

Presentation Abstract for SOT 2010 in Salt Lake City UT, March 7-11, 2009

Symposium TITLE: FASTER SCIENCE FOR BETTER DECISIONS: CHARACTERIZING ENVIRONMENTAL CONTAMINANT RISK FROM HIGH THROUGHPUT DATA

Presentation Title: HIGH THROUGHPUT SCREENING FOR HAZARD AND RISK OF ENVIRONMENTAL CONTAMINANTS

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ABSTRACT: High throughput toxicity testing provides detailed mechanistic information on the concentration response of environmental contaminants in numerous potential toxicity pathways. High throughput screening (HTS) has several key advantages: (1) expense orders of magnitude less than animal testing; (2) direct study of human gene, protein and cell targets is possible; and (3) hundreds to thousands of contaminants can be studied simultaneously. Quantitative HTS hazard assessment can thus identify potential mechanisms and pathways by which a contaminant can lead to specific adverse outcomes. EPA's ToxCast project is evaluating the use of HTS for understanding the types of molecular and pathway perturbations caused by environmental chemicals, and building initial predictive models of in vivo toxicity for prioritization and hazard assessment. To date we have tested 309 pesticide active and industrial chemicals in 467 assays across 9 HTS technologies. These include cell-free assays, as well as cell-based assays in a variety of human and rodent primary cells and cell lines. Both individual assays and composite assays for effects on genes and pathways demonstrated a broad spectrum of chemical activity at the molecular and pathway levels. Many expected interactions were seen in the data, including endocrine and xenobiotic metabolism enzyme activity. Chemicals show widely varying promiscuity across pathways, from no activity to activity in dozens of pathways. This diversity of behavior is seen even within well-defined chemical classes. This approach promises to provide meaningful data on thousands of untested environmental chemicals, and to guide more intelligent, targeted testing of environmental contaminants in the future. *This abstract may not necessarily reflect Agency policy.*