

Group 1

The first task was to ascertain studies from the literature that provide evidence of the terminal half-life of PFOA in the human population. Renal reabsorption of PFOA provides the primary pathway that drives the long terminal half-life of PFOA (Andersen et al. 2007; Han et al. 2012). Analysis of the available literature that have reported quantitative analysis of the PFOA half-life in humans yielded 12 studies that had sufficient data to be included in our evaluation. These studies range in size from small subject groups such as the analysis of retired 3M workers reported by Olsen et al. (2007) and airport workers (Xu et al. 2020) to larger population studies using NHANES data over several sampling intervals (Gomis et al. 2017). Across all studies, the range of half-lives reported was 1.77 to 8.5 years which is surprisingly small (<factor of 5). Based on the reported half-lives, a reasonable central estimate would fall between the median and mean 2.4 to 3.2 years of the reported PFOA half-lives. Cofactors that may impact the terminal half-life of PFOA in environmentally exposed individuals include variability in renal transporter expression, life-stage associated changes in renal transport and glomerular filtration, renal tubule diseases, continued exposure to background PFOA in the assessed population, sex specific loss of PFOA (i.e., episodic loss to fetus and menstrual excretion), and the mixture of PFOA molecules of the exposure population (i.e., branched PFOA has shorter half-life than linear PFOA).

The second task was to evaluate the reported volume of distributions (VD) reported for PFOA. Two estimates in primates were found. Andersen et al. (2007) estimated the VD (0.14 L/kg) from a kinetic dataset in orally exposed monkeys. This estimate is close to the VD in humans, 0.17 L/kg, provided by Thompson et al. (2010). The 0.17 L/kg VD has been generally accepted and was used in many, if not all, of the PFOA half-life assessments that have been reported.

References

Andersen ME, Clewell HJ III, Tan YM, Butenhoff JL, Olsen GW. Pharmacokinetic modeling of saturable, renal resorption of perFLuoroalkylacids in monkeys—probing the determinants of long plasma half-lives. *Toxicology*. 2006; 227:156–164.

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Thompson J, Lorber M, Toms LL, Kato K, Calafat AM, Mueller JF. Use of simple pharmacokinetic modeling to characterize exposure of Australians to perfluorooctanoic acid and perfluorooctane sulfonic acid. *Environ Int*. 2010; 36(4):390-397.