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Exposure Considerations for Chemical Prioritization and Toxicity Testing
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Globally there is a need to characterize potential risk to human health and the environment that arises from the manufacture and use of tens of thousands of chemicals. Currently, a significant research effort is underway to apply new technologies to screen and prioritize chemicals for toxicity testing as well as to improve understanding of toxicity pathways. The 2007 National Research Council report, *Toxicity Testing in the 21st Century: A Vision and a Strategy*, calls for a collaborative effort across the toxicology community to rely less on animal studies and more on *in vitro* tests using human cells and cellular components to identify chemicals with toxic effects. A framework for implementing this long-range vision is provided by the recently formalized collaboration between two NIH institutes and the EPA to use high-speed, automated screening methods to efficiently test compounds for potential toxicity (Science Feb 15, 2008). More immediately, the US EPA is completing the Phase I pilot for a chemical prioritization research program, called ToxCast^{TM}. Here EPA is developing methods for using computational chemistry, high-throughput screening, and toxicogenomic technologies to predict potential toxicity and prioritize limited testing resources.

These high visibility efforts in computational toxicology raise important research questions for exposure scientists. As the NAS points out, population-based data and human exposure information are required at each step of their vision for toxicity testing. In addition, the ToxCast^{TM} program has identified the need to include exposure considerations for chemical prioritization. Two major areas of exposure research are required to meet immediate needs for chemical screening, prioritizing and toxicity testing. First, it is imperative that exposure data be accessible and linked to the rapidly growing base of toxicity data. Development of consolidated data and knowledge bases for exposure is a high priority. Second, novel computational approaches are required to ensure that information on biological effects is developed at environmentally relevant exposures. Computational tools and approaches for characterizing and prioritizing exposure are required: to provide input for selection of chemicals; to select doses for toxicity tests; and to interpret and extrapolate results of in vitro tests.

Examples of tools available for further development and application to address this need can be found by considering state-of-the-art research in modeling exposure of phthalates and other semi-volatile organic compounds (SVOCs) from emitting source to metabolic sink or dose. Data analysis and modeling to understand behavior of phthalates provides insight on determinants of exposure that can be applied to a broad range of compounds. In this presentation, the need for exposure science to address chemical screening, prioritizing, and toxicity testing in the 21st century is identified; examples of relevant computational research activities are highlighted; and an approach forward for exposure scientists is proposed. *This work has been reviewed and approved by the USEPA for publication but does not necessarily reflect Agency policies.*