Parsimonious Development of a Physiologically-Based Pharmacokinetic Model for PFOA

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We examine pharmacokinetic (PK) models of varying complexity with respect to a large data set for female CD1 mice (Lau *et al.*) exposed to a range of single and repeated oral doses of PFOA. These data can be broadly grouped into 1) plasma concentrations 2) liver and kidney concentrations, and 3) liver weights. Depending upon the model assumed, different data groups can be predicted. For simple empirical (*e.g*. one-compartment) models or the "saturable resorption" model of Andersen et al. (2006), only plasma concentrations can be predicted. For more complicated physiologically-based PK (PBPK) models specific tissue concentrations, including kidney and liver, as well as liver weights can all be predicted. Adding model complexity requires sufficient data to parameterize the additional dynamics. We use Bayesian analysis to examine on a case-by-case basis whether models of varying complexity are supported by the available data. We consider a physiologic kidney with glomerular filtration and saturable resorption of PFOA from the proximal tubules; a growing liver with growth proportional to PFOA concentration in the liver; and dynamic, saturable plasma binding of PFOA. We use our results to establish the minimal PBPK model supported by the available data. We then compare the predictions of this model to limited PFOA data for male CD1 mice (Lau *et al*.) and female C57/B6 mice (DeWitt *et al.*). *EPA reviewed this work but it does not necessarily reflect official Agency policy*.