Kavlock RJ, Dix D.J., Houck K, Judson R, Knudsen T, Martin M, Richard A ToxCast: Developing predictive signatures of chemically induced toxicity. National Center for Computational Toxicology, ORD, US EPA, RTP, NC 27711.

ToxCast, the United States Environmental Protection Agency's chemical prioritization research program, is developing methods for utilizing computational chemistry, bioactivity profiling and toxicogenomic data to predict potential for toxicity and prioritize limited testing resources. In the proof-of-concept phase, we are focused upon evaluating chemicals with an existing, rich toxicological database in order to provide an interpretive context for the high throughput screening data. This set of 320 reference chemicals is largely derived from active ingredients in food-use pesticides and represents numerous structural classes and phenotypic outcomes, including tumorigens, developmental and reproductive toxicants, neurotoxicants and immunotoxicants. The goal of the program is to develop signatures predicitve of *in vivo* toxicity, based on the combined use of physicochemical properties, the traditional independent variables in structure activity models, as well as *in vitro* bioactivity data derived from a broad spectrum of more than 400 biochemical, cell-based, or gene expression assays. The signatures derived for chemicals with toxicity data gaps could then be compared with those of the well-characterized chemicals, and those with significant signature matches would become priority candidates for further testing in traditional animal bioassays. These data are being generated through a series of external contracts, and by collaborations within EPA and with the National Institutes of Health Chemical Genomics Center. Results of the proof-of-concept phase and development of the supporting chemo-informatic infrastructure will be presented. *[This work was reviewed by EPA and approved for publication but does not necessarily reflect official Agency policy.]*