PER- and POLYFLUOROALKYL SUBSTANCES (PFAS), including the US EPA UCMR3 analytes[1]:	CASRN:	June 8, 2018
Perfluorooctane Sulfonic Acid (PFOS)	1763-23-1	
Perfluorooctanoic Acid (PFOA)	335-67-1	
Perfluorohexane Sulfonic Acid (PFHxS)	355-46-4	
Perfluorononanoic Acid (PFNA)	375-95-1	
Perfluorohepatanoic Acid (PFHpA)	375-85-9	

[1]The listed compounds and associated CAS registry numbers (CASRN) are for the acid forms of these PFAS compounds. The information presented in this document and the ORSG are also applicable to the respective anionic forms of these compounds. These anions may form salts with any of a number of cations resulting in a variety of possible chemical species, each having a unique CASRN.

Current Massachusetts Regulatory Limit: ORSG = 0.00007 mg/L. When all or some of these compounds occur together in drinking water, the detected concentrations for these PFAS should be summed and compared to 0.00007 mg/L. This value is also applicable to the individual compounds.

Federal Regulatory Limit: The US EPA has not published an MCL for any of these PFAS.

Basis for Criteria:

The ORSG is based on information used by the US EPA to develop Health Advisories (HAs) for PFOS and PFOA (detailed below) as well as on information on the molecular structure and available toxicological data for PFHxS, PFNA and PFHpA.

The US EPA Reference Dose (RfD) for PFOS is based on effects (e.g., decreased pup body weight) on the developing fetus resulting from exposures that occur during gestation and lactation. This RfD was developed based on a human-equivalent dose (HED) of 0.00051 mg/kg/day that corresponds to a no-observed-adverse-effect level (NOAEL) for decreased pup body weight in rats, where dams were exposed by gavage 6 weeks prior to mating, during mating and through gestation and lactation (Luebker *et al.*(2005a,b). A total uncertainty factor (UF) of 30 (10 to account for sensitive individuals in the human population and 3 to account for differences between animals and humans in the effects of the chemical) was applied to the HED NOAEL to derive an RfD of 0.00002 mg/kg/day.

The US EPA RfD for PFOA is based on effects on the developing fetus (e.g., reduced ossification in pups and accelerated puberty in male pups). The RfD was derived from a HED of 0.0053 mg/kg/day that corresponds to a lowest-observed-adverse-effect level (LOAEL) for developmental effects in mice where dams were exposed for 17 days during gestation and lactation, in a study by Lau *et al.* (2006). A total UF of 300 (10 to account for sensitive individuals in the human population, 3 to account for differences between animals and humans in the effects of the chemical, and 10 to account for use of LOAEL instead of a NOAEL) was applied to the HED LOAEL to derive an RfD of 0.00002 mg/kg/day.

The PFOA and PFOS HAs were both derived using the water ingestion rate and body weight

for a lactating woman (e.g., 54 mL/kg-day representing the consumers-only estimate of combined direct and indirect community water ingestion at the 90th percentile for lactating women) and incorporate a relative source contribution factor of 0.2. Basing exposure on the lactating woman is also protective for the pregnant women.

The US EPA HAs for PFOA and PFOS were both calculated to be 0.00007 mg/L. Because the adverse effects following exposure to both PFOA and PFOS are similar and include effects on the developing fetus, as well as effects on the liver, immune system and changes in organ and body weights, they have similar chemical structures and their US EPA HAs are both 0.00007 mg/L, the US EPA recommends that the concentrations of both compounds be summed and compared to 0.00007 mg/L.

The available data for PFHxS, PFNA and PFHpA demonstrate that these PFAS compounds are very similar in molecular structure to PFOS and PFOA, have long biological half-lives like PFOS and PFOA and elicit similar types of effects at similar dose ranges as PFOA and PFOS. Based on the analysis presented in the, "*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*" (MassDEP 2018), which was reviewed and endorsed by the MassDEP Health Effects Advisory Committee, the ORSG extends the additivity approach used by the US EPA for PFOS and PFOA to PFHxS, PFNA and PFHpA. When these five compounds occur alone, together, or in any combination, the sum of their concentrations should be compared to 0.00007 mg/L.

Cancer Assessment:

Using the US EPA *Guidelines for Carcinogen Risk Assessment* (US EPA 2005), there is "suggestive evidence of carcinogenic potential" for PFOA (US EPA, 2016a). This designation is based upon epidemiological evidence for kidney and testicular tumors in highly exposed members of the general population as well as two chronic animal bioassays with PFOA that produced liver, kidney and pancreatic tumors in rats. The US EPA developed an oral cancer potency factor (CPF) based upon the incidence of testicular tumors, assuming a default adult body weight of 80 kg and drinking water rate of 2.5 liters/day, but determined that a guideline derived based on the developmental endpoint used in the derivation of the PFOA HA is protective for the cancer endpoint.

There is also "suggestive evidence of carcinogenic potential" for PFOS (US EPA 2005, 2016b). This designation is based upon the results of a chronic oral toxicity and carcinogenicity study of PFOS in rats. In this study, liver, thyroid and mammary fibroadenomas were identified, though only the liver tumors significantly increased in experimental animals over controls.

Though data on carcinogenicity is not available for PFHxS, PFNA and PFHpA, given the similarities in structure and toxicity of these PFAS to PFOA and PFOS, the potential for the carcinogenicity of these other PFAS cannot be ruled out.

Class: Organic

Analytical Information:

Lowest Concentration Minimum Reporting Level (LCMRL):

Table 1. LCMRL[1] of PFAS

Analyte	LCMRL (ng/L)
PFOA	5.1
PFOS	6.5
PFHxS	8.0
PFNA	5.5
PFHpA	3.8

[1] The single laboratory LCMRL is the lowest true concentration for which the future recovery is predicted to fall, with high confidence (99%), between 50 and 150% recovery.

Analytical Methods: US EPA Method 537 (US EPA, 2009)

LCMRLs and analytical methods may have been updated since this guidance value was last revised. Updated analytical methods for drinking water and their associated LCMRLs may be found at https://www.epa.gov/measurements-modeling/collection-methods#2

Other Regulatory Data:

Any HAs, RfDs, cancer assessments or CPFs referenced in this document pertain to the derivation of the current guidance value. Updated information may be obtained from the following sources:

HAs – The US EPA provides guidance for shorter-term exposures for chemicals based on their non-cancer effects. Current HAs may be more current than those used to derive MCLs and may be found at https://www.epa.gov/sites/production/files/2018-03/documents/dwtable2018.pdf.

RfDs, cancer assessments and CPFs – For specific information pertaining to derivation of drinking water criteria, consult the Federal Register notice that announces the availability of the most current guidance for that chemical. In addition, information on other current RfDs and CPFs as well as cancer assessments for specific chemicals may be found in the US EPA Integrated Risk Information System (IRIS) at https://www.epa.gov/iris https://www.epa.gov/iris. Please note that the information in IRIS may differ from that used in the derivation process as published in the Federal Register notice.

References:

Lau, C., J.R. Thibodeaux, R.G. Hanson, M.G. Narotsky, J.M. Rogers, A.B. Lindstrom, and M.J. Strynar (2006). Effects of perfluorooctanoic acid exposure during pregnancy in the mouse. *Toxicological Sciences* 90:510–518.

Luebker, D.J., R.G. York, K.J. Hansen, J.A. Moore, and J.L. Butenhoff (2005a). Neonatal

mortality from in utero exposure to perfluorooctanesulfonate (PFOS) in Sprague-Dawley rats: Dose-response and biochemical and pharmacokinetic parameters. *Toxicology* 215:149–169.

Luebker, D.J., M.T. Case, R.G. York, J.A. Moore, K.J. Hansen, and J.L. Butenhoff (2005b). Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats. *Toxicology* 215:126–148.

MassDEP (2018). Massachusetts Department of Environmental Protection (MassDEP). Final Recommendations for Interim Toxicity and Drinking Water Guidance Values for Perfluorinated Alkyl Substances Included in the Unregulated Chemical Monitoring Rule 3. Office of Research and Standards.

US EPA (2005). United States Environmental Protection Agency. Guidelines for Carcinogen Risk Assessment. Risk Assessment Forum. EPA/630/P-03/001B.

US EPA (2009). United States Environmental Protection Agency. Method 537, Determination of Selected Perfluorinated Alkyl Acids in Drinking Water By Solid Phase Extraction and Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS) Version 1. US EPA, Office of Research and Development, National Exposure Research Laboratory. EPA/600/R-08/092.

US EPA. (2016a). United States Environmental Protection Agency. Drinking Water Health Advisory for Perfluorooctaanoic Acid (PFOA) and Health Effects Support Document for Perfluorooctaanoic Acid (PFOA). US EPA Office of Water. EPA 822-R-16-005

US EPA. (2016b). United States Environmental Protection Agency. Drinking Water Health Advisory for Perfluorooctane Sulfonate (PFOS) and Health Effects Support Document for Perfluorooctane Sulfonate (PFOS). US EPA Office of Water. EPA 822-R-16-004.