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 Phase I, our proof-of-concept component, 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 550 readouts from biochemical assays, cell-based phenotypic assays, and genomic analyses of cells) that are relevant to the mechanisms by which toxic responses are induced 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 (NCGC). All data generated within the ToxCast will be made publicly available, affording others the opportunity to conduct their own data analysis procedures and interpretations. Phase 1 data collection is currently being completed, and plans are underway to launch Phase II in mid 2009. Phase II will involve upwards of 700 additional chemicals to test the validity of bioactivity signatures and to extend the types of chemicals being tested. Results of the proof of concept phase and supporting chemo-informatic infrastructure will be presented. . ToxCast is part of a larger government effort (Tox21) being conducted jointly by EPA, the National Toxicology Program of NIEHS, and the NCGC that is obtaining high throughput screening data on more than 2000 chemicals, with plans to expand to more than 6000 chemicals in 2009. *This is an abstract of a proposed presentation.*