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Uncertainty, variability, and sensitivity analysis in physiological pharmacokinetic models.

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Summary: Physiologically based pharmacokinetic (PBPK) models are now commonly used to predict the dose of toxic metabolites of chemical substances reaching target tissues. A typical PBPK model can involve 20 or more physiological, physiochemical, and biochemical parameters, each of which is estimated with some degree of error. In this article, methods for assessing the impact of uncertainty in the parameter values on prediction of tissue dose are proposed, along with methods for identifying those parameters to which predictions of tissue doses are most sensitive. Many of the model parameters are related to body weight, which is assumed to vary in accordance with a doubly truncated normal distribution. The application of the proposed methods is illustrated using a PBPK model for benzene.

#### MSC:

[62P10](#) Applications of statistics to biology and medical sciences; meta analysis

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[92C45](#) Kinetics in biochemical problems (pharmacokinetics, enzyme kinetics, etc.)

#### Keywords:

Michaelis-Menten kinetics; physiological model; sensitivity analysis; uncertainty analysis; Monte Carlo simulation; benzene

#### Software:

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Full Text: [DOI](#)

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