

Invited presentation abstract

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EPA's ToxCast Program for Predicting Hazard and Prioritizing the Toxicity Testing of Environmental Chemicals

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Only a fraction of the 30,000 chemicals in U.S. commerce have been fully characterized for toxicity, and defining toxicity can take years and cost millions of dollars per chemical. An alternative is to perform a set of relatively inexpensive and rapid high throughput screening (HTS) assays, derive signatures predictive of effects or modes of chemical toxicity from the HTS data, then use these predictions to prioritize chemicals for more detailed analysis. The U.S. EPA has made a significant investment in this approach through its ToxCastTM program (www.epa.gov/comptox/toxcast), with the goal of building accurate predictive models for thousands of antimicrobials, pesticide inert ingredients, new and existing industrial chemicals, and drinking water candidate contaminants with limited toxicity data available for hazard and risk assessments. Phase I of ToxCast is a proof-of-concept utilizing 300 chemicals of known toxicity in over 400 HTS and genomic assays to generate a set of bioactivity profiles to develop and validate predictive toxicity signatures. Phase I chemicals are primarily pesticide active ingredients that have been extensively tested, with known properties relative to carcinogenicity, and developmental, reproductive and neural toxicity. Phase I data generation and analysis is expected to be complete in 2008. Phase II will focus on expansion of ToxCast predictive signatures, generating HTS data for additional chemicals and confirming the sensitivity and specificity of the signatures. Assuming success in the earlier phases, regulatory application of ToxCast in Phase III will measure ToxCast signatures for thousands of environmental chemicals of unknown toxicity, generating prioritization scores for more extensive testing and providing an affordable, science-based system for categorizing chemicals. *This work was reviewed by U.S. EPA and approved for publication but does not necessarily reflect official Agency policy.*