Pharmacokinetic Modeling of Perfluoroalkyl Acids in Rodents Hugh A. Barton US EPA, ORD, National Center for Computational Toxicology Research Triangle Park, NC 27711

Perfluorooctanoic acid (PFOA) has pharmacokinetic properties that appear consistent with a number of processes that are currently not well understood. Studies in mice exposed orally at lower doses (1 and 10 mg/kg) demonstrated blood, liver, and kidney concentration time courses consistent with a one-compartment model, although the tissue distribution is clearly not uniform. Blood time course concentrations following a single 60 mg/kg oral dose were consistent with a two-compartment model. Repeated exposures (20 mg/kg/day for 7 and 17 days) produced exposures inconsistent with the one-compartment predictions, but reasonably predicted by the two compartment fit based upon the single high dose. The three-compartment saturable resorption model can be parameterized to fit all the blood time course data. A more complex physiologically based pharmacokinetic model would be required to predict the tissue distribution characteristics. Improved knowledge of the biological processes controlling the pharmacokinetics of these compounds will better inform cross-species extrapolation and understanding of mode of action. (This abstract does not present Agency policy).