

Predictive *In Vitro* Screening of Environmental Chemicals – The ToxCast Project

Dr David Dix

Acting Deputy Director, National Center for Computational Toxicology

Office of Research & Development

U.S. Environmental Protection Agency

Research Triangle Park, NC USA

Email: dix.david@epa.gov

ToxCast, the United States Environmental Protection Agency's chemical prioritization research program, is developing methods for utilizing computational chemistry and bioactivity profiling to predict potential for toxicity and prioritize limited testing resources (www.epa.gov/toxcast). This presentation will provide an overview of the rationale, design and status of ToxCast. In Phase I, our proof-of-concept component, we have 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, largely food use pesticides, and represents numerous structural classes and phenotypic outcomes. The in vivo datasets include standard chronic bioassays in the rat and the mouse as well as developmental toxicity and multigenerational studies. All the toxicity information is contained in a relationship database, ToxRefDB, facilitating comparison with the in vitro data. The bioactivity data is derived from a broad spectrum of more than 500 readouts from cell-free biochemical assays, cell-based phenotypic assays, and model organisms. A sampling of data analysis that will be presented includes both supervised (selecting particular assays or pathways known to be associated with toxicities and testing for association with phenotypes) and unsupervised (univariate, multivariate and clustering) approaches. *This is an abstract of a proposed presentation.*