MEMORANDUM

SUBJECT: Recommendations on the Use of State PFAS Reference Values for Superfund Human Health Risk Assessments

FROM: OLEM's Human Health Regional Risk Assessment Forum's (OHHRRAF) Toxicity Workgroup

TO: Regional Screening Levels Workgroup

PURPOSE

The purpose of this memorandum is to provide recommendations from the Office of Land and Emergency Management's (OLEM) Human Health Regional Risk Assessment Forum's (OHHRRAF) Toxicity Workgroup regarding the use of state toxicity values for five per- and polyfluoroalkyl substances (PFAS) as noted in the attachment.

This recommendation is based on OHHRRAF Toxicity Workgroup evaluation of Tier 3 toxicity values for five PFAS. The Workgroup recommends the use of four toxicity values derived by the state of Wisconsin. The Workgroup does not recommend the use of the fifth toxicity value. OHHRRAF concurs with the Toxicity Workgroup recommendations. The Workgroup's recommendations may be applicable to EPA regional offices' activities to evaluate and address hazardous waste releases under the Comprehensive Environmental Response, Compensation and Liability Act's authorities (e.g., Hazard Ranking System scoring, remedial investigation and feasibility study process, removal actions, and five-year reviews) and other OLEM risk evaluation efforts.

BACKGROUND

The Office of Solid Waste and Emergency Response[1] (OSWER) Directive 9285.7-53 **(***Human Health Toxicity Values in Superfund Risk Assessments*; December 5, 2003; commonly referred to as "the 2003 hierarchy guidance"), identifies an updated source hierarchy for human health toxicity values to consider when carrying out Superfund site risk assessments. It also states that "[t]his revised hierarchy recognizes that EPA should use the best science available on which to base risk assessments." Furthermore, the 2003 hierarchy guidance states that, "EPA and state personnel may use and accept other technically sound approaches," acknowledging "that there may be other sources of toxicological information," referring specifically to OSWER Directive 9285.7-16 (*Use of IRIS Values in Superfund Risk Assessment*; December 21, 1993), which offers similar guidance.[2] The 2003 hierarchy guidance states that Tier 3 "includes additional EPA and non-EPA sources of toxicity information. Priority should be given to those sources of information that are the most current, the

[1] The former name of what is now EPA's Office of Land and Emergency Management.

[2] See OSWER Directive 9285.7-53, page 2, quoting OSWER Directive 9285.7-16: "...IRIS is not the only source of toxicology information, and in some cases more recent, credible and relevant data may come to the Agency's attention. In particular, toxicological information other than that in IRIS may be brought to the Agency by outside parties. Such information should be considered along with the data in IRIS in selecting toxicological values; ultimately, the Agency should evaluate risk based upon its best scientific judgement and consider all credible and relevant information available to it."

basis for which is transparent and publicly available, and which have been peer reviewed." The guidance provides examples of Tier 3 toxicity values such as California Environmental Protection Agency (Cal EPA) and Agency for Toxic Substances and Disease Registry (ATSDR) Minimal Risk Levels (MRLs) and notes that additional sources may be identified for Tier 3. While the recommended state (Wisconsin) reference values were derived by a state whose toxicity values have not been used before, the state's toxicity information was determined by the OHHRRAF's Toxicity Workgroup to be based on similar methods and procedures as those used for other Tier 3 values.

The OHHRRAF Toxicity Workgroup performed a comprehensive review of toxicity values and supporting information developed by states at the time of the evaluation. The workgroup identified several oral toxicity values derived by states. Of these, the Workgroup identified a subset of five originally derived toxicity values for a PFAS where there was no final or planned federal chronic toxicity value. The five PFAS identified are perfluorooctadecanoic acid (PFODA), perfluorotetradecanoic acid (PFTetDA), perfluorododecanoic acid (PFDoDA), perfluoroundecanoic acid (PFUDA), and 4,8-dioxa-3H-perfluorononanoic acid (DONA, sometimes called ADONA). This memo is intended to summarize the conclusions of the OHHRRAF Toxicity Workgroup with respect to the use of a state reference value. These evaluations are based on assessments of the quality of the principal study and the methodology used to derive the reference value for each chemical. Table 1 provides a summary of the recommended toxicity values, and Table 2 provides details on the toxicity values as well as the rationale for each toxicity value's recommendation.

The recommendations in the memorandum will be re-evaluated in the future as toxicity values are updated.

Please contact Linda Gaines (202) 566-1054 if you have any questions or require additional information.

REFERENCES

Texas Commission on Environmental Quality. (2016). "Perfluoro Compounds (PFCs)." https://www.tceq.texas.gov/downloads/toxicology/pfc

Wisconsin Department of Health Services. (2020). "Summary and Scientific Support Documents for Cycle 11 Recommended Groundwater Standards." https://www.dhs.wisconsin.gov/publications/p02807.pdf

Table 1: Selected toxicity values

PFAS	Chronic Toxicity Values (mg/kg-day)	Source of Value
Perfluorooctadecanoic acid (PFODA, 16517-11-6)	4E-02	Wisconsin (2020)
Perfluorotetradecanoic acid (PFTetDA, 376-06-7)	1E-03	Wisconsin (2020)
Perfluorododecanoic acid (PFDoDA, 307-55-1)	5E-05	Wisconsin (2020)
Perfluoroundecanoic acid (PFUDA, 2058-94-8)	3E-04	Wisconsin (2020)

Table 2. Information Summary of Screening Toxicity Value Recommendations for PFAS			
PFAS	**Toxicity Values[a] (mg/kg-day)**	**Principal study (species) and critical effect for selected value**	**Rationale**
Perfluorooctadecanoic acid (PFODA)	**4E-02 (WI)**	• Principal study: Hirata-Koizumi et al. 2012 (reproductive/developmental study in rats) • Critical effect: Decreased maternal body weight gain and food consumption; damage to pancreas and liver (females)	Strengths: • Derivation was consistent with EPA methodology with respect to selection of the principal study and critical effects, and application of UFs to the POD to derive a toxicity value. • Principal study encompassed pre-mating, mating, gestation, and lactation. Limitations: • Principal study was subchronic in duration (42d); UF_S ideally would be higher than 1. • Sensitive endpoints (e.g. endocrine/thyroid effects) were not evaluated. • Acceptable daily intake is less sensitive than toxicity values for other PFAS.
Perfluorotetradecanoic acid (PFTetDA)	**1E-03 (WI)**	• Principal study: Hirata-Koizumi et al. 2012 (reproductive/developmental study in rats) • Critical effect: Decreased maternal body weights	Strengths: • Derivation was consistent with EPA methodology with respect to selection of the principal study and critical effects, and application of UFs to the POD to derive a toxicity value. • Principal study encompassed pre-mating, mating, gestation, and lactation. Limitations: • Principal study was subchronic in duration (42d); UF_S ideally would be higher than 1. • Sensitive endpoints (e.g. endocrine/thyroid effects) were not evaluated.
Perfluorododecanoic acid (PFDoDA)	**5E-05 (WI)** 1.2E-05 (TX)	• Principal study: Shi et al. 2009 (110-day study in rats) • Critical effect: Decreased testosterone	• The use of a longer-term study by WI (110d) was considered more appropriate than the short-term (14d) study used by TX. • TX did not apply UFs in a manner consistent with EPA methodology. • TX relied on an older version of the ATSDR Toxicological Profile for PFAS and its literature search identified Shi et al. (2007) as the only available study. WI relied on a later version of the ATSDR profile and an additional literature search to identify relevant studies.
Perfluoroundecanoic acid (PFUDA)	**3E-04 (WI)**	• Principal study: Takahashi et al. 2014 (reproductive/developmental study in rats) • Critical effect: Decreased body weight in pups	Strengths: • Derivation was consistent with EPA methodology with respect to selection of the principal study and critical effects, and application of UFs to the POD to derive a toxicity value. • Principal study encompassed pre-mating, mating, gestation, and lactation. • Critical effect was observed in pups of exposed mothers. Limitations: • Principal study was subchronic in duration (42d) and no UF_S used. • Sensitive endpoints (e.g. endocrine/thyroid effects) were not evaluated. • Although it would be preferable to have additional chronic-duration studies evaluating sensitive endpoints, the principal study encompassed pre-mating, mating, gestation, and lactation.
4,8-dioxa-3H-perfluorononanoate (DONA)	3E-04 (WI)	• Principal study: Gordon et al. 2011 (90-day study in rats) • Critical effect: Decreased hemoglobin and hematocrit (males)	Limitations: • Critical effects did not show a clear dose-response. • Magnitude of changes was small (4-5% lower than controls). • Clinical parameters fell within the range for historical controls (same strain/age). • Toxicological significance/adversity of hemoglobin/hematocrit decrease was uncertain.

			• Principal study also identified decreased litter size in a developmental study, but WI did not indicate why this acceptable daily intake was excluded.

[a]Selected value indicated in **bold** font

POD = Point of departure; WI = Wisconsin; TX = Texas, UF = uncertainty factor, UF_S = Subchronic to Chronic uncertainty factor