

Reconstructing Exposures to Populations: Are Complex Models Necessary?

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This presentation explores whether physiologically-based pharmacokinetic models can be used for reconstructing population-scale source-to-dose relationships and, if they can, how complex must they be to achieve the objective. We know that complex physiologically-based pharmacokinetic models are well suited for conducting scoping studies to, for example, (i) understand how a physical or environmental mechanism affects the exposure-to-dose pathway, (ii) determine what biomarkers or environmental data to obtain in a study and (iii) generate exploratory data during the development of a study. However, the level of complexity required to use these models often exceeds the data available for generating model inputs or for calibrating and validating the models. For example, biomarker data are snap-shots of exposure events and thus provide limited description of the temporal history of the exposure. Also, biomarkers and the estimated (or predicted) pollutant concentrations in foods, air, water, and soils are subject to wide inter-individual variability and uncertainty. This presentation explores the difficulties and tradeoffs between using a complex five-compartment model and a simple one-compartment model to reconstruct the exposure to a TCE-exposed cohort. Using Bayesian statistics, we estimate the likely exposure profile using biomarker data and compare how well the models accurately represents the true exposures. We find, in this example, that because variability in the biomarker dataset and uncertainty in exposure input parameters are large, the simple one-compartment model characterizes the exposure-to-dose relationship as well as the more complex model.

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