Applying Uncertainty Analysis to a Risk Assessment for the Pesticide Permethrin

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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 derived from an understanding of the uncertainty of the component distributions describing pesticide use and parameters governing pesticide fate and human behavior relating to exposure. The final output of the coupled model is a probability distribution of exposures that characterizes the distribution of internal 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.*