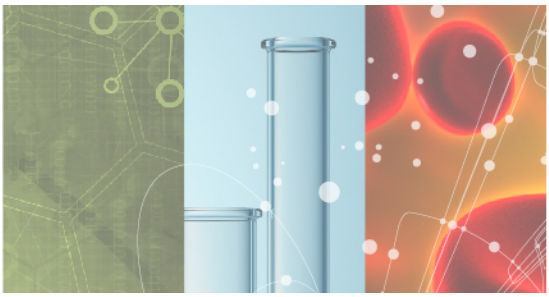

May 23, 2019

American Chemistry Council

ACC Science and Research Highlights

Improving Chemical Exposure Evaluation: A New Framework to Encompass the "Production-to-Dose Continuum"

Risk-based decision making requires integration of quantitative exposure values with relevant hazard information. However, in many cases, chemical use and exposure information are not readily available, or the reliability of such data is uncertain.

To address such challenges, aided in part by support from the ACC-LRI, Jon Arnot (ARC Arnot Research and Consulting) and colleagues at the University of Toronto have developed a novel framework that encompasses the "production-to-dose" continuum for estimating aggregate exposures of humans to organic chemicals.

A Framework for Improved Exposure Estimation

This integrated exposure estimation framework couples a new screening-level version of the Chemicals in Products-Comprehensive Anthropospheric Fate Estimation (CiP-CAFE) model with the Risk Assessment IDentification And Ranking (RAIDAR) and RAIDAR-Indoor and Consumer Exposure (RAIDAR-ICE) models (**Figure 1**). The goal of this framework is to facilitate high-throughput exposure, risk prioritization efforts, and screening-level decisions for relatively "data poor" chemicals—substances for which only limited chemical information (i.e., tonnage in commerce and chemical structure) may be available.

The new CiP-CAFE model can be used to estimate the lifecycle multi-pathway release rates of thousands of chemicals. The output of CiP-CAFE then serves as input for RAIDAR and RAIDAR-ICE. By coupling these modeling approaches, the "production-to-dose" continuum can be approximated. Each model is further described in the following text (with hyperlinks to original articles).

The original CiP-CAFE substance flow model has been revised to derive multimedia emission rates of thousands of chemicals at a time. The model describes chemical flows throughout lifecycle stages such as production, industrial processes, instantaneous use (e.g., the use of personal care products), in-use stock (e.g., chemicals in articles), and waste disposal. The new screening-level version of CiP-CAFE requires two basic inputs, i) yearly-averaged chemical tonnage and ii) molecular structure. It provides estimates of emission rates to outdoor air, surface water, soil, and indoor air, as well as rates of contact with human skin.

The RAIDAR mass balance model combines outdoor environmental fate simulations (air, water, soil, sediment), aquatic and terrestrial food web bioaccumulation, exposure estimates, and, if desired, toxicity information for risk estimation (**Figure 2**). RAIDAR calculates chemical concentrations in the environment, including a range of representative ecological receptors, as well as exposure metrics like intake rates (e.g., human exposure through consumption of drinking water and food or inhalation of outdoor air). It describes the absorption, metabolism, and elimination processes of chemicals in humans and other vertebrate species.

The RAIDAR-ICE mass balance model combines all near-field (indoor and consumer) exposure pathways associated with chemical use and release into indoor compartments or product application onto hands and skin (**Figure 3**). RAIDAR-ICE builds from the Indoor Chemical Exposure Classification/Ranking Model (ICECRM) mass balance framework.

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by Richard A. Becker Ph.D., DABT, ACC's Science and Research Division, Regulatory & Technical Affairs Department

Figure 1. Integrated exposure estimation framework simulating the "production-to-dose" continuum

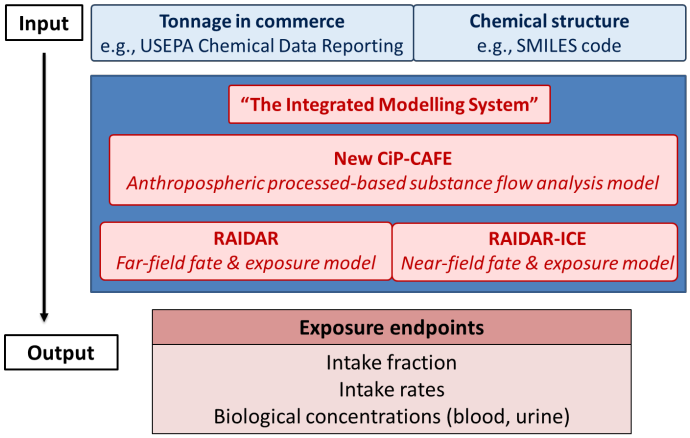
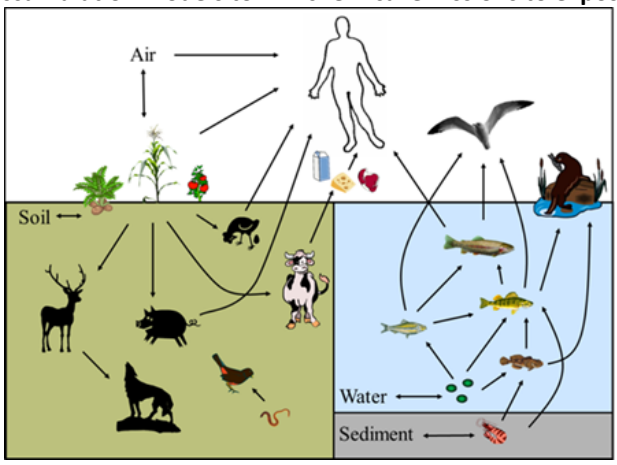


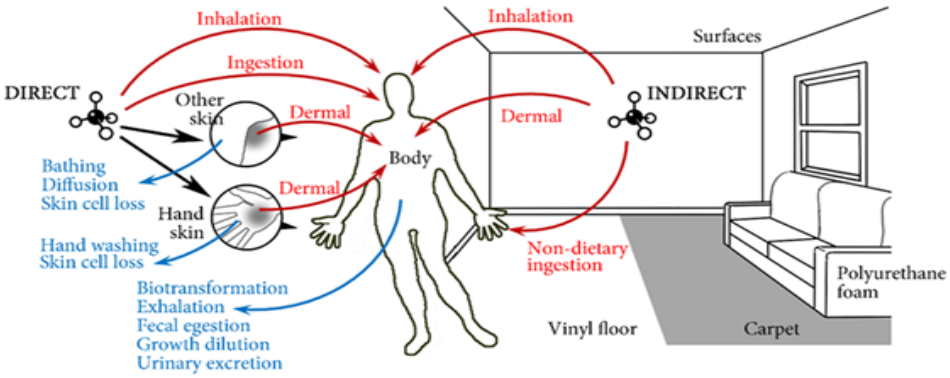
Figure 2. RAIDAR model (ver.3.0) combines mass balance fate and bioaccumulation models to link chemical emissions to exposure



RAIDAR-ICE's indoor chemical fate module (**Figure 3**) consists of seven compartments (indoor air, polyurethane foam, carpet, vinyl floor, and organic films on vertical, up-facing, and down-facing surfaces). RAIDAR-ICE also includes a physiologically-based toxicokinetic (PBTK) model which quantifies dosimetry (e.g., in blood and urine) from inhalation, dermal absorption, and ingestion. This combination of exposure and PBTK modeling provides a seamless connection between chemical use and external and internal exposures (doses). Derived human exposure levels can then be combined with user-defined toxicity (hazard) data to support risk-based prioritization and decision making.

Figure 3. RAIDAR-ICE (ver.1.0) combines mass balance indoor fate and PBTK models to link chemical and product use to exposure

Download the new RAIDAR-ICE model using this link: https://arnotresearch.com/RAIDAR-ICE/



A Model for Risk-Based Screening and Prioritization of Human Exposure to Chemicals from Near-Field Sources (Li et al, 2018. Environ. Sci. Technol. 2018, 52, 24, 14235-14244)

Scientists from ARC, EPA, and the University of Toronto collaborated to verify RAIDAR-ICE model performance by comparing predictions to NHANES human biomonitoring data; the model performed well and was shown to be comparable to SHEDS-HT for the limited set of substances evaluated. Additional case studies demonstrate the feasibility of linking the CiP-CAFE model with RAIDAR and RAIDAR-ICE for estimating human exposure based on two basic inputs—chemical tonnage and molecular structure. In addition, the RAIDAR and RAIDAR-ICE models provide a systematic and harmonized approach for the evaluation of aggregate human exposure. By enabling generation of blood and urine concentrations (not just external concentration at the point of contact), RAIDAR-ICE facilitates comparisons of exposure predictions directly with biomonitoring and toxicity data or bioactivity data from *in vivo* or *in vitro* assays, respectively.

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