LINKING MULTIMEDIA ENVIRONMENTAL AND PBPK MODELS TO ASSESS HEALTH RISKS – A CASE STUDY

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Background and aims: Human exposure to chemicals through multiple pathways is classically estimated by the so-called 'multimedia models', calculating the distribution of contaminants among products of interest for humans (like drinking water, inhaled air, vegetables, meat, milk, etc). Combined to data describing human behavior (diet composition, time spent outside, etc), such multimedia models provide an estimation of the daily quantity inhaled or ingested by the population of interest. Once the exposure scenario is identified, the dose-response assessment is typically achieved by comparing exposure outputs (*e.g*, the daily intake) to reference doses, estimated from toxicological data. Coupling multi-media models for different exposure pathways with a generic physiologically based pharmacokinetic (PBPK) model for the human population enables to assess directly the impact of the exposure scenarios on the chemical's concentration in the target tissues.
Methods: One aim of the European 2-FUN project (Full-chain and UNcertainty Approaches for Assessing Health Risks in FUture ENvironmental Scenarios) was to develop an integrated 'multimedia-PBPK' toolbox that also incorporates uncertainty and inter-individual variability analyses and different kinds of sensitivity analysis.
Results: In the present study, an integrated modeling approach was demonstrated for predicting internal tissue concentrations of chemicals by coupling a multimedia environmental model and a PBPK model. A case study was designed for a region situated on the Seine river watershed, downstream of the Paris megacity and for some chemicals (for example benzo(a)pyrene or lead) emitted from industrial zones in the region. In order to take into account the parametric uncertainty in the model inputs, some input parameters relevant for the multimedia model were given by probability density functions (PDFs); some generic PDFs were updated with site-specific measurements by a Bayesian approach.
Conclusions: This case study demonstrated the feasibility of a full-chain assessment combining multimedia environmental predictions and PBPK modeling, including uncertainty analysis.
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