

Kavlock, R.J. The Future of Toxicity Testing - the NRC Vision and EPA's ToxCast Program
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The EPA requested the National Research Council (NRC) to develop a vision and strategic plan for toxicity testing in the 21st century. The 2007 report called for transforming toxicology to provide a robust scientific basis for assessing adverse health effects of environmental agents; enable broad coverage of chemicals, mixtures, outcomes, and life stages; and reduce the cost and time of testing. The core of the strategy involved mapping 'toxicity pathways' in human tissues, and identifying perturbations in critical pathways responsible for toxicity using in vitro assays. ToxCast (www.epa.gov/toxcast), an EPA chemical prioritization research program, seeks to enable that vision by applying computational chemistry and high-throughput-based bioactivity profiling to predict the toxicity of chemicals and thus prioritize them for subsequent targeted testing. Phase I, a proof-of-concept component, focused on 320 reference chemicals with existing toxicological data to provide an interpretive context for the bioactivity profiles. These chemicals are primarily pesticides with available chronic, multigenerational and developmental toxicity bioassays. The bioactivity profiles are derived from more than 550 biochemical and cell-based phenotypic assays, and genomic analyses that are related to the mechanisms of toxicity in animal bioassays. The data are being generated through contractual and collaborative agreements within EPA and with the NIH Chemical Genomics Center (NCGC). All data generated for ToxCast will be publicly available, affording others the opportunity to analyze and interpret the dataset. Results of the proof of concept phase of ToxCast and supporting chemo-informatic infrastructure will be presented. *This is an abstract of a proposed presentation.*