Improving Exposure Models and Integrating Exposure and Risk Information for High-Throughput Chemical Screening (Prioritization) and Higher Tiered Assessments

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Thousands of chemicals require ecological and human health assessment; however, relatively few measured data required for these assessments exist. There are practical limitations to testing and monitoring all of these chemicals; therefore, predictive models are needed. Uncertainty in chemical exposure, hazard, and risk assessment exists whether the data are measured or predicted. In an effort to meet the American Chemistry Council’s Long-Range Research Initiative (ACC-LRI) goals to (i) advance scientific tools for chemical assessment (method development) and (ii) establish a basis for safe chemical use to enhance public confidence and decision-making (application, evaluation, testing or “ground-truthing” of methods), this project aims to improve models and data for chemical assessment.

In this project we seek to advance exposure science through the development and evaluation of chemical property databases and through the development, testing and improvement of predictive quantitative structure–activity relationship (QSAR) and mass balance models for chemical assessment. We also seek to integrate exposure and hazard information for risk assessment through the development and evaluation of new tools for linking the data, i.e., new data and models for biotransformation (metabolism) and degradation rates, and to improve chemical safety testing technologies, i.e., develop and apply *in vitro* models to better interpret *in vitro* bioassay data (e.g. ToxCast). We are evaluating models used for chemical assessments to (i) address uncertainty in the models and available measured data, (ii) further establish a scientific foundation for applying models for decision-making, (iii) foster public and regulatory confidence in their application, and (iv) help prioritize future research needs. The specific components that comprise this project are as follows:

1. Evaluate chemical dermal permeation data and models used in high-throughput (prioritization) and screening-level assessments.
2. Develop and evaluate databases of *in vitro* biotransformation (metabolism) rates in humans and models to predict biotransformation (metabolism) rates from chemical structure.
3. Develop and improve “generic” physiologically-based pharmacokinetic (PBPK) models.
4. Evaluate (ground-truth) far-field (RAIDAR) and near-field (RAIDAR-ICE) exposure and risk assessment models.
5. Develop and apply *in vitro* mass balance models to improve the interpretation and use of data from *in vitro* bioactivity assays.
6. Develop databases and QSARs for chemical partitioning and environmental degradation.

**Implications:** This research builds capacity to evaluate and better understand chemical hazard, exposure and potential risk to humans and the environment through the development and evaluation of measured datasets and predictive models.

**Collaborations:** US Environmental Protection Agency, Environment and Climate Change Canada

**Key words:** hazard assessment, exposure and risk estimation, multimedia mass balance models, QSARs, *in vitro*, model evaluation, biotransformation

**Project start and end dates:** April 2015 – March 2018

This abstract was prepared by the principal investigator for the project. Please see [www.americanchemistry.com/lri](http://www.americanchemistry.com/lri) for more information about the LRI.
Peer-reviewed publications:


Papa E, Sangion A, Arnot JA, Gramatica P. Development of human biotransformation QSARs and application for PBT assessment refinement. *Food Chem Toxicol Accepted*

Manuscripts in preparation for peer-review:

Falls A, Armitage JM, Toose L, Gouin T, Bonnell M, Arnot JA. Applying and evaluating the RAIDAR model to address data gaps for chemical exposure assessment: A case study for organic flame retardants. *In prep.*


Conference and Workshop Presentations:

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Arnot, J; Foster, KL; Looky, AB; Brown, TN; Armitage, J; Papa, E; Wetmore, B; Nichols, J. Comparisons of in vitro, in vivo and in silico biotransformation rates in fish and humans. Society of Environmental Toxicology and Chemistry (SETAC) North America Annual Meeting, Orlando, FL, November 6-10, 2016

Arnot J; Armitage J; Westgate J; Embry M; Gouin T. Examining underlying assumptions when translating in vitro bioassay results to in vivo conditions. International Society of Exposure Science (ISES) Meeting, Utrecht, The Netherlands, October 9-13, 2016

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Arnot J; Armitage J; Embry M; Gouin T. Examining underlying assumptions when translating in vitro

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