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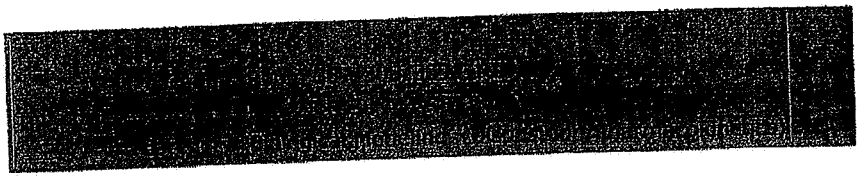

CONSIDERATIONS RELEVANT TO CONSTRUCTING A HUMAN PBPK MODEL FOR PERFLUOROOCTANOIC ACID (PFOA)

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Perfluorooctanoic acid (PFOA) is a surfactant, which has received significant interest in recent years due to its reported prevalence in blood samples from many US citizens. Consequently, there has been some activity associated with constructing a human PBPK model to relate inhalation and oral exposures to PFOA levels in plasma. While there have been many kinetic studies conducted on rodents, the rodent kinetic data have not been useful in extrapolation to PFOA kinetics in humans. There are several considerations relevant to the construction of a human PBPK model that will determine how, or even if, such a model is appropriate for PFOA. First, PFOA is a surface-active chemical, which will affect its behavior in biological systems and has thus far complicated any efforts to determine tissue to blood partition coefficients. Second, PFOA is reported to be unmetabolized in mammalian systems, thereby eliminating the need for explicit description of metabolizing organs or tissues. Third, the elimination rate is dramatically different between humans and rodents. The reported half-life in humans is approximately 4 years as compared to 2 hours in the female rat. Further, rats have sex dependent elimination rates, which do not appear to be relevant to humans. Fourth, controlled human exposures to PFOA are lacking; therefore, any attempts to validate a PBPK model would be severely limited. This is further complicated by the fact that elimination mechanisms have not been completely elucidated in rats and humans. These considerations and gaps in the understanding of species-specific elimination of PFOA make it impractical to construct and apply a human PBPK or generic kinetic model to predict PFOA concentrations in plasma following ingestion or inhalation of PFOA. The basis for constructing and validating a human PBPK model for PFOA was described and evaluated.

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