Applying Uncertainty Analysis to a Risk Assessment for the Pesticide Permethrin

R. Woodrow Setzer[1], Jimena Davis[1], Rogelio Tornero-Velez[2], Jianping Xue[2], Valerie Zartarian[2]
[1]National Center for Computational Toxicology, USEPA, RTP, NC
[2]National Exposure Research Laboratory, US EPA, RTP, NC

We discuss the application of methods of uncertainty analysis from our previous poster to the problem of a risk assessment for exposure to the food-use pesticide permethrin resulting from residential pesticide crack and crevice application. Exposures are simulated by the SHEDS (Stochastic Human Exposure and Dose Simulation) model, which is loosely coupled to a PBPK model for human internal dose estimation. This presentation discusses approaches for quantifying the uncertainties at several points in the coupled model: parameter estimation in the PBPK model; extrapolation to a human model; exposure parameters in SHEDS; and evaluation of overall uncertainty of the predictions of the coupled model and application of sensitivity analysis to identify the most important contributors to that uncertainty. Uncertainties in each component model are characterized as probability distributions on the parameters of that model. In the case of the PBPK model, the uncertainty distribution is derived from prior information about parameter values as well as *in vitro* data specific to permethrin pharmacokinetics, and is computed using Bayesian statistical methods. Extrapolating the PBPK model from rodents to humans involves changing physiological parameters and extrapolating from rodent to human chemical-specific parameter values. Uncertainties here are estimated both from limited human data and from experience in using similar extrapolation methods in other chemicals. Uncertainties in the SHEDS model are quantified using bootstrap and two-stage Monte Carlo techniques, accounting for uncertainty of input parameters related to chemical usage, human activity patterns, environmental concentrations, and various exposure factors. The output of the coupled SHEDS-PBPK model is a probability distribution that characterizes the distribution of modeled dose for a defined population. We use Monte-Carlo methods to propagate the uncertainty in each of the components to make confidence bands around this probability distribution. Finally, global sensitivity analysis allows us to identify individual components of uncertainty which contribute most to the overall uncertainty in the coupled model's predictions. *This work was reviewed by EPA and approved for publication but does not necessarily reflect official Agency policy.*