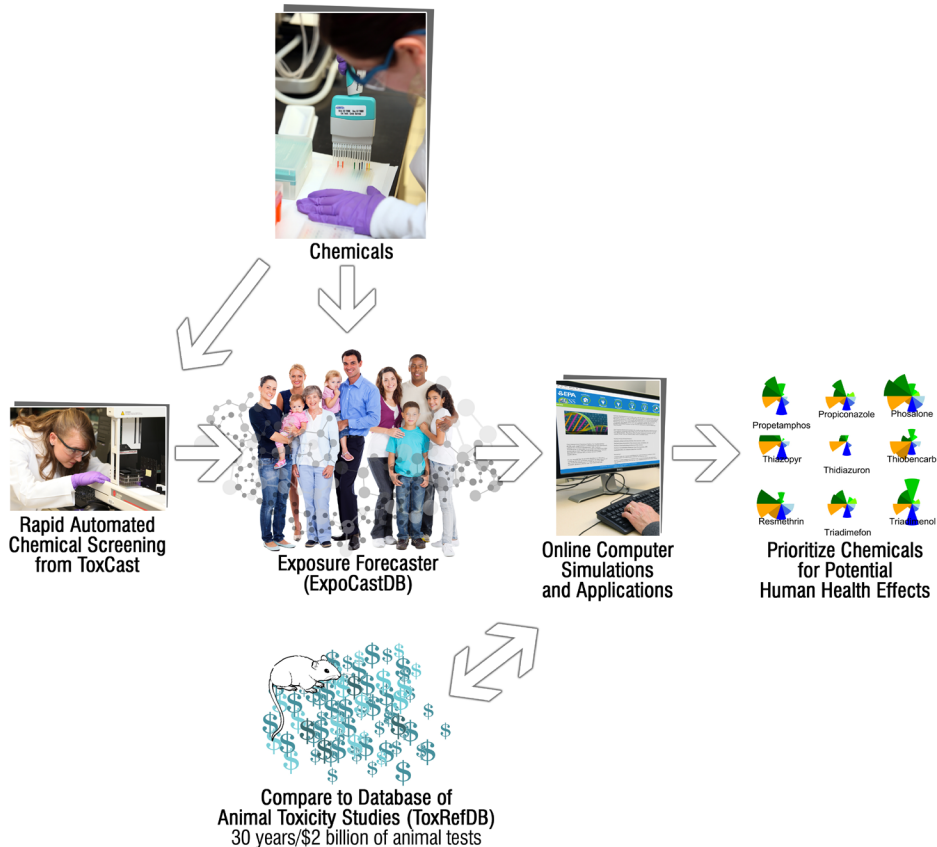
## Toxicity Forecaster (ToxCast™)

### ADVANCING THE NEXT GENERATION OF CHEMICAL SAFETY EVALUATION

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.

A major part of EPA's CompTox research is the Toxicity Forecaster (ToxCast™). ToxCast is a multiyear effort launched in 2007 that uses automated chemical screening technologies, called "high-throughput screening assays", to expose living cells or isolated proteins to chemicals. The cells or proteins then are screened for changes in biological activity that may suggest potential toxic effects. These innovative methods have



the potential to limit the number of required animal-based laboratory toxicity tests while, quickly and efficiently screening large numbers of chemicals.

The first phase of ToxCast, called "proof of concept", was completed in 2009, and it evaluated more than 300 well studied chemicals (primarily pesticides) in more than 500 high-throughput screening assays. Because most of these chemicals already have undergone extensive animal-based toxicity testing, this enables EPA researchers to compare the results of the high-throughput assays with those of the traditional animal tests.

Completed in 2013, the second phase of ToxCast evaluated over 2,000 chemicals from a broad range

of sources, including industrial and consumer products, food additives, and potentially "green" chemicals that could be safer alternatives to existing chemicals. These chemicals were evaluated in more than 700 high-throughput assays covering a range of high-level cell responses and approximately 300 signaling pathways. ToxCast research is ongoing to determine which assays, under what conditions, may lead to toxicological responses. The results of this research then can be used to suggest the context in which decision makers can use the data. The EPA's Endocrine Disruptor Screening Program already has begun the scientific review process necessary to begin using ToxCast data to prioritize the thousands of chemicals that need to be tested

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for potential endocrine-related activity. Other potential uses include prioritizing chemicals that need testing under the Toxic Substances Control Act and informing the Safe Drinking Water Act's contaminant candidate lists.

EPA contributes the results of ToxCast to a Federal agency collaboration called Toxicity Testing in the 21st Century (Tox21). Tox21 pools those results with chemical research, data and screening tools 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. Thus far, Tox21 has compiled high-throughput screening data on nearly 10,000 chemicals.

As part of EPA's commitment to gather and share its chemical data openly and clearly, all ToxCast chemical data is publicly available for anyone to access and use through user-friendly Web applications called interactive Chemical Safety for Sustainability (iCSS) Dashboards. Currently, iCSS dashboards provide an accessible portal for users to search and query the ToxCast chemical screening data. Users can select the chemicals and data of interest and then explore and export this information. Making ToxCast data available through the iCSS dashboards creates an environment that encourages external stakeholders to interact with new data, identify potential issues, and suggest improvements.

## Collaboration Opportunities

To continue to advance EPA's CompTox research, EPA scientists are partnering and collaborating with EPA regions and program offices, industry, academia, trade associations, other Federal agencies, State and local government agencies and nongovernmental organizations with an interest in revolutionizing the current approach to assessing chemical toxicity risk to humans and the environment.

EPA actively engages partners to give feedback about how to improve ToxCast data and hosts workshops, webinars and training to inform partners and to solicit feedback about how to improve its research programs. EPA has hundreds of research partnership agreements in place with outside organizations to share research data and studies.

For more information, go to:

**ToxCast:**

<http://epa.gov/ncct/toxcast/>

**ToxCastDB:**

<http://actor.epa.gov/actor/faces/ToxCastDB/Home.jsp>

**ACToR:**

<http://actor.epa.gov/actor>

**ToxRefDB:**

<http://actor.epa.gov/toxrefdb>

**CSS Dashboards:**

<http://actor.epa.gov/actor/faces/CSSDashboardLaunch.jsp>

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