MEMORANDUM

TO: Emily Boedecker, Commissioner

FROM: Mark A. Levine MD, Commissioner

DATE: July 10, 2018

SUBJECT: Drinking Water Health Advisory for Five PFAS (per- and polyfluorinated alkyl substances)

Summary
The Department of Health (Department) has derived a Drinking Water Health Advisory (Health Advisory) of 20 parts per trillion (ppt) applicable to the sum of PFOA (perfluorooctanoic acid), PFOS (perfluorooctane sulfonic acid), PFHxS (perfluorohexane sulfonic acid), PFHpA (perfluoroheptanoic acid) and PFNA (perfluorononanoic acid). These chemicals belong to the PFAS family (per- and polyfluorinated alkyl substances). According to the Centers for Disease Control and Prevention, “some studies in people show that certain PFAS may affect growth, learning and behavior of infants and older children; lower a woman’s chance of getting pregnant; interfere with the body’s natural hormones, increase cholesterol levels, affect the immune system, and increase the risk of cancer.” Until 2018, the PFAS species predominantly found in drinking water in Vermont was PFOA. Recently, other PFAS including PFHxS and PFHpA were found in drinking water in Vermont at concentrations that warrant review. This Health Advisory updates the Drinking Water Health Advisory for the sum of PFOA and PFOS that was issued on June 22, 2016.

During the evaluation of PFHxS, PFHpA and PFNA, the Department looked to federal and other state partners. The Department consulted with colleagues at U.S. Environmental Protection Agency (US EPA) and the Agency of Toxic Substances and Disease Registry (ATSDR). The Department reviewed work conducted by the Connecticut Department of Health, as Connecticut issued a Drinking Water Action Level of 70 ppt for the sum of the five PFAS. The Department reviewed Massachusetts Department of Environmental Protection’s Drinking Water Guidance Values for the sum of five PFAS, equal to 70 ppt. Colorado issued a Health Advisory of 70 ppt applicable to the sum of PFOA, PFOS and PFHpA. Minnesota Department of Health recommends the drinking water level for PFOS be used as a surrogate for PFHxS.

There is no federal maximum contaminant level (MCL) for PFOA, PFOS, PFHxS, PFHpA, PFNA or any other PFAS. No finalized toxicity values exist for PFHxS, PFHpA and PFNA from authoritative sources (such as US EPA and ATSDR). The Department has not derived a noncancer toxicity value for PFHxS, PFHpA or PFNA. These five PFAS meet the criteria for grouping chemicals under one Health Advisory level according to the Department’s chemical grouping process for the following reasons:

1. PFOA, PFOS, PFHxS, PFHpA and PFNA are currently being investigated in Vermont and have been found in drinking water.
2. PFHxS, PFHpA and PFNA are members of the PFAS family along with PFOA and PFOS and are considered sufficiently similar to PFOA and PFOS.
PFHxS, PFHpA, PFNA, PFOA and PFOS are often found together. PFHxS, PFHpA and PFNA elicit similar health effects as PFOA and PFOS.

PFOA, PFOS, PFHxS, PFHpA and PFNA are all long-chain members of the PFAS family. PFOA and PFOS are man-made fluorinated chemicals that contain eight carbons. PFHxS, PFHpA, and PFNA contain six, seven and nine carbons and are structurally similar to PFOA and PFOS. These PFAS have similar and long biological half-lives. PFAS chemicals are often found together in the environment, and some PFAS chemicals degrade to other PFAS chemicals.

ATSDR published a draft Toxicological Profile for PFAS on June 20, 2018. This draft Toxicological Profile provides intermediate oral minimal risk levels for PFOA and PFOS that are roughly an order of magnitude more stringent than the chronic oral reference dose provided by US EPA Office of Water in 2016. The draft Toxicological Profile also provides intermediate oral minimal risk levels for PFHxS and PFNA, which are equal to or lower than the 2016 US EPA Office of Water chronic oral reference dose for PFOA and PFOS. The intermediate oral minimal risk levels are provided as draft, and the ATSDR draft Toxicological Profile for PFAS is subject to revision in response to public comments and when additional data become available. The Department has not used the intermediate oral minimal risk levels to derive Health Advisories for individual PFAS. The draft Toxicological Profile supplements the Department’s understanding of PFAS, and supports Vermont’s approach of summing the five PFAS.

Supporting Information
PFOA and PFOS are the most well-studied of the PFAS. The US EPA Office of Water has provided toxicity values for PFOA and PFOS, and advice to apply a single guidance value to the sum of them. PFOA and PFOS target many organ systems, including but not limited to the liver, endocrine and the immune system. The National Toxicology Program, a Division of the National Institute of Environmental Health Sciences, concludes that PFOA and PFOS are presumed to be immune hazards to humans, based on a high level of evidence in animals that PFOA and PFOS suppress the antibody response. Exposure to PFOA and PFOS is also associated with developmental toxicity. The offspring of mice exposed to PFOA showed neurodevelopmental effects, skeletal alterations, and reduced ossification and accelerated puberty in males. The offspring of rats exposed to PFOS showed delayed eye opening and decreased pup weight. Toxicity information for PFHxS, PFHpA and PFNA is summarized below.

PFHxS- A single dose of PFHxS in mice at postnatal day 10 resulted in altered spontaneous behavior and habituation at two and four months. Increased thyroid follicular cell damage was observed in male rats given PFHxS for 42 days. In vitro studies show PFHxS has the potential to bind thyroid transporter protein.

PFHpA- Data from two in vitro studies suggest PFHpA has the potential to exhibit developmental toxicity and bind PPARα. Colorado Department of Public Health and Environment issued a Health Advisory applicable to the sum of PFOA, PFOS and PFHpA, as they concluded PFHpA may have similar effects as PFOA and PFOS.

PFNA- Toxicity studies indicate that exposure to PFNA may have similar impacts as exposure to PFOA and PFOS including but not limited to; immunotoxicity, developmental toxicity, and liver toxicity. Decreased thymus and/or spleen weight, and changes in immune cell ratios were observed in rats and mice after PFNA exposure. Decreased pup weight and delayed development was observed in mice exposed...
gestationally to PFNA\textsuperscript{26}. The New Jersey Drinking Water Quality Institute developed an MCL for PFNA of 13 ppt, based on increased liver weight in mice\textsuperscript{27}.

**Derivation of the Health Advisory**

The Health Advisory of 20 ppt for the combination of PFOA, PFOS, PFHxS, PFHpA and PFNA is based on a non-cancer endpoint and derived\textsuperscript{6} using the oral reference dose of 0.00002 mg/kgBW-d provided in US EPA’s 2016 Health Effects Support Documents for PFOA\textsuperscript{11} and PFOS\textsuperscript{12}. The Department applied the oral reference dose for PFOA and PFOS to the sum of PFOA, PFOS, PFHxS, PFHpA, and PFNA. The Department also calculated a candidate drinking water advisory for consideration based on the cancer endpoint using the information provided in EPA’s 2016 Health Effects Support Documents for PFOA\textsuperscript{11} and PFOS\textsuperscript{12} and determined that derivation of the Health Advisory based on the noncancer endpoint is more protective.

The Health Advisory for the combination of PFOA, PFOS, PFHxS, PFHpA and PFNA is based on direct exposure via ingestion of drinking water only. As is standard practice\textsuperscript{28,29}, a relative source contribution is incorporated in the development of the advisory value to account for potential exposure to these chemicals from other sources.

Details of the derivation of the Drinking Water Health Advisory of 20 ppt are found below.

**Drinking Water Health Advisory - Noncancer**

1. The general equation used to derive a noncancer-based Drinking Water Health Advisory:

\[
\text{DWHA} = \text{HQ} \times \text{RfD}_o \times (1/\text{BW}_{\text{IR}}) \times \text{CF} \times \text{RSC}
\]

\(\text{DWHA} = \text{Drinking Water Health Advisory}\)

HQ = Hazard Quotient

RfD\(_o\) = chronic oral reference dose

\(\text{BW}_{\text{IR}}\) = Body Weight adjusted Water Intake Rate

CF = Units Conversion Factor

RSC = Relative Source Contribution

2. Derivation of the Health Advisory for the combination of PFOA, PFOS, PFHxS, PFHpA and PFNA

\[
\text{DWHA} = (1)(2 \times 10^{-5} \ \text{mg/kg BW-day})(1/0.175 \ L/kg BW-day)(1000 \ µg/mg)(0.2)
\]

\[
= 0.02285 \ µg/L \ (ppb)
\]

\[
= 0.02285 \ µg/L \ (ppb) \times 1000 \ ng/µg = 22.9 \ ng/L \ (ppt) \approx 20 \ ppt
\]

**Exposure Assumptions, Parameter Values and Descriptions**

HQ = 1

Target Hazard Quotient employed in the development of Department of Health Drinking Water Guidance Values

\(\text{RfD}_o = 2 \times 10^{-5} \ \text{mg/kgBW-d}\)

Oral reference dose provided in EPA’s 2016 Health Effects Support Documents for PFOA\textsuperscript{11} and PFOS\textsuperscript{12}
BW_{\text{IR}} = 0.175 \text{ L/kgBW-d}

The 2016 US EPA Drinking Water Health Advisories for PFOA\textsuperscript{10} and PFOS\textsuperscript{30} state that “the developing fetus and newborn are particularly sensitive to PFOA- and PFOS-induced toxicity.” US EPA has recommended that fine age groupings be used in the assessment of potential exposure to children\textsuperscript{31}. A series of ten ranges between birth and 21 years of age is recommended for consideration as appropriate. The 95\textsuperscript{th} percentile Body Weight Adjusted Water Intake Rate for the first year of life based on combined direct and indirect water intake from community water supplies for consumers only is 0.175 L/kgBW-d\textsuperscript{32,33}.

CF = 1000 \mu g/mg

Unit conversion from milligrams to micrograms

RSC = 0.2 (20%)

Consistent with US EPA guidance\textsuperscript{28,29}, an RSC is incorporated in the development of Health Advisories that are based upon a threshold type, primarily noncancerogenenic, health effect. The RSC represents the portion of an individual’s total daily exposure to a specific chemical that is attributed to or allocated to drinking water. An RSC of 20% is incorporated to account for exposure to PFOA, PFOS, PFHxS, PFHpA and PFNA from other sources. This follows EPA’s recommendation to use an RSC of 20% when quantitative data on other sources of exposure are not available. The 2016 US EPA PFOA Health Advisory states “In cases where environmental or exposure data are lacking, the Exposure Decision Tree approach results in a recommended RSC of 20%. This 20% RSC value may be replaced where sufficient data are available to develop a scientifically defensible alternative value.”\textsuperscript{10}

References


13. Office of Health Assessment and Translation, Division of the National Toxicology Program, National Institute of Environmental Health Sciences, National Institutes of Health. U.S. Department of Health and Human Services, 2016. NTP monograph of immunotoxicity associated with exposure to perfluorooctanoic acid (PFOA) or perfluorooctane sulfonate (PFOS).


25. Rockwell, CE., et. al., 2017. Persistent alterations in immune cell populations and function from a single dose of perfluorononanoic acid (PFNA) in C57Bl/6 mice. Food and Chemical Toxicology 100, 24e33.


