Analysis of Pooled Banked Blood Samples to Augment Chemical Risk Assessment Prioritization Using High Throughput Screening

Lesa Aylward1, Sean Hays1, John Wambaugh2, Barbara Wetmore2, and Jon Arnot3. 1Summit Toxicology, LLP. 2US EPA. 3ARC Arnot Research & Consulting.

Two reports from the National Academy of Sciences (NAS), Toxicity Testing in the 21st Century and Exposure Science in the 21st Century, provide a vision for transforming the approach to chemical risk assessment. The existing risk assessment paradigm is based on a chemical-by-chemical approach that is resource-intensive and ill suited to the comprehensive assessment of a chemical landscape involving tens of thousands of chemicals and their environmental and biotransformation products. The NAS reports envision transitioning to a high-throughput screening (HTS) approach to initial chemical evaluation for both toxicity and exposure potential in order to provide a basis for prioritization among chemicals for more intensive tiered assessment of both toxicity and exposure. A key element of this vision is the ability to conduct in silico exposure modeling for integration with in vitro toxicity testing to provide screening on a basis that is not simply hazard-based. Development and validation of these exposure modeling approaches remains a key challenge for the 21st century vision outlined in the NAS reports.

This pilot project is designed to evaluate the feasibility of using pooled banked blood samples to generate initial data on actual population blood concentrations for compounds not to date routinely biomonitored in order to allow comparison to blood concentrations predicted using HTS exposure models and active concentrations in ToxCast assays. This project is designed to be less resource intensive than an effort such as the National Health and Nutrition Examination Survey (NHANES) program, and, therefore, will produce data that are less detailed and descriptive of the U.S. population. However, the effort should provide data that are useful in the development and verification/validation of screening level exposure models. The data generated would be, in essence, estimates of central tendency blood concentrations and thus could also be potentially used for direct comparison to active concentrations observed in the U.S. Environmental Protection Agency’s (EPA) ToxCast™ assays. The feasibility study will be limited to a select set of substances sufficient to permit evaluation of the scientific strength and limitations of the approaches and methods.

Results to date include prioritization of 542 chemicals using established criteria, assembling of serum pools, and an initial analytical evaluation to derive calibration curves and estimate limits of detection. Next steps include evaluation of serum-based detection limits and the analysis of the pooled samples.

Implications: Data and experience gathered through this pilot project will guide development and refinement of high-level exposure models used in the HTS process, including both in vitro to in vivo (IVIVE) and external exposure models. The project will provide information useful for developing additional strategies and tools for increasing the confidence in HTS approaches to chemical assessment.

Collaborations: EPA, ScitoVation, Arnot Research and Consulting

Key words: high-throughput screening, chemical risk assessment, biomonitoring

Project start and end dates: October 2015 – June 2020

Peer-reviewed publication(s): None to date.

Presentation(s): None to date.

Other publication(s): None to date.

Abstract revision date: July 2019

This abstract was prepared by the principal investigator for the project. Please see lri.americanchemistry.com for more information about the LRI.