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EPA Develops an Information Resource on the Application of Physiologically-Based Pharmacokinetic Models in Risk Assessment

The U.S. Environmental Protection Agency's (EPA) research and development office, a leader in the area of human health risk assessment, has written a report on physiologically based pharmacokinetic (PBPK) modeling that should become a standard desk reference for risk assessors and risk managers who want to know more about using PBPK models in their work. This peer-reviewed report -- *Approaches for the Application of Physiologically Based Pharmacokinetic (PBPK) Models and Supporting Data in Risk Assessment* -- is both an important learning tool for novices in risk assessment, as well as an information resource for experienced risk assessors and risk managers.

Pharmacokinetics is the study of the biological processes that affect the absorption, distribution, metabolism and excretion of a substance, such as a drug or a toxicant. Pharmacokinetic data and models have important applications in risk assessment. Given sufficient physiological and pharmacokinetic data, physiologically-based pharmacokinetic (PBPK) models, which mathematically represent pharmacokinetic processes based on known biological properties, can be developed. Such models can then predict an internal dose (generally blood level or target tissue level) that would result from different exposure regimens or in different species. In risk assessment, PBPK models allow for the extrapolation of data for species and exposure scenarios where you may not have enough data from existing studies. Also, they allow a risk assessor to incorporate variability into the model.

This report gives an overview of the PBPK modeling process, and

- *explains in depth how PBPK models can be used in risk assessment,*
- *describes the data needed to develop these models,*
- *includes examples of certain models and their use,*
- *provides considerations for evaluating these models prior to using them to perform interspecies, intraspecies, and other extrapolations needed in risk assessment, and*
- *describes the types of data and models that EPA requires for consideration of a model for use in risk assessment.*

The report also explains how PBPK models can and cannot be used in risk assessment, as well as highlighting the benefits of using PBPK modeling. In addition, the appendix compiles a list of relevant publications current as of the end of 2005. The report does not, however, issue Agency guidance on the use of PBPK modeling and does not specify when to use a PBPK model in risk assessment.

The report can be found on the Office of Research and Development's National Center for Environmental Assessment Web site at www.epa.gov/ncea under *Recent Additions*.