Kavlock, RJ, Dix, D, Houck K, Judson, R. T. Knudsen, Martin, M. and 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 (www.epa.gov/tocast). 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 through put screening data. This set of 320 reference chemicals are largely derived from the active ingredients in food use pesticides and represent numerous structural classes and phenotypic outcomes, including tumorigens, developmental and reproductive toxicants, neurotoxicants and immunotoxicants. The goal of the program is to develop signatures based on the combined use of physico-chemical properties (the traditional independent variables in structure activity models) and the bioactivity data (derived from a broad spectrum of more than 400 readouts from biochemical assays, cell-based phenotypic assays, and genomic analyses of cells) that are predictive of responses in animal bioassays. The signatures derived for chemicals with toxicity data gaps could then be compared with those of the well characterized chemicals, and those with significant signatures would become priority candidates for testing in traditional animal bioassays. These data are being generated through a series of external contracts, and through collaborations within EPA and with the National Institutes of Health Chemical Genomics Center. Results of the proof of concept phase and supporting chemo-informatic infrastructure will be presented. *This is an abstract of a proposed presentation.*