Assuring the Safety of Chemicals through Improved Exposure Science

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Thousands of chemicals are currently in commercial use and hundreds more are introduced each year. Of these, only a small fraction has been assessed adequately for potential risks. Existing chemical testing and exposure measurement protocols are expensive and time consuming. Furthermore, the specific nature of the Toxic Substances Control Act (TSCA) led to many existing chemicals being deemed safe with little knowledge of exposure and toxicity. As a result, federal regulators have not had adequate information to fully evaluate chemical safety. In September of 2009, the US EPA Administrator announced principles for modernizing TSCA (Jackson, 2009). These principles highlight the need to review all manufactured chemicals against safety standards protective of human health and the environment, with special consideration for exposures and effects on vulnerable groups including children.

The US EPA National Center for Computational Toxicology (NCCT) has a mission to integrate modern computing and information technology with molecular biology to improve Agency prioritization of data requirements and risk assessment of chemicals. Assessing complex human-health risks associated with exposures to chemicals requires that hazard, susceptibility, and exposure are all reliably characterized. Recognizing the critical need for exposure information to inform chemical design, evaluation and health risk management, the ExpoCast™ research program has been initiated by the NCCT in collaboration with partners and stakeholders. The goal of ExpoCast is to address global needs for rapid exposure assessment and to advance exposure characterization required to translate findings in computational toxicology to information that can be directly used to support decision making and improved public health. Combining information from ExpoCast with information from ToxCast™, a battery of rapid screens EPA is studying to determine whether they can predict toxicity (Dix et al, 2007), will help EPA identify priority chemicals for evaluation based on potential to harm human health.

Translation will occur by two routes. In the first, identification of toxicity pathways coupled to identification of important environmental factors (exposures) provides new opportunities to inform decision making and public health protection at the population level. Decision support tools developed along this route may include: (1) biomarkers, metrics and indicators for measuring and monitoring environmental exposures as well as providing early indication of toxicological impacts; (2) extrapolation models for risk assessment based on detailed understanding of relevant environmental stressors and associated perturbations to toxicity pathways; and (3) public policy to prevent or mitigate exposures to protect human health and welfare.

The second translational route lies through using knowledge of individual patterns of exposure and disease predisposition to develop more personalized approaches to health risk management. Here,

toxicology research and public policy can only fully empower individuals to manage risks by providing a clear understanding of important exposures and where these can be voluntarily controlled. Considerations of individual variation based on genetic susceptibility, lifestage, and interaction of non-chemical stressors is required context for both routes and for holistic assessment of risk factors associated with complex environmental disease.

This abstract does not necessarily reflect U.S. EPA policy.

Dix DJ, Houck KA, Martin MT, Richard AM, Setzer RW, Kavlock RJ. (2007) The ToxCast program for prioritizing toxicity testing of environmental chemicals. *Toxicol Sci.* 95(1):5-12.

Jackson, LP. (2009) Administrator Lisa P. Jackson, Remarks to the Commonwealth Club of San Francisco, As Prepared 09/29/2009