Agency for Toxic Substances and Disease Registry
Comments on the Interagency Science Discussion (Step 6)
Draft IRIS Toxicological Review of Perfluorodecanoic Acid (PFDA) and Related Salts
April 2024

Date: 05/22/2024

Thank you for providing ATSDR with the opportunity to review the Step 6 Draft IRIS Toxicological Review of Perfluorodecanoic Acid (PFDA) and Related Salts. This draft is much improved from the previous draft reviewed by ATSDR. ATSDR would like to thank EPA for addressing some of the concerns raised by ATSDR during the Step 3 review. ATSDR would like to provide the following additional comments:

- Use of ATSDR sources
    - The citations for ATSDR 2018a (An overview of perfluoroalkyl and polyfluoroalkyl substances and interim guidance for clinicians responding to patient exposure concerns) and 2018b (Toxicological Profile for Perfluoroalkyls – Draft for Public Comment) are outdated and should be replaced with ATSDR's current products or another appropriate citation.
        - Please utilize this 2024 source in place of ATSDR 2018a: ATSDR PFAS Information for Clinicians: Factsheet (cdc.gov)
        - Where applicable, ATSDR 2018b should be replaced with ATSDR 2021. Additionally, the hyperlink in the list of references for ATSDR 2018b (draft Tox Profile) directly leads to ATSDR 2021 (final Tox Profile). The exception to replacing ATSDR 2018b with ATSDR 2021 is the use of the ATSDR 2018b in "Literature Search and Screening Results" in section 2.1.
- Errors
    - On page 391, there appears to be an error in Table 5-14. For Wikstrom et al., 2020, two different POD_{HED} are listed using the same health effect basis. Under the osRfD, the POD is 5.44×10^{-8}, but under "Overall lifetime RfD", the POD is listed as 5.44×10^{-9}.
- PFAS Confounding
    - The discussion surrounding concerns of cofounding for multiple PFAS has been updated and improved in this draft. EPA clearly discusses confounding related to the use of epidemiological studies for PFDA hazard identification (i.e., identifying associations between PFDA exposure and decreased birth weight or decreased antibody titers), but the draft and disposition falls short of adequately addressing confounding concerns regarding the use of these studies for quantitative risk assessment and derivation of toxicity factors. The draft and disposition could benefit from additional discussion directly addressing these concerns.
- Immune Effects
    - EPA cites the World Health Organization/International Programme on Chemical Safety (WHO/IPCS) (IPCS, 2012) in support of the use of decreased antibody titers for PFAS risk assessment; however, in September 2022, WHO released their own draft "PFOS and PFOA in Drinking-water, Background document for development of

WHO Guidelines for Drinking-water Quality" for public review. This review from WHO considered the clinical implications of using this endpoint uncertain. WHO also adds (citing CDC 2019) that the number of new cases of diphtheria in the United State over a 40-year period was less than one per year on average. EPA should take this into consideration when citing the WHO immunotoxicity guidelines published in 2012.

    - On page 148 of the PDF (3-106; lines 22-23), the sentence "The lack of clear association with infectious disease outcomes does not reduce certainty in this effect because these studies are expected to be biased toward the null." This statement is also utilized in the appendix. The meaning behind this statement should be clarified. The concerns pointed out by reviewers in earlier drafts were related to the clinical implications of the effect rather than uncertainty of the effect itself.

- Endocrine Effects
    - EPA acknowledges the critical role thyroid hormones play in bone growth and brain development at various life stages (Section 3.2.8, page 3-282). Due to this role thyroid hormones play in neurodevelopment/development, EPA could consider briefly discussing the hazard conclusions for neurodevelopmental and developmental effects in the evidence integration for endocrine effects.