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Massachusetts Department of Environmental Protection Office of Research and Standards Final Recommendations for Interim Toxicity and Drinking Water Guidance Values for Perfluorinated Alkyl Substances Included in the Unregulated Chemical Monitoring Rule 3

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Summary and Recommendations

The United States Environmental Protection Agency (USEPA) included six perfluorinated alkyl substances (PFAS) in the Unregulated Contaminant Monitoring Rule 3 (UCMR 3) (77 FR 26072, 2012). Under UCMR 3 many public drinking water supplies across the US, including in Massachusetts (MA), were tested for a number of emerging contaminants of concern. The UCMR 3 PFAS compounds included perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA), perfluorohexane sulfonate (PFHxS), perfluorononanoic acid (PFNA), perfluorohepatanoic acid (PFHpA) and perfluorobutane sulfonate (PFBS).

All of the UCMR 3 PFAS have been detected in one or more MA water supplies, as well as in some groundwater and surface water samples. Because USEPA has only issued drinking water health advisory (HA) values and toxicity values (Reference Doses or RfDs) for PFOS and PFOA, the Massachusetts Department of Environmental Protection (MassDEP) Drinking Water and Waste Site Cleanup Programs requested the Office of Research and Standards (ORS) assistance in evaluating the potential health risks associated with detections of the other four UCMR 3 PFAS. Currently, USEPA, MA and most other states do not address the additional UCMR 3 PFAS analytes in drinking water guidance or risk assessments. This is tantamount to a default assumption that these compounds are not toxic and do not present any additional health risk. In light of the structural similarities of these compounds; available data relating to biological half-lives, which are long; and toxicity, which includes developmental endpoints, it is not reasonable or health-protective to treat these compounds as being non-toxic. The following document presents ORS recommendations regarding how health risks posed by these compounds should be evaluated based on a review of key information relating to their toxicity, chemical structures and biological persistence.

In summary, the available data demonstrate that PFHxS, PFNA and PFHpA are very similar in molecular structure to PFOS and PFOA, with all three compounds having six to eight fluorinated carbons (plus or minus one compared to PFOS and PFOA). They also exhibit similarly long

biological half-lives ranging from approximately 3-7 years, which is strongly associated with the toxicity of these compounds. Although toxicity test data are more limited for the three additional compounds compared to PFOS and PFOA, the available results demonstrate that these compounds elicit similar types of effects and these are observed at similar dose ranges. PFBS has only four fluorinated carbons, and available data, although limited, indicates that it exhibits lower toxicity than PFOS and PFOA and is less persistent in the body, with a serum half-life of weeks compared to years for PFOS and PFOA[1]. The USEPA has issued a provisional RfD, but no drinking water guidance, for PFBS, and the Minnesota Department of Health (MNDH) recently issued a revised drinking water guidance value of 2,000 ppt for this compound.

Based on the information reviewed by ORS and to address the gaps in guidance from USEPA regarding toxicity and drinking water guidance values for PFHxS, PFNA, PFHpA and PFBS, ORS:

a. Recommends that the USEPA HAs and RfDs derived for PFOS and PFOA be applied to PFHxS, PFNA and PFHpA.
b. Recommends that an additive toxicity approach be used for these compounds when they occur together. For example, when all or some of the five compounds PFOS, PFOA, PFHxS, PFNA and PFHpA occur together in drinking water, the detected concentrations for these PFAS should be summed and compared to 0.07 ug/L (70 ppt).
c. Does not recommend treating PFBS as being equipotent to the longer-chain PFAS considered in this document and is further assessing appropriate toxicity and drinking water guidance values for this compound. In the interim, the MNDH drinking water guidance value of 2 ug/L (2,000 ppt) and RfD (0.00043 mg/kg-day) are recommended for PFBS for risk screening purposes pending further ORS review.

The recommendation regarding additivity of PFHxS, PFNA and PFHpA, with PFOS and PFOA, is an extension of the approach used by USEPA for PFOS and PFOA, which treats these two compounds as being toxicologically equivalent and additive. Extending this approach and applying the PFOS and PFOA RfD and HA values to the other longer-chain UCMR 3 PFAS is supported by the similarities in molecular structures, toxicology and serum half-lives exhibited by these five compounds.

This approach is consistent with that used by the Connecticut (CT) Department of Public Health (CTDPH) in establishing the CT Drinking Water Action Levels for the UCMR 3 PFAS (CT DPH, 2016) and is further supported by stated concerns and decisions about long-chain PFAS

[1] With respect to the other USEPA Method 537 PFAS, PFHxA has been found to be considerably less toxic and persistent than PFOS and PFOA. Very little *in vivo* data was located on C10 and longer chain PFAS included in EPA Method 537. These longer compounds exhibit greater cytotoxicity in *in vitro* bioassays but there are considerable uncertainties regarding their toxicokinetics and indications that they may not be as well absorbed following ingestion. At this time, no RfD or HA values have been issued or proposed for these compounds by USEPA or ORS.

risks by: 1) USEPA (USEPA, 2017a); 2) the Arizona Department of Health Services (AZDHS) and the Agency for Toxic Substances and Disease Registry (ATSDR), Health Consultation on the Ottoman Water Company (Arizona DHS, 2016); and, 3) the Colorado Department of Public Health and Environment (CODPHE) and USEPA Region 8 decision to include PFHpA together with PFOA and PFOS in their assessment of contaminated drinking water near Colorado Springs, CO (CODPHE, 2017).

Due to the lack of USEPA drinking water guidance and toxicity values for several of the UCMR 3 PFAS, the potential risks of these compounds to sensitive populations, in particular the developing fetus and nursing infants may not be adequately addressed. The proposed recommendations fill this gap by providing clear drinking water guidance and toxicity values.

As information is evolving on PFAS toxicity and exposures, ORS will continue to track scientific developments on these compounds, in particular regarding potential mechanisms of action that may further improve the understanding and extrapolation of effects in animals to humans, and will update these recommendations as appropriate.

Introduction and Background

PFAS are a group of man-made fluorinated chemicals containing diverse functional groups and carbon chain lengths. They are known to be persistent and bioaccumulative, explaining their worldwide environmental presence. To begin to gather data on the occurrence of PFAS compounds in US drinking water, six of these compounds were included in USEPA's nationwide testing of public drinking water supplies (PWS) under the Unregulated Contaminant Monitoring Rule 3 (UCMR 3) (Table 1). Under this program all large public water systems and some smaller systems were tested for six PFAS compounds. In MA, 170 PWS were sampled for the six PFAS. This testing is required under the Safe Drinking Water Act. The six compounds included PFOS, PFOA, PFHxS, PFNA, PFHpA and PFBS. All of these compounds have been detected at some level in one or more MA water supplies[2].

USEPA has established identical toxicity values (reference doses or RfDs), of 0.00002 mg/kg/day for PFOS and PFOA (USEPA 2016 a,b). USEPA also issued Drinking Water Health Advisories (HA) of 0.07 ug/L (70 ppt) for PFOS and PFOA (USEPA, 2016a,b). USEPA states that these RfD values "apply to both short-term and chronic risk assessment scenarios, including exposure scenarios of weeks to months to PFOA and PFOS in drinking water during pregnancy and lactation". Based on USEPA's extensive assessments of PFOS and PFOA, USEPA decided it was appropriate and health protective to treat these compounds as having equal and additive toxicity and thus applies the HA concentration of 70 ppt to the sum of both compounds when

[2] The UCMR 3 testing included six PFAS. USEPA Method 537 includes an additional eight PFAS. The UCMR 3 and USEPA Method 537 compounds are listed in Table 1.

they occur together (USEPA, 2016 a,b)[3]. MassDEP is currently relying on the USEPA HA and RfD values to inform decisions regarding drinking water and disposal sites contaminated with PFOS and PFOA and is using the USEPA additivity approach.

USEPA has also published a provisional RfD value for PFBS of 0.02 mg/kg/day but has not issued a drinking water HA for this compound (USEPA, 2017b). The Minnesota Department of Health recently revised their chronic RfD for PFBS from 0.0014 mg/kg-day to 0.00043 mg/kg-day and health based drinking water guidance value from 7 ug/L (7,000 ppt) to 2 ug/L (2,000 ppt) (MN DH, 2017).

USEPA has not derived drinking water HAs or RfDs for the other PFAS compounds included under UCMR 3.

While most states are relying on the USEPA HA's for PFOS and PFOA, some, including CT, MN, NJ, AZ and CO have also addressed other UCMR 3 PFAS compounds as well. NJ, VT and MN have derived lower drinking water targets for PFOS and PFOA, largely due to differences in exposure parameters selected, choice of relative source contribution adjustments, and the application of uncertainty factors (Table 2).

- The CTDPH has applied the USEPA PFOS and PFOA drinking water HA to PFHxS, PFNA and PFHpA, and uses USEPA's additivity approach for all five compounds. The USEPA, and, by extension, CTDPH, used body weights and water intakes for a nursing woman, and a relative source contribution factor of 0.2, in their drinking water guidance derivations. The MNDH has published Drinking Water Guidance values for PFOS (27 ppt) and PFOA (35 ppt) and recommends the use of the PFOS value for PFHxS (MNDH, 2017).
- MNDH used exposure parameters for the nursing infant and a relative source contribution factor of 0.5 in deriving their drinking water guidance. Based on technical analyses by the NJ Drinking Water Quality Institute, the NJ DEP is in the process of promulgating an MCL of 13 ppt for PFNA and 14 ppt for PFOA.
- The NJ Drinking Water Quality Institute also recently recommended an MCL of 13 ppt for PFOS (Table 2). Regarding the potential for additive toxicity with other PFASs, the NJ Health Effects Subcommittee noted that the available information indicates that the target organs and modes of action may be generally similar for certain (longer chain) PFAS and may be additive. However, the potential for additive toxicity was not explicitly considered in development of the NJ Health-based MCL(s). NJ used default adult exposure parameters and a relative source contribution factor of 0.2 in deriving their

[3] USEPA states: "Adverse effects observed following exposures to PFOA and PFOS are the same or similar…..The RfDs for both PFOA and PFOS are based on similar developmental effects and are numerically identical; when these two chemicals co-occur at the same time and location in a drinking water source, a conservative and health-protective approach that USEPA recommends would be to compare the sum of the concentrations ([PFOA] + [PFOS]) to the HA (0.07 µg/L)" USEPA 2016 a,b.

drinking water values. NJ also applied an additional uncertainty factor to account for limitations in the toxicological database.

- In a November, 2016 Health Consultation report, the Arizona Department of Health Services (AZDHS), in consultation with ATSDR, stated that it considers the effects from all PFAS exposures to be additive (AZDHS, 2016).
- The Colorado Department of Public Health and Environment, in consultation with USEPA Region 8, is summing PFHpA, along with PFOA and PFOS, to compare with the health advisory level of 70 ppt due to the potential for PFHpA to have similar effects as PFOS and PFOA (CODPHE, 2017).

To address the gap in national USEPA drinking water and toxicity guidance regarding the other UCMR 3 PFAS, the MassDEP Drinking Water and Waste Site Cleanup program requested ORS support in evaluating drinking water supplies with detectable concentrations of multiple UCMR 3 PFAS. The following presents an evaluation of available data relating to the toxicity and biological persistence of the UCMR 3 PFAS compounds, with recommendations on how to address their potential risks.

Recommended Approach to Addressing Potential Risks Posed by the UCMR 3 PFAS

Environmental research and toxicology on PFAS initially focused on PFOS and PFOA the historically most common PFAS, resulting in an extensive data base regarding their toxicity, biological persistence and environmental fate. USEPA derived RfDs and drinking water HAs for PFOS and PFOA based on extensive analyses of the toxicity of these two compounds. MassDEP is relying on the USEPA RfD and HA values to inform drinking water and waste site cleanup decisions for PFOA and PFOS. ORS will follow the developing toxicological and exposure data for these and related compounds and may update the recommended values in the future.

In addition to PFOS and PFOA, USEPA has also stated that it is concerned about other longer-chain PFAS chemicals because they are persistent and cause reproductive, developmental, and systemic toxicity in laboratory tests, effects similar to those by PFOS and PFOA. USEPA considers long chain PFAS to include perfluoroalkyl carboxylic acids with eight or more carbons, which includes PFOA and PFNA, and perfluoroalkane sulfonates with six or more carbons, which includes PFOS and PFHxS. USEPA notes that, while persistent in the environment, shorter-chain PFAS, such as PFHxA and perfluorobutane sulfonic acid (PFBS), are generally less toxic and less bioaccumulative in wildlife and humans (USEPA, 2017a). PFHpA, with seven carbons, falls one carbon below the USEPA definition of a long chain PFAS compound. However, as noted above, in consultation with USEPA Region 8, the Colorado Department of Public Health and Environment (CDPHE) decided to sum PFHpA, along with PFOA and PFOS, to compare with the HA of 70 ppt due to the potential for PFHpA to have similar effects as PFOS and PFOA (CDPHE, 2017).

Overall, the available data on PFAS indicates that the toxicities of these compounds are related in part to their bioaccumulation and elimination rates (which determine biological half-lives). These attributes are related to their chemical structures, including carbon chain lengths (in particular the number of fluorinated carbons) and functional group type (Kudo et al., 2006; Mulkiewicz et al., 2007; Ohmori et al., 2003).

The following summarizes key available information on the UCMR 3 PFAS compounds PFNA, PFHxS, PFHpA and PFBS. Data from laboratory studies on animals, chemical structures, and biological half-lives are considered. Where available, values derived by other states are noted. Cross compound comparisons of toxicity, especially for PFHpA and PFHxS, are difficult due to limited published test data and variability in the toxicology data available. Differences in dosing, endpoints evaluated, reported responses, statistical analyses, test species and strains are all limiting factors in quantifying potency differences across compounds. Thus, no attempt has been made to develop precise toxic equivalency factors for these compounds. Instead, compounds have been evaluated based on weight-of-the-evidence concordance in the key attributes noted above. Where concordance exists, toxic equivalency has been applied.

In addition to *in vivo* studies, a number of *in vitro* cell culture studies of PFOS, PFOA and other PFAS have been completed. ORS has not focused on these studies due to uncertainties relating to mechanisms of action and how the *in vitro* potencies quantitatively relate to *in vivo* effects. However, it is important to note that additive and synergistic responses were reported in multi PFAS treated cell cultures, demonstrating that interactive effects between the tested compounds occurred (Hu et al. 2014).

Key information, including guidance values adopted by other states; chemical structures; serum half-lives; and toxicity data are summarized in Tables 2 to 4 and in Appendix A. These are discussed, by PFAS compound, below.

The recommendations below provide an interim approach to assessing potential risk posed by closely related compounds for which no USEPA toxicity or drinking water health advisory values are available. As information is evolving on PFAS toxicity, exposures and guidance values, ORS will continue to track developments on these compounds at USEPA and in the scientific literature and will update these recommendations as appropriate.

UCMR 3 PFAS Compounds

PFHxS: PFHxS has a chemical structure that is very similar to PFOS (Table 3). It shares the same sulfonic acid functional group and has six fluorinated carbons (compared to seven for PFOA and eight for PFOS), and falls within USEPA's definition of a long-chain PFAS of concern. Although limited, the available data indicates that PFHxS may be more persistent in the human body than PFOA and PFOS. PFOA, PFOS, and PFHxS

have reported geometric mean serum elimination half-lives in humans of 3.5, 4.8, and 7.3 years, respectively, although estimated half-lives on an individual basis overlap for all three compounds (Table 4). Limited *in vivo* toxicity data exist for PFHxS (Appendix A). A repeated dose reproductive/developmental study in rats demonstrated that PFHxS exposure resulted in decreases in body weight and cholesterol levels and an increase in prothrombin time at a lowest observed adverse effect level (LOAEL) of 0.3 mg/kg/day in males in the parental generation (Appendix A, Table A1) (Butenhoff et al., 2009a). This LOAEL is in the range of those identified for various endpoints by USEPA in its derivation of the PFOS and PFOA RfDs and HAs (USEPA 2016 a,b). The same laboratory group published a companion study on PFOS using the same strain of rats (Butenhoff et al., 2009b). Unfortunately, the dose regimes differed and results were not reported for the endpoints noted above, limiting the ability to directly compare PFOS and PFHxS responses. The authors did, however, report that no statistically significant results were observed in either study on maternal health and reproductive outcomes at the same dose of 0.3 mg/kg/day, the only overlapping data with respect to dose and reported endpoints (Butenhoff et al., 2009 a,b).

Two states are addressing PFHxS. The Connecticut Department of Health is applying the PFOS and PFOA Health Advisory to PFHxS (CTDPH, 2016) and the Minnesota Department of Health (MNDH, 2017) recommends that its state derived PFOS drinking water guidance value of 27 ppt be used as a surrogate[4] for PFHxS until more toxicological research is available, stating that PFHxS appears to be similar in toxicity to PFOS[5].

Taken together, the structural similarity and half-life data indicate that PFHxS is likely to exhibit toxicity similar to PFOS and PFOA. The available toxicity data, while limited, is consistent with this conclusion. Based on these similarities, ORS recommends applying the PFOA and PFOS RfD and HA to PFHxS. Consistent with USEPA's approach for PFOS and PFOA, ORS also recommends that PFHxS toxicity should be treated as additive with the other longer-chain UCMR 3 analytes.

PFNA: PFNA has a chemical structure that is very similar to PFOA (Table 3). It shares the same functional group (carboxylic acid) and has an eight fluorinated carbon chain (vs. seven for PFOA)[6], falling within USEPA's definition of a long-chain PFAS of concern. The serum half-life for PFNA in the mouse is longer than PFOA's. The geometric mean half-life estimates for human males and females are somewhat lower, but on an individual basis, overlap those for PFOS, PFOA and PFHxS.

[4] See http://www.health.state.mn.us/divs/eh/hazardous/topics/pfcshealth.html#levels
[5] In 2017 MN DH issued updated state Drinking Water Guidance Values for PFOS (27 ppt) and PFOA (35 ppt).
[6] PFOA has 7 fluorinated carbons with a total of 8 carbons, counting the carboxylic acid group.

The most comprehensive assessment of PFNA toxicity was undertaken by NJ in response to groundwater contamination attributable to an industrial facility. In 2015, after extensively reviewing the available toxicity data, the New Jersey Drinking Water Quality Institute (NJ DWQI, 2015) developed a health-based maximum contaminant level (MCL) for PFNA of 0.013 ug/L (13 ppt). This value is based on toxicity results observed in a developmental study conducted in laboratory animals. Key data considered by NJ are summarized in Appendix A. The New Jersey DWQI (2017a,b) has also proposed health based MCLs of 0.014 ug/L (14 ppt) for PFOA and 0.013 ug/L (13 ppt) for PFOS. While lower than USEPA values for PFOA and PFOS, the NJ values are all essentially identical.

Regarding the potential for additive toxicity between related PFAS, NJ states in their MCL technical support documents "that available information indicates that the target organs and modes of action may be generally similar for the compounds assessed (PFOA, PFNA and PFOS) and other related PFAS. Therefore, the toxicity of these compounds and other related PFAS may be additive." The authors of developmental toxicity studies on PFOA and PFNA conducted in Dr. Christopher Lau's laboratory in the Toxicity Assessment Division, U.S. Environmental Protection Agency, Research Triangle Park, NC, concluded that the "developmental toxicity of PFNA in mice is comparable to that of PFOS and PFOA, and these adverse effects are likely common to perfluoroalkyl acids that persist in the body" (Das et al., 2015)

Taken together, the structural similarity, half-life and toxicity data indicate that PFNA is likely to exhibit toxicity similar to PFOS and PFOA. Based on these similarities, ORS recommends applying the RfD and HA for PFOA and PFOS to PFNA. Consistent with USEPA's approach for PFOS and PFOA, PFNA toxicity should be treated as additive with the other longer-chain UCMR 3 analytes.

PFHpA: PFHpA has a chemical structure very similar to PFOA (Table 3). It shares the same functional group but has a total of 7 carbons, with 1 fewer fluorinated carbons, compared to PFOA. Very little data were identified for this compound. No biological half-life determinations or estimates were identified for PFHpA. Based on structural similarity, its serum half-life is likely to fall between the estimates for PFOA (human serum half-life of 3.5 years (Table 4) and PFHxA (human serum half-life of approximately one month (Nilsson et al., 2010)). No animal toxicity data were identified for PFHpA. A limited epidemiological study showed higher asthma incidence in children with higher serum levels of PFHpA compared to children that have lower serum levels of the compound (Dong et al., 2013) but this study is insufficient to derive quantitative toxicity values.

Two state health departments have decided to assess PFHpA the same as PFOA and PFOS. The Connecticut Department of Public Health is applying the PFOS and PFOA Health Advisory to PFHpA (CTDPH, 2017), as is the Colorado Department of Public Health and Environment (CODPHE). CODPHE, in consultation with EPA Region 8, has added in PFHpA along with PFOA and PFOS when comparing drinking water levels to the 70 ppt PFOS and PFOA health advisory level due to the potential for PFHpA to have similar effects (CODPHE, 2017).

In light of the structural similarity to PFOA, the lack of serum half-life and *in vivo* toxicity data, ORS recommends that a prudent approach be taken for this compound until sufficient toxicological and biological half-life data in animals and humans become available to better assess this compound. Towards this end ORS recommends that PFHpA be assessed similarly to PFOS, PFOA, PFHxS and PFNA. This approach is consistent with the actions by CTDPH and CODPHE.

PFBS: ORS is reviewing recent data and water guidance values for this compound. At this time ORS does not recommend treating PFBS as being equipotent to the other long chain compounds addressed in this document. ORS recommends that the recent MN drinking water guidance value (2,000 ppt) and RfD (0.00043 mg/kg-day) is recommended pending further assessment by ORS.

Conclusions

Four of the six PFAS tested for under UCMR 3 do not have USEPA drinking water guidance values and three lack toxicity values (RfDs). The lack of USEPA drinking water guidance for PFHxS, PFHpA, and PFNA complicates decision making in response to detections of these compounds in MA drinking water and ground water. To provide guidance for these situations, ORS recommends that these three compounds be treated as being toxicologically equivalent to PFOS and PFOA and that the USEPA HA and RfD for PFOA and PFOS be used for these compounds. Following USEPA's approach for PFOS and PFOA, ORS also recommends that additivity be applied to all five of these compounds when assessing situations where more than one is present. These recommendations are based on the similarities in chemical structure, available *in vivo* toxicity and biological half-life data. Taken together, the data indicate that PFHxS, PFHpA, and PFNA are likely to exhibit toxicities similar to PFOS and PFOA. This approach is consistent with that adopted by the CTDPH in deriving the CT Drinking Water Action levels for PFAS (CTDPH, 2016) as well as statements and actions taken by the AZDHS in consultation with ATSDR; CODPHE in consultation with USEPA Region 8; and USEPA (USEPA, 2017).

For PFBS, the MN Department of Health recently published a revised drinking water guidance value of 2,000 ppt, based on an RfD of 0.00043 mg/kg/day (MNDH, 2017). The USEPA Provisional Peer Reviewed Toxicity Value (PPRTV) program issued a provisional RfD of 0.02 mg/kg/day for PFBS in 2014 (USEPA, 2017b). At this time ORS recommends that the MN values, which are more recent and more health protective, be used for risk screening purposes pending further review of the MN and USEPA RfD values and their supporting technical documentation by ORS.

No RfD or drinking water guidance values were identified for other PFAS addressed under USEPA Method 537 and ORS has not derived guidance values applicable to these compounds at this time.

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Tables and Figures

Table 1. UCMR 3 and USEPA Method 537 PFAS

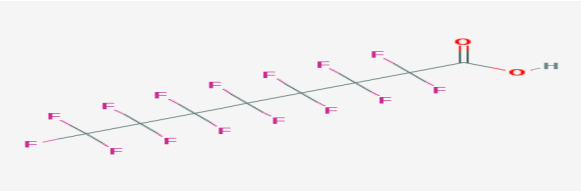
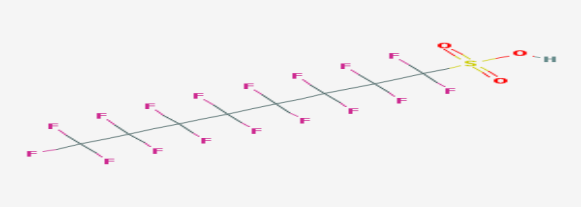
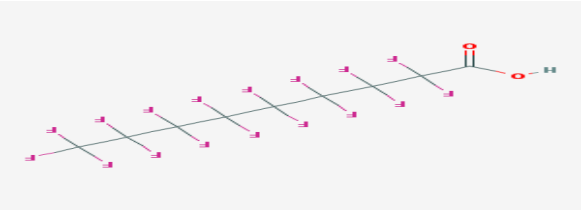
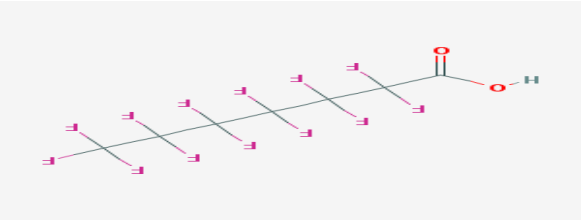
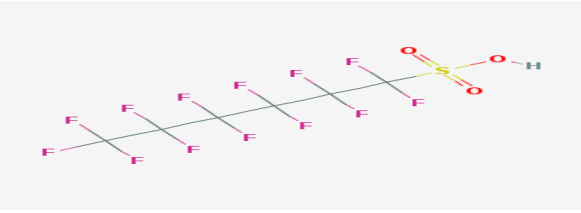
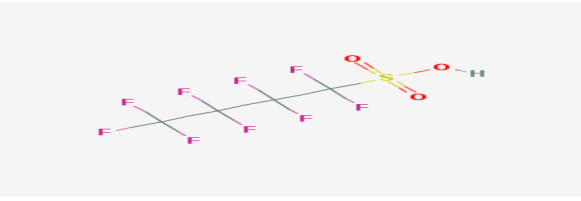
PFAS (CAS)	Abbrev.	UCMR 3 Analyte	EPA 537 Analyte
Perfluorobutanesulfonic acid (375-73-5)	PFBS	x	x
Perfluorohexanoic acid (307-24-4)	PFHxA		x
Perfluorohexanesulfonic acid (355-46-4)	PFHxS	x	x
Perfluoroheptanoic acid (375-85-9)	PFHpA	x	x
Perfluorooctanoic acid (335-67-1)	PFOA	x	x
Perfluorooctanesulfonic acid (1763-23-1)	PFOS	x	x
N-ethyl perfluorooctane-sulfonamidoacetic acid	NEtFOSAA		x
N-methyl perfluorooctane-sulfonamidoacetic acid	NMeFOSAA		x
Perfluorononanoic acid (375-95-1)	PFNA	x	x
Perfluorodecanoic acid (335-76-2)	PFDA		x
Perfluoroundecanoic acid (2058-94-8)	PFUnA		x
Perfluorododecanoic acid (307-55-1)	PFDoA		x
Perfluorotridecanoic acid (72629-94-8)	PFTrDA		x
Perfluorotetradecanoic acid (376-06-7)	PFTA		x

Table 2. State Drinking Water Values for UCMR 3 PFAS Including Values for Compounds Other Than PFOS and PFOA (parts per trillion; ppt)

	PFOS	PFOA	PFNA	PFHxS	PFHpA	PFBS
USEPA[1] Health Advisories	70 Sum of both					
NJ[2] DEP/Drinking Water Institute Proposed MCLs	13	14	13			
CT[3] DPH Drinking Water Action Levels	70 Sum of all five					
MN[4] DH Drinking Water Guidelines	27	35		27		2,000
VT[5] DH Drinking water and Groundwater standards	20 Sum of both					

[1] USEPA 2016 a,b; [2] NJ DEP and DWQI 2015, 2017; [3] CT DPH, 2016; [4] MNDH 2017; VT DPH, 2016. Most states are using the USEPA HAs for PFOS and PFOA, individually and summed. Some additional states have established groundwater screening values (e.g. Texas CEQ has issued TIER 1 groundwater values for PFOS (560 ppt); PFOA (290 ppt); PFBS (34,000 ppt); PFHxS (93 ppt); PFHpA (560 ppt); PFNA (290 ppt).

Table 3. UCMR 3 PFAS: Comparative Structures, Toxicity and Half-life Data

UCMR 3 PFAS	Chemical Structure	*In vivo* toxicity*	Half-life In body
Perfluorooctanoic acid **335-67-1** **Carbons = 8** **Fluorinated Carbons = 7**	PFOA 	1	3.5 years
Perfluorooctanesulfonic acid **1763-23-1** **Carbons = 8** **Fluorinated Carbons = 8**	PFOS 	1	4.8 years
Perfluorononanoic acid **375-95-1** **Carbons = 9** **Fluorinated Carbons = 8**	PFNA 	1	3.2 years
Perfluoroheptanoic acid **375-85-9** **Carbons = 7** **Fluorinated Carbons = 6**	PFHpA 	NA	NA
Perfluorohexanesulfonic acid **355-46-4** **Carbons = 6** **Fluorinated Carbons = 6**	PFHxS 	1	7.3 years
Perfluorobutanesulfonic acid **375-73-5** **Carbons = 4** **Fluorinated carbons = 4**	PFBS 	Significant-ly lower than those above	0.1 year

NA = not available; * relative to PFOA or PFOS; see Table 4

Table 4. Relative Toxicity Values and Serum Half-lives for UCMR3 PFAS and PFHxA

Chemicals	PFOS	PFOA	PFNA	PFHxS	PFHpA	PFBS
Carbon Chain	C8	C8	C9	C6	C7	C4
In Vivo Toxicity Relative to PFOA	1[1]	1[1]	1[2]	1.3[3]	No comparative data	0.02[4]
Half-life (Human) Years, geometric mean (range)	4.8 years (2.4 – 21.7) N=26[5]	3.5 years (1.5 – 9.1) N=26[5]	3.2 years (M and F > 50 yrs.) (0.34 - 20) N=50[6]	7.3 years (2.2 - 27) N=26[5]	No data	26 days[7]
Half-life (Mouse) Days	36 - 43 (M) 30 - 38 (F)[8]	17 (F)[9] 19 (M)	26[10] - 68 (F)[11] 34[10] - 69 (M)[11]	25 – 27[12]	No Data	No data

[1]Based on US EPA RfD values for PFOA and PFOS
[2]Based on comparison of New Jersey proposed MCL values of 0.014 ug/L for PFOA and 0.013 ug/L for PFNA
[3]Based on reproductive/developmental LOAELS of PFOS and PFHxS
[4]Based on MNDHDW values
[5]Olsen et al. (2007); based on serum concentrations over 5 years
[6]NJDWQI (2015); modeled based on urinary clearance
[7]Olsen et al. (2009)
[8]Chang et al. (2012)
[9]Lau et al. (2007); F= female; M= male
[10]Tatum-Gibbs et al. (2011)
[11]Ohmori et al. (2003)
[12]Sundström et al. (2012); F= female; M= male

Appendix A. In Vivo Toxicity and Epidemiology Data

Table A1. Summary of Toxicity and Epidemiology Studies on Select PFAS

PFAS	Carbon chain length	Dose	Dose duration	Study species/cell type	Endpoint	LOAEL/NOAEL	Remarks
PFHxS	C6	0, 0.3, 1, 3 or 10 mg/kg/d	During cohabitation, gestation and lactation through to study day 42 (males) or PND 21 (females).	Rats	P1males-reduced serum cholesterol (all doses), decreased prothrombin time (0.3, 3 and 10 mg/kg/d), increased liver-to-body and liver-to-brain weight ratio, centrilobular hypertrophy, hyperplasia of thyroid follicular cells, decreased haematocrit (3 and 10 mg/kg/d). No effects in F1 pups reported	LOAEL = 0.3 mg/kg/d (decreased serum cholesterol and prothrombin time)	Butenhoff et al., 2009
		30 mg/kg/d	16 weeks	Mice	Altered serum lipid profile and transport proteins	30 mg/kg/d	Bijland et al., 2011.
		Environmental exposure	2 ng/ml (serum level)	Maternal exposure	Decreased birth weight	NA	Maisonet et al., 2012
		Environmental exposure	1 µg/L increase in PFHxS (serum level)	Children	Increased ADHD	NA	Hoffman et al., 2010
		Environmental exposure	highest quartile (10.1-276.4 ng/mL) (serum level)	Children	Prevalence of ADHD	NA	Stein and Savitz, 2011
		Environmental exposure	2.5 ng/mL (median	Maternal	Increased asthma incidence	NA	Dong et al., 2013

			serum Level)				
		Environmental exposure	2.86 nmol/L	Children	Increased risk of maternal hypothyroxinemia	NA	Chan et al., 2011
		Environmental exposure		Children	A 2-fold increase in PFHxS concentrations at age 5 years was associated with decreased antibody response at age 7	NA	Grandjean et al., 2012
PFNA	C9	0, 0.2, 1 or 5 mg/kg/d	14 days	Rats	Absolute and relative liver weight increase	LOAEL = 1 mg/kg/d	Fang et al., 2012
		0, 1, 3 or 5 mg/kg	14 days	Mice	Altered immune responses	LOAEL = 1 mg/kg/d	Fang et al., 2008
		0, 1, 3 or 5 mg/kg/d	14 days	Rats	Thymus weight was increased at 1 mg/kg/d and decreased at 3 and 5 mg/kg/d	LOAEL = 1 mg/kg/d	Fang et al., 2009
		0, 1, 3 or 5 mg/kg	14 days	Rats	Change in serum testosterone	LOAEL = 1 mg/kg/d (significantly increased); unchanged at 3 mg/k/d and decreased at 5 mg/kg/d. Other effects included changes in testicular ultrastructure at 3 mg/kg/d and histology at 3 and 5 mg/kg/d	Fang et al., 2009, 2010
		0, 0.83, 1.1, 1.5 or 2.0 mg/kg/d	GD 1-18	Mice	Increased relative liver weight in dams and pups	LOAEL =1.1 mg/kg/d (dams) 0.83 mg/kg/d (pups)	Wolf et al., 2010
		Environmental exposure levels		Human	Reproductive effects (endometriosis; correlation with age at menopause	Endometriosis (n = 495) were reported to be more likely in women with serum PFNA concentrations in the highest tertile (0.8405-4.0996 ng/mL) relative to women without endometriosis	Taylor et al., 2013