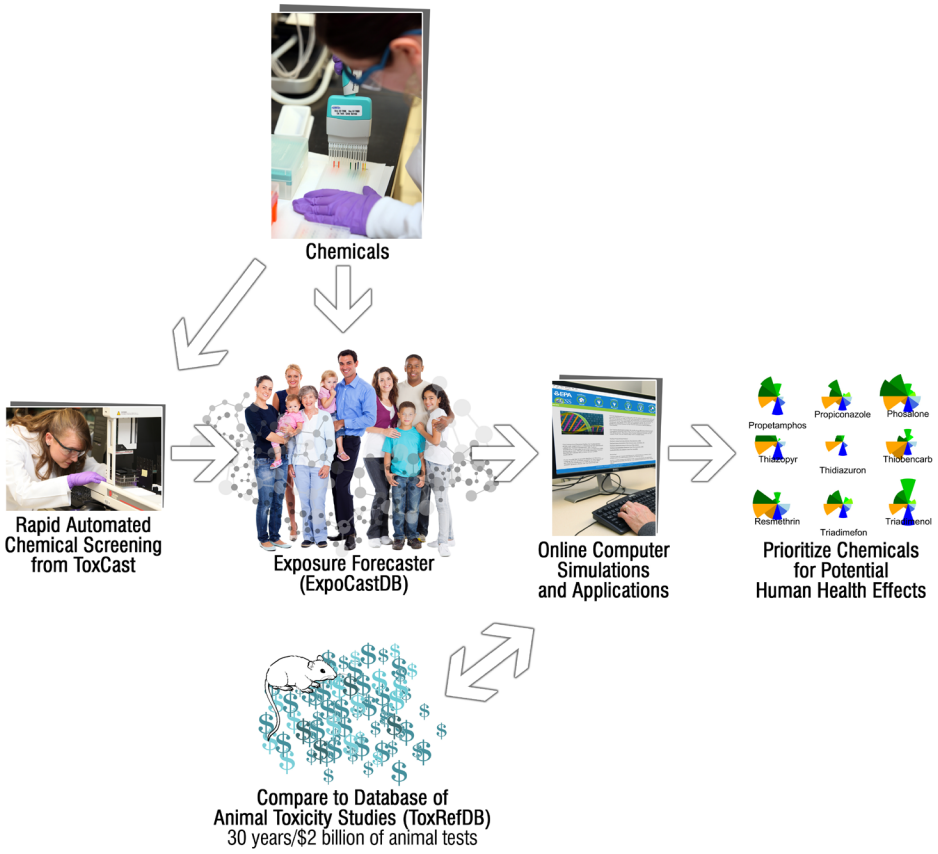
Toxicity Forecaster (ToxCast™)

ADVANCING THE NEXT GENERATION OF CHEMICAL SAFETY EVALUATION

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

Through its computational toxicology research (CompTox), 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 tracing 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 multi-year 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 are then screened for changes in biological activity that may suggest potential toxic effects. These innovative methods have the potential to limit the number of required laboratory animal-based toxicity tests while quickly and efficiently screening large numbers of chemicals.



The first phase of ToxCast, appropriately called "Proof of Concept", was completed in 2009 and it evaluated over 300 well studied chemicals (primarily pesticides) in over 500 high-throughput screening assays. Most phase one chemicals already have undergone extensive animal-based toxicity testing, which allows EPA researchers to compare results of the high-throughput assays with 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 2,000 chemicals were evaluated in over 700 high-throughput assays that cover 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 can then be used to inform the context in which decision makers can use the data. The EPA's Endocrine Disruption Screening Program has already started the scientific review process needed to begin using ToxCast data to prioritize the thousands of chemicals that

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

EPA contributes the results of ToxCast to a federal agency collaboration called Toxicity Testing in the 21st Century (Tox21). Tox21 pools chemical research, data and screening tools from multiple federal agencies including the National Toxicology Program/ National Institute of Environmental Health Science, National Center for Advancing Translational Sciences and the Food and Drug Administration. Together, Tox21 has compiled high-throughput screening data on nearly ten thousand chemicals.

As part of EPA's commitment to gather and share its chemical data in open and transparent ways, all ToxCast chemical data is publicly available for anyone to access and use through a user-friendly web application. Currently, the ToxCast dashboard provides an accessible portal for users to search and query the ToxCast chemical screening data. Users can select the chemicals and data of interests and then explore and export this information. Making ToxCast data available through the Toxcast dashboard makes it easier for EPA to ask external stakeholders to interact with new data, identify potential issues, and provide suggestions for improvements.

Collaboration Opportunities

To continue to advance EPA's computational toxicology 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 non-governmental organizations with an interest in revolutionizing the current approach to assessing chemical toxicity risk to humans and the environment.

EPA actively engages partners to get feedback about how to improve ToxCast data. EPA hosts workshops, webinars and training to inform partners and to solicit feedback about how to improve our research program. 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:
https://actor.epa.gov/dashboard/

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