



ACC Science & Research Highlights

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PLETHEM: 21st Century Dosimetry to Improve Risk-Based Decision Making

PLETHEM - the open source [population lifecourse exposure-to-health-effects model](#)

Making PBPK modeling, reverse dosimetry and *in vitro* to *in vivo* extrapolation more accessible, easier to conduct, and more transparent

Advancing Exposure Science: A Key Objective of ACC's Long-Range Research Initiative (LRI)

Every risk-based chemical safety evaluation requires integrating knowledge of chemical hazards with information on chemical exposure. Developing and applying new approaches to understand the potential hazards of chemicals have received significant attention from EPA over the years. But, evaluating exposure potential has received much less attention. Therefore, one of the core objectives of [ACC's LRI strategic research plan](#) is to enhance the development of exposure methods and models and harnessing 21st century approaches for quantifying potential exposures.

Since its inception ACC's LRI has supported research to develop, verify, and apply PBPK modeling to improve chemical risk assessments. Physiologically-based pharmacokinetic (PBPK) models, based on knowledge of absorption, distribution, metabolism and excretion, are designed for this purpose.

Making PBPK Modeling More Accessible: Research to integrate PBPK modeling with open source computational tools and source to contact exposure methods are paying off

The PLETHEM software platform ([see this abstract](#)), which is built around a core PBPK model, is an ACC LRI research project conducted by ScitoVation scientists.

- PLETHEM is an open-source package for PBPK modeling written in R statistical language.
- PLETHEM integrates PBPK modeling workflows in an easy-to-use and intuitive user interface.
- PLETHEM provides a quantitative bridge between external chemical exposure and internal dose to better understand and evaluate potential health effects at realistic levels of exposure.

- ScitoVation has just announced the [public launch of PLETHEM](#)

PLETHEM software installation and instructions can be found on [GitHub](#) and on the [Comprehensive R Archive Network](#).

PLETHEM has been designed to address a number of exposure challenges, including:

- Simulation of exposure across the entire lifespan from the beginning of gestation to senescence to determine the effect of growth and physiological change on the relationship of exposure and internal dose.
- Reverse dosimetry modeling to estimate exposures to environmental chemicals from human biomonitoring data.
- Quantitative in vitro to in vivo extrapolation (IVIVE) to translate the concentration of a chemical that elicits a biological response in vitro to predict the equivalent in vivo dose.
- The capability for rapidly predicting chemical dosimetry to support risk assessments ranging from high-throughput screening to in-depth risk evaluations.

The PLETHEM User Guide ([click here](#)) provides detailed step-wise instructions and all data files needed to illustrate and run (and familiarize new users with):

- installing R and Rstudio / installing PLETHEM from the Comprehensive R Archive Network (CRAN)
- loading and running an existing PLETHEM project for PBPK modeling
- creating, running, and saving a new PLETHEM project for PBPK modeling
- importing exposure estimates for PBPK modeling
- running HT-IVIVE for estimating equivalent dose from in vitro point of departure
- a recorded [PLETHEM demo illustrating IVIVE](#) application is also available

Additional research and development of PLETHEM in 2019 will devoted to:

- creating case examples and step by step demos for importing exposure estimates from the exposure tools such as TRA, SHEDS-HT, ConsExpo, and CEM and running forward dosimetry models in PLETHEM
- development of case examples and step by step demos demonstrating IVIVE workflows in PLETHEM
- Refactoring user interfaces for importing exposure estimates to improve ease of use

To learn more about the ACC LRI visit our website

<https://lri.americanchemistry.com/>

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