SRA Exposure Assessment Guidance Update Symposium

Abstract for Presentation: PBPK modeling for exposure and dosimetry

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Physiologically based pharmacokinetic (PBPK) and pharmacodynamic (PBPD) models are tools that describe and predict internal dose and changes in endogenous physiology and biochemistry resulting from that dose. Here we define dose as a toxicologically active entity at the target tissue. The choice of the metric of dose is dependent upon the mode of action and could be various measures of the parent compound, one or more of the metabolites, or an amount bound with an endogenous molecule. Qualitative and quantitative evaluations of the relationship between exposure, dose, and response are improved with the use of computational models. Genomic and other "omic" information offers the promise to greatly aid the characterization of toxic pathways after exposure and help define and identify truly susceptible populations. The challenge will be to use such information not only to identify pathways and susceptibility but also to quantify changes in those pathways over dose and time. When this challenge is met, then PBPK and PBPD models can be extended to describe systems of cells, tissues, organs, and organisms and their response to exposure to environmental factors and chemicals. These models will further describe the relationship between those exposures and background endogenous processes that reflect underlying genetics, disease and behavior, and ultimately adverse health effects. EPA has developed the Exposure Related Dose Model (ERDEM), a system where PBPK models can easily be configured for specific chemicals. It is particularly well suited to examine the impacts of different body size and physiological parameters, including those that change as a result of underlying disease. It is designed so that the user may construct a model as complex or parsimonious as necessary. This presentation will highlight application of ERDEM to show its use for dose analysis. *While EPA has approved this abstract for publication it does not necessarily reflect Agency Policy.*