Explicit Pharmacokinetic Modeling: Tools for Documentation, Verification, and Portability

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Quantitative estimates of tissue dosimetry of environmental chemicals due to multiple exposure pathways require the use of complex mathematical models, such as physiologically-based pharmacokinetic (PBPK) models. The process of translating the abstract mathematics of a PBPK model description into a computational implementation is typically a tedious process fraught with the potential for error. Sometimes key information, such as parameters or even whole equations, is unintentionally omitted from published results. Furthermore, complex models are often interpreted by a wide community of scientists and policy makers, it is important that the language used to communicate the model be explicit and coherent. Fields allied with toxicology, such as systems biology, have created markup languages (*i.e.* Systems Biology Markup Language) to standardize the syntax of mathematics and documentation, allowing models to be disseminated as supplemental material in articles or through on-line databases. We propose a formal declarative description of PBPK models, PhLexicOn, to assure published models are thoroughly documented and can be readily translated into popular simulation software. Completeness of a model is not sufficient, it must make sense in terms of the relationships among tissue volumes, blood flows and other fundamental biology. Plausibility is assessed though an ontology that defines the appropriate constituents of physiologically-based systems. Tools are in development to: efficiently verify semantic validity based on the ontology, and automate translation into executable simulations to evaluate consistency with published results. PhLexicOn a framework for documenting, verifying, and translating legacy and state-of-the-art models for re-usability and efficient dosimetry estimation of chemicals for use in human health risk assessments. *This abstract does not necessarily reflect U.S. EPA policy.*