National Institute for Occupational Safety and Health (NIOSH)
Comments on the Interagency Science Consultation
Draft IRIS Toxicological Review of Perfluorohexanesulfonic Acid (PFHxS)
January 2023
(Date Received February 3, 2023)

All comments pertain to the main document.

Page 1-2, line 2 and multiple other locations: Consider updating the ATSDR 2018a and b references to the most up-to-date ATSDR reference published in its final form, ATSDR 2021: [Toxicological Profile for Perfluoroalkyls (cdc.gov)](#).

Page 1-3, lines 3-5: Suggest addition of text (see yellow highlight): "PFHxS has been used as a surfactant to make fluoropolymers, and in water- and stain-protective coatings for carpets, paper, and textiles including textiles used in some protective clothing (NTP, 2018c)." The use of PFAS in protective clothing is of particular interest as the compounds *may* be protecting from one hazard while introducing another, potentially making its elimination from these textiles more challenging than textiles used for recreation or sports performance. We do not yet know if it is a contributing source, but the title of section 1.1.2 includes "Use" and its application to protective clothing has different implications than its use for other textiles.

Page 1-3, lines 5-8: Suggest expanding the overview of sources, production, and use that contain PFHxS across multiple occupational sectors and/or products including wood particle board, rubber insulation, electrowinning metal wire, metal treatments, paints, varnishes, and flame retardants [Glüge et al. 2020; OECD 2022].

Page 1-3, lines 8-9: Suggest addition of text: "It has also been used in aqueous film-forming foam (AFFF) for ~~fire~~ suppression of liquid fuel fires (Laitinen et al., 2014)." This text is important, because the reader may misinterpret it as being in all fire suppression products. Additionally, it is important that the reader understand that alternative products must meet performance specifications related to liquid fuel fires instead of fires in only the built environment as a fuel source.

Page 1-4, lines 16-18: Suggest addition of text: "Long-chain PFAS have been found at sites, including private and federal facilities, and have been associated with various sources, including AFFF for ~~fire~~ suppression of liquid fuel fires, and PFAS manufacturers and industries that use PFAS (e.g., textiles) (ATSDR, 2018a)."

Comments on Table 1-1 Physical-chemical properties of PFHxS and related salts, page 1-3

Melting point: 190 C; For comparison, PubChem gives perfluorooctanesulfonic acid (PFOS, C_8) as a liquid (i.e., melting point < 25 C). Sigma-Aldrich reports perfluorobutanesulfonic acid (C_4) as a liquid with a freezing point at -21 C. Given these, it seems highly unlikely that perfluorohexanesulfonic acid (C_6) could have a melting point of 190 C.

Boiling points: Two of the 3 salts have listed boiling points very similar to the parent acid and the potassium salt with a boiling point only moderately higher than the parent acid. It is normal for a salt to have a boiling point much, much higher than its parent acid. The ammonium salt could appear to have a similar boiling point if it loses ammonia to reform the parent acid.

Vapor pressure: The listed vapor pressure of the parent acid seems very low based on comparisons with similar PFAS and its own reported boiling point. The Comp Tox Chemicals Dashboard gives a vapor pressure for perfluorooctanesulfonic acid (PFOS, C_8) of 2.48 x 10^{-6} mm Hg. For perfluorobutanesulfonic acid (C_4), PubChem and Sigma-Aldrich give 2.7 x 10^{-2} mm Hg and 5 x 10^{-2} mm Hg, respectively. If those values are reasonably accurate, the expectation would be for perfluorohexanesulfonic acid to have a vapor pressure falling between these values. However, the listed vapor pressure is 8.10 x 10^{-9} mm Hg. This extremely low vapor pressure is also not consistent with a boiling point of 246 C. Finally, the 3 salts all are given boiling points nearly identical to the parent acid. It should be noted that, just as the boiling points of salts are typically much, much higher than that of their parent acid, vapor pressures of salts are typically much, much lower than that of their parent acid.

Bioconcentration factors: This reviewer does not have experience with bioconcentration factors; however, it seems odd that the perfluorohexanesulfonic acid, its potassium salt, and its ammonium salt would have bioconcentration factors that are very similar, yet the sodium salt has a value that is radically lower.

Page 3-5, line 9: “No data on absorption of PFHxS through the respiratory tract has been found.” This statement appears to be the only justification for not deriving an RfC (inhalation reference concentration). Please elaborate on whether any useful extrapolations can be made between oral and inhalation absorption and describe whether a rough model of inhalation absorption (e.g., assuming 100% absorption of inhaled compound) would have any potential application and what limitations that would put on deriving a value for inhalation.

Page 5-24, lines 3-4: “No studies examining inhalation effects of short-term, subchronic, chronic, or gestational exposure for PFHxS in humans or animals have been identified, precluding the derivation of an RfC.” In light of the fact that the kinetics of systemically absorbed PFHxS in humans are known well enough to determine a human equivalent dose (HED) for the derivation of the oral reference dose (RfD) values, and the fact that the adverse effects are caused by systemically absorbed PFHxS, please briefly elaborate on why it is not practicable to extrapolate an RfC from blood PFHxS levels.

<u>References</u>

Glüge J, Scheringer M, Cousins IT, DeWitt JC, Goldenman G, Herzke D, Lohmann R, Ng CA, Trier X, Wang Z [2020]. An overview of the uses of per- and polyfluoroalkyl substances (PFAS). Environ Sci Processes Impacts 22(12):2345–2373, https://doi.org/10.1039/d0em00291g. PMID: 33125022.

OECD [2022]. Per- and Polyfluoroalkyl substances and alternatives in coatings, paints and varnishes (CPVs), Report on the commercial availability and current uses. OECD Series on Risk Management, No. 70, Environment, Health and Safety, Environment Directorate, OECD, https://www.oecd.org/chemicalsafety/portal-perfluorinated-chemicals/per-and-polyfluoroalkyl-substances-alternatives-in-coatings-paints-varnishes.pdf.