Rapid Chemical Exposure and Dose Research

Exposure Forecasting (ExpoCast)

EPA is responsible for ensuring the safety of thousands of chemicals, but quantitative exposure data are available for only a small fraction of registered chemicals. As part of its ongoing efforts to support implementation of the Toxic Substance Act as revised by the Frank R. Lautenberg Chemical Safety for the 21st Century Act, EPA researchers are developing innovative methods to make exposure estimates for thousands of chemicals. These type of exposure data are combined with toxicity data to help thoroughly evaluate chemicals for potential health effects.

Rapid, also called high-throughput, exposure predictions or ExpoCast provide rapid exposure estimates for thousands of chemicals. ExpoCast quickly and efficiently looks at multiple routes of exposure to provide exposure estimates. ExpoCast uses, enhances and evaluates two well-known exposure models to provide exposure predictions.

Farfield Exposure Models

Farfield Exposure Models are used to predict exposures from chemicals that are released into the outdoor environment through industrial releases. ExpoCast uses “off-the-shelf models, USETox and RAIDAR, to estimate outdoor environment exposures. These models estimate the average amount of chemical that gets into the air, water, and soil. The estimates from these models are used in combination with the estimates from the nearfield models to make exposure predictions.

Nearfield Exposure Models

Nearfield exposure models provide estimates of exposure to chemicals used in consumer and in-home products. The model used to estimate the range of total chemical exposures in a population is the EPA’s Stochastic Human Exposure and Dose Simulation (SHEDS) model. There is a SHEDS high-throughput model that estimates exposure for thousands of chemicals, and a more precise traditional SHEDS model which needs more input data to make more accurate exposure predictions.

- SHEDS High-Throughput: Models population level distributions of exposure to nearfield chemical sources. SHEDS-HT can produce a model for thousands of chemicals. This model accounts for the multiple routes, scenarios, and pathways of exposure to understand the total exposure to these chemicals while retaining population and life stage information. SHEDS-HT is useful for the quick evaluation of many chemicals as it has broad applicability, is flexible for what inputs are allowed, and can add new chemicals easily.

Pictured Above: Farfield Exposure Examples

Pictured Above: Examples of Nearfield Exposure, Consumer Use and Indoor

- Traditional: Estimates the range of total chemical exposures in a population from different exposure pathways (inhalation, skin contact, dietary and non-dietary ingestion) over different time periods, given a set of demographic characteristics. The estimates are calculated using available data, such as dietary consumption surveys; human activity data drawn from EPA's Consolidated Human Activity Database (CHAD); and observed chemical levels in food, water, air, and on surfaces like floors and counters. Data on chemical concentrations and exposure factors used in SHEDS are based on measurements collected in EPA field studies and published literature values. SHEDS is useful for considering all exposure scenarios.

EPA is currently evaluating the effectiveness of high-throughput exposure models using the Systematic Empirical Evaluation of Models (SEEM) framework. SEEM includes calibration and evaluation of the models using chemical concentrations found in blood and urine samples from the National Health and Nutrition Examination Study. EPA’s high-throughput models are continually refined as more data is gathered for consumer product use, non-targeted chemical exposure screening, and from estimates for oral doses. It also allows for the systematic evaluation of whether additional data improves the exposure predictions.

Continued on back

Rapid Chemical Exposure and Dose Research

Chemical and Products Database

High-throughput exposure predictions from SHEDS high-throughput use a simple indicator of consumer product use. The high-throughput exposure models are being improved by adding more refined indoor and consumer use information. More refined consumer use information is available in the EPA Chemical and Product Category Database (CPDat), which is a database that maps more than 49,000 chemicals to a set of terms categorizing their use or function in 16,000 consumer products (e.g. shampoo, soap) types based on what chemicals they contain.

The information in the database comes from collating electronic material safety data sheets (MSDS), analyzing consumer product purchasing behavior and data resulting from testing consumer products for the presence of chemicals using a technology called non-targeted analysis. CPDat is a part of EPA's Computational Toxicology (CompTox) Chemicals Dashboard.

Non-Targeted Analysis

Most exposure sampling techniques are chemical-specific and designed to test for chemicals that are suspected to be present. EPA researchers are using "Non-Targeted Screening" methods to test indoor environmental samples such as dust for all chemicals present in the samples.

The objective of non-targeted analysis methods is to identify unknown chemicals in water, soil and other types of samples, without having a preconceived idea of what chemicals are present.

Evaluating Chemical Concentrations in Humans

EPA researchers are developing more precise methods for estimating chemical concentrations in humans following exposure. EPA scientists developed a method to make its high-throughput results more applicable to humans by replacing the traditional constant exposure rate with more realistic human exposure pathways.

EPA researchers developed four toxicokinetic models within a R software package called high-throughput toxicokinetics (httk) to estimate chemical concentrations in humans. The package can currently use human in vitro data to make predictions for 391 chemicals in humans, rats, mice, dogs, and rabbits, including 76 pharmaceuticals and 282 ToxCast chemicals.

Exposure Predictions for Varying Demographics and Life Stages

When evaluating the risk of chemicals, uncertainty exists in hazard identification and exposure predictions. There is also variability in exposure due to differences in key populations. General population exposure estimates are helpful, but population specific exposure values for children, older adults, and other key populations are needed to account for group level variability.

High-throughput toxicokinetics can also be used to provide a more rapid and less resource intensive method for understanding population specific differences in exposure and dose. For example, there is biological variability in the rate that a chemical is cleared from the body across different age and ethnic subpopulations due to differing amounts and activities of metabolic enzymes. This method allows you to adjust exposure models to account for these population specific susceptibilities.

For more information:

ExpoCast webpage: http://www.epa.gov/ncct/expocast/

CPCat webpage: http://actor.epa.gov/cpcat/faces/ho me.xhtml

ToxCast webpage: http://www.epa.gov/ncct/toxcast/

Contact:

Monica Linnenbrink Communications Director, linnenbrink.monica@epa.gov

Kristin Isaacs Project Lead, isaacs.kristin@epa.gov

John Wambaugh Project Lead, wambaugh.john@epa.gov

Main Office:

919-541-4219

http://www.epa.gov/comptox

109 T.W. Alexander Drive

Research Triangle Park, NC 27711

December 2018