Perfluorooctanoic Acid (PFOA) and Perfluorooctanesulfonate (PFOS)
Peer Review

Background:

PFOA and PFOS are environmentally persistent organic fluorocarbons that have been identified in ambient waters, ground water, drinking water, and biosolids. They are metabolically inert but have the ability to bind to and interact with a variety of biomolecules leading to responses in living organisms. Both compounds have a substantial database of epidemiological, pharmacokinetic, toxicological and mechanistic studies.

The two documents submitted for peer review include health assessment chapters that will be used 1) to provide information to drinking water treatment plant operators regarding the significance of monitoring results with respect to potential health outcomes and 2) to determine whether the perfluorinated compounds currently being monitored at Public Drinking Water Systems require regulation. The health information at that time will be accompanied with chapters on environmental fate, occurrence at public drinking water systems and occurrence in other media. The quantitative aspects of the Health Assessment documents will also be used to develop lifetime Health Advisories for both compounds.

Charge to the Peer Reviewers:

1. Please comment on the strengths, weaknesses, and characterization of the studies selected as key for quantification.

2 Please provide citations (and, where possible, pdfs or hard copies) for any references you suggest EPA consider adding to the document. Describe where you suggest these references be incorporated.

3. The OW concluded that the human epidemiology data for PFOS/PFOA do not provide adequate quantifiable dose-response information for use as the basis of a candidate RfD because of uncertainty regarding the routes, levels and timing of exposures plus the confounding influences of other PFCs present in serum. Please comment of the OW characterization of the data.

4. Please comment on the transparency and characterization of the epidemiological data.

5. The OW has concluded that the cancer classifications for PFOA and PFOS are most consistent with respective classifications of s*uggestive evidence for carcinogenicity* as described the EPA Guidelines for Carcinogen Risk Assessment (pp. 2-56, 2-57). Please comment on the strengths and weaknesses of this classification.

6. Significant interspecies differences in pharmacokinetics exist for both PFOA and PFOS. Adjusting for interspecies differences was an important step in developing candidate RfDs given the totality of the human and animal data. Please comment on the strengths and

weaknesses of the pharmacokinetic model adjustments to accommodate the impact of albumin binding and renal tubule transporters in determining average serum values.

7. Table 5-7 lists the parameters used for the ORD pharmacokinetic models that provide the final serum and AUC values for calculating the internal dose point of departure for the RfD calculation. Please comment on the strengths and weaknesses of the selected parameters.

8. The volume of distribution (Vd) and half-life values are critical in the derivation of the interspecies uncertainty factor applied in derivation of candidate RfDs from a NOAEL, LOAEL or a BMDL. The available data for both values are provided in Section 3.5.2 and 3.5.3 of both documents. Please comment the strengths and weaknesses of the values selected.

9. A variety of endpoints and studies were used to compare points of departure and the resultant RfDs for both PFOA and PFOS. In addition, comparisons were provided across RfD outcomes based on the model outputs compared to those for the NOAEL, LOAEL and BMDL points of departure. The range of candidate RfDs derived from the different points of departure is fairly narrow. Please comment on the strengths, weaknesses and transparency of this analysis.

10. The RfDs for PFOS and PFOA are derived from the modeled steady state serum concentrations and their association with effects that include short term and longer term exposures with associated diverse effects. The studies considered included effects due to exposure durations that ranged from 11 to 182 days, and occur at comparable human equivalent dose (HED) levels. The current, draft RfDs do not include an uncertainty factor for study duration because of the apparent concordance HEDs despite duration differences. Given this pattern of response, is it appropriate to conclude that the candidate RfDs are applicable to both short-term and lifetime exposures?

11. In addition to using the average serum values from animal studies to calculate internal doses for humans, the animal to human extrapolation can be accomplished by dividing animal average serum values by the human to animal clearance ratios to project a human average serum point of departure in units of mg/L serum. Please provide recommendations for applying uncertainty factors to the extrapolated average human serum values to determine serum-based thresholds that are protective for humans. A NOAEL expressed in average human serum units would be useful in interpreting NHANES population monitoring data.

12. Please describe any suggestions you have for improving the clarity, organization, and/or transparency of the draft documents.