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HEALTH ADVISORY FOR PERFLUOROOCTANOIC ACID (PFOA) CHEMICAL ABSTRACT SERVICES REGISTRY NUMBER (CASRN) 335-67-1

Prepared by
Office of Toxicity Assessment
Illinois Environmental Protection Agency
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REASON FOR ACTION

As a result of a Per- and Polyfluoroalkyl Substances (PFAS) sampling initiative of community water supplies (CWS), undertaken by the Illinois Environmental Protection Agency (Illinois EPA), Perfluorooctanoic Acid (PFOA) has been confirmed in a well at a CWS. In accordance with 35 Illinois Administrative Code 620.605(a), the Illinois EPA is issuing a health advisory for Perfluorooctanoic Acid. Section 620.605(a) directs the Illinois EPA to issue a health advisory for a chemical substance if all of the following conditions are met:

1) A community water supply well is sampled, and a substance is detected and confirmed by resampling;

2) There is no standard under Section 620.410 for such chemical substance; and

3) The chemical substance is toxic or harmful to human health according to the procedures of Appendix A, B, or C.

The health advisory guidance level for PFOA is 0.000002 milligrams per liter (mg/L), or 2 nanograms per liter (ng/L) or parts per trillion (ppt).

The health advisory will be published in the Environmental Register (publication of the Illinois Pollution Control Board) and placed at the website: https://pcb.illinois.gov/Resources/News

The health advisory will also be placed on Illinois EPA's website at: https://www2.illinois.gov/epa/topics/water-quality/pfas/Pages/pfas-healthadvisory.aspx

PURPOSE OF A HEALTH ADVISORY

In accordance with 35 Ill. Adm. Code 620.601, the purpose of a health advisory is to provide guidance levels that, in the absence of an applicable groundwater quality standard under Section 620.410, must be considered by Illinois EPA in: 1) establishing groundwater cleanup or action levels whenever there is a release or substantial threat of a release of a hazardous substance, pesticide, or another contaminant that represents a significant hazard to public health or the environment; 2) determining whether a community water supply is taking its raw water from a site or source consistent with regulatory requirements; and 3) developing Illinois Pollution Control Board (Board) rulemaking proposals for new or revised numerical standards.

Health advisories serve as informal technical guidance, intended to provide information about contaminant exposures and potential public health impacts. The guidance level represents concentrations in drinking water at which no adverse health effects are expected to occur. Guidance levels are not enforceable or intended to be used as drinking water standards, also known as maximum contaminant levels (MCLs).

HEALTH ADVISORY GUIDANCE LEVEL FOR PFOA

Through issuance of this Health Advisory, Illinois EPA is providing public notice of its guidance level for PFOA in drinking water. PFOA meets the definition of a carcinogen pursuant to the relevant provisions of the Board's Part 620 regulations. In 2017, the World Health Organization's International Agency for Research on Cancer (IARC) classified PFOA as a "2B" carcinogen (possibly carcinogenic to humans).

For carcinogenic health effects, the guidance level is 0.000002 milligrams per liter (mg/L), or 2 nanograms per liter (ng/L) or parts per trillion (ppt). For non-carcinogenic health effects, the guidance level is 0.000021 milligrams per liter (mg/L), or 21 nanograms per liter (ng/L) or parts per trillion (ppt). Illinois EPA designated the guidance level for carcinogenic effects as the final guidance level for PFOA, as it is protective for both cancer and non-cancer effects.

Section 620.605 prescribes the methods for developing guidance levels for carcinogens and non-carcinogens. Briefly, this method specifies that the United States Environmental Protection Agency (U.S. EPA) MCL or maximum contaminant level goal (MCLG) is the guidance level, if available. If there is no MCL or MCLG for the substance, the guidance level for the chemical is either the Human Non-Threshold Toxicant Advisory Concentration (HNTAC) for carcinogens or the Human Threshold Toxicant Advisory Concentration (HTTAC) for non-carcinogens as determined in accordance with procedures in Section 620.Appendix A. U.S. EPA has not published an MCL or MCLG for PFOA.

Appendix A specifies, in prescribed order, the toxicological data to be used in developing guidance levels. To determine appropriate toxicological data in accordance with nationally accepted guidelines, pursuant to the Illinois Groundwater Protection Act (415 ILCS 55-8(a)), Illinois EPA relied upon U.S. EPA guidance titled, *"Tier 3 Toxicity Value White Paper"* (paper), dated May 16, 2013, prepared by the U.S. EPA Office of Solid Waste and Emergency Response

(OSWER) Human Health Regional Risk Assessors Forum. The paper lists a hierarchy of sources to be used when determining an appropriate toxicological value for use in human health assessments. The hierarchy for selection of toxicity values is as follows:

Tier 1: U.S. EPA Integrated Risk Information System (IRIS).

Tier 2: U.S. EPA Provisional Peer-Reviewed Toxicity Values (PPRTVs).

Tier 3: In the order in which they are presented:

1) U.S. Health and Human Services Agency for Toxic Substances and Disease Registry (ATSDR) Dose Minimal Risk Levels (dose MRLs).

2) California EPA Office of Environmental Health Hazard Assessments (OEHHA).

3) PPRTV "Appendix" Values.

4) Health Effects Assessment Summary Table (HEAST).

Cancer Assessment

As stated above, PFOA meets the definition of a carcinogen pursuant to the relevant provisions of the Board's Part 620 regulations and a determination by IARC.

California EPA's OEHHA developed a cancer oral slope factor (SF_o) of 143 (1.43E+02) $(mg/kg\text{-}day)^{-1}$ for liver and pancreatic tumors in male rats, based on an extrapolation of data from PFOA cancer studies by the United States Department of Health and Human Services, National Toxicology Program (NTP), titled, "*TR-598: Technical report pathology tables and curves – PFOA*", published in 2018. Using a 5% benchmark response, OEHHA calculated an animal benchmark dose lower bound ($BMDL_{05}$) of 0.000648 mg/kg-day from animal bioassay data, yielding a human $BMDL_{05}$ (equivalent to a human equivalency dose or HED) of 0.00035 milligrams per kilogram per day (mg/kg-day) and an SF_o equal to 143 $(mg/kg\text{-}day)^{-1}$.

Using California EPA's OEHHA SF_o of 143 (1.43E+02) $(mg/kg\text{-}day)^{-1}$, and the procedures outlined in Section 620.Subpart F, the calculated HNTAC for drinking water equivalent to a one in one million cancer risk is 0.0000006 mg/L, or 0.6 ng/L or ppt.

Non-Cancer Assessment

ATSDR published a peer reviewed toxicological (tox) profile titled, "*Toxicological Profile for Perfluoroalkyls"* (tox profile), for four PFAS, including PFOA, in the Federal Register on July 19, 2018 for a 60-day public comment period. The comment period closed on September 17, 2018. The toxicity values in the tox profile are considered "draft" until they have been finalized following the public comment period. Following the close of the comment period, ATSDR

submitted their toxicological profile to the Office of Management and Budget in December 2019. In November 2018, ATSDR published health-based drinking water MRLs using the recommended dose MRLs included within the tox profile.

ATSDR's tox profile recommends an intermediate dose MRL equal to 0.000003 (3E-06) mg/kg-day. The value is based on skeletal alterations and altered motor function in mice from exposure through gestation and lactation from developmental toxicity studies by Onishchenko et al., titled, "*Prenatal exposure to PFOS or PFOA alters motor function in mice in a sex-related manner",* published in 2011, and Koskela et al., titled, "*Effects of developmental exposure to perfluorooctanoic acid (PFOA) on long bone morphology and bone cell differentiation*", published in 2016. The Wambaugh pharmacokinetic (PK) model was used to derive a predicted time-weighted average (TWA) serum concentration from a lowest observed adverse effects level (LOAEL) of 0.3 mg/kg-day in mice. A no observed adverse effects level (NOAEL) was not determined from the studies. The TWA serum concentration was then used to calculate a HED of 0.000821 in units of mg/kg-day.

A total uncertainty factor (UF) of 300 (UF of 10 to account for intrahuman variability, UF of 3 to account for toxicodynamic differences between animals and humans, and UF of 10 for account for a LOAEL to NOAEL conversion factor) was applied to the HED to derive its dose MRL.

$$dose\ MRL = \frac{HED}{UF}$$

$$dose\ MRL = \frac{0.000821\ mg/kg\text{-}day}{300}$$

$$dose\ MRL = 0.0000027\ mg/kg\text{-}day$$

Rounded to one significant digit:

$$dose\ MRL = 0.000003\ mg/kg\text{-}day$$

Using the ATSDR dose MRL of 0.000003 (3E-06) mg/kg-day, and the procedures outlined in Section 620.Appendix A, the calculated HTTAC for drinking water is 0.000021 mg/L, or 21 ng/L or ppt for non-carcinogen effects.

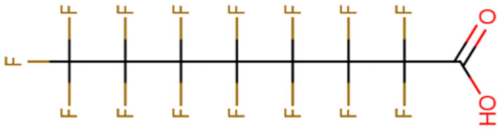
CHEMICAL CHARACTERISTICS AND POTENTIAL ADVERSE HEALTH EFFECTS

General Description of PFOA

Perfluorooctanoic Acid (CASRN 335-67-1), also known as pentadecafluoro-octanoic acid, or PFOA, is a synthetic chemical which is part of a larger class of chemicals referred to as per- and

polyfluoroalkyl substances. PFAS have been manufactured since the middle 20th Century and are known for their chemical and physical properties that impart oil and water repellency, temperature resistance, and friction reduction to a wide range of products, including, but not limited to, textile coatings, paper products, food wrappers, cosmetic and personal care products, non-stick cookware and fire-fighting foams. PFAS are also used in the semiconductor, aerospace, oil production, mining, and metal plating industries, to name a few. PFAS enter the environment through industrial manufacturing and the use and disposal of PFAS-containing products. The chemical and physical properties of PFOA make it mobile, persistent, and bioaccumulative, meaning fish and other animals may accumulate PFOA in animal tissue when their food sources are contaminated with PFOA. PFOA is not known to degrade in the environment.

Structural Identifier



Chemical Identifier

$C_7F_{15}COOH$

Potential Adverse Health Effects of PFOA

Epidemiology studies on humans suggest associations between PFOA exposure and several possible health outcomes, such as:

- Pregnancy-induced hypertension/pre-eclampsia
- Liver damage
- Increased serum lipids, primarily total cholesterol and LDL cholesterol
- Increased thyroid disease
- Decreased antibody response to vaccines
- Decreased fertility
- Decreased birth weight

Most information regarding health effects of PFOA is derived from animal studies, primarily via the ingestion, or oral exposure, route. Laboratory studies observed the following effects in animals exposed to PFOA:

- Liver damage
- Neurodevelopmental effects
- Suppressed immune response
- Skeletal malformations

- Decreased weight of offspring

Carcinogenic Potential

Section 620.110 defines a carcinogen as a contaminant that is classified as: 1) a Category A1 or A2 Carcinogen by the American Conference of Governmental Industrial Hygienists (ACGIH); 2) a Category 1 or 2A/2B Carcinogen by IARC; 3) a "Human Carcinogen" or "Anticipated Human Carcinogen" by the U.S. Department of Health and Human Service National Toxicological Program (NTP); or 4) a Category A or B1/B2 Carcinogen by the U.S. EPA in IRIS or a Final Rule issued in a Federal Register notice by the U.S. EPA. PFOA meets the definition of a carcinogen, as it is classified as a 2B possible carcinogen by IARC. The classification is based on evidence of increased risk for kidney and testicular cancers in humans. Additional research has found evidence of liver and pancreatic cancers.

ATTACHMENT TO HEALTH ADVISORY
FOR
PERFLUOROOCTANOIC ACID (PFOA)
CASRN 335-67-1

OVERVIEW OF KEY STUDIES

For information regarding the studies used by California OEHHA for derivation of its SF_o and ATSDR for derivation of its dose MRL, refer to the following documents:

California OEHHA SF_o: https://oehha.ca.gov/media/downloads/water/chemicals/nl/final-pfoa-pfosnl082119.pdf

ATSDR dose MRL: https://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=1117&tid=237

DERIVATION OF THE HEALTH ADVISORY FOR PFOA

The first step in the derivation of a health advisory is to determine whether the chemical substance presents a carcinogenic risk to humans. In 2017, the IARC classified PFOA as a "2B" carcinogen. The classification meets the definition of a carcinogen pursuant to Section 620.110.

For a guidance level equal to a one-in-one million cancer risk, the human non-threshold toxicant advisory concentration is calculated by the following equation specified at Section 620.605(b):

$$HNTAC = \frac{TR \bullet BW \bullet AT \bullet 365 \frac{days}{year}}{SF_o \bullet IR \bullet EF \bullet ED}$$

Where:

HNTAC = Human non-threshold toxicant advisory concentration in milligrams per liter (mg/L).

TR = Target cancer risk equal to one in one million risk (1.0E-06).

BW = Body weight equal to an average adult (70 kg).

AT = Averaging time for carcinogens (70 years).

SF_o = Oral slope factor for PFOA (143 $(mg/kg\text{-}day)^{-1}$).

IR = Daily water ingestion rate equal to an average adult equal to 2 liters per day (L/day).

EF = Exposure frequency (350 days/year).

ED = Exposure duration (30 years).

The calculation for a carcinogen guidance level is as follows:

$$HNTAC\ (mg/L) = \frac{0.000001 \bullet 70\ kg \bullet 70\ years \bullet 365\ days/year}{143\ (mg/kg\text{ - }day)^{-1} \bullet 2\ L/day \bullet 350\ days/year \bullet 30\ years}$$

$$HNTAC\ (mg/L) = \frac{1.7885}{3{,}003{,}000}$$

$$HNTAC = 0.0000006\ mg/L$$

or:

0.6 ng/L or ppt

In deriving a guidance level to protect against a health effect for which there is a threshold dose below which no damage occurs (i.e., non-carcinogen effects), Section 620.605 specifies that U.S. EPA's MCLG, if available, is the guidance level. U.S. EPA has not published a MCLG for PFOA; therefore, Illinois EPA must calculate the HTTAC as the guidance level, using the procedures specified in Appendix A of Section 620.

Appendix A specifies in subsection (a) that the HTTAC is calculated as follows:

$$HTTAC = \frac{RSC \bullet ADE}{W}$$

Where:

HTTAC = Human threshold toxicant advisory concentration in milligrams per liter (mg/L).

RSC = Relative source contribution, the relative contribution of the amount of exposure to a chemical via ingestion of drinking water when compared to total exposure to that chemical from all sources. Valid chemical-specific data shall be used if available. If valid chemical-specific data are not available, a value of 20% (= 0.20) must be used.

ADE = Acceptable daily exposure of a chemical in milligrams per day (mg/d) as determined in accordance with Appendix A, subsection (b).

W = Per capita daily water consumption equal to 2 liters per day (L/d).

Subsection (b) of Appendix A specifies that the ADE be calculated using, in specified order: a U.S. EPA verified RfD (an estimate of a daily exposure to a chemical which is expected to be without adverse health effects for humans for a lifetime of exposure in units of mg/kg-day); a

NOAEL which has been identified as a result of human exposures; a LOAEL which has been identified as a result of human exposures; a NOAEL which has been determined from studies with laboratory animals; and a LOAEL which has been determined from studies with laboratory animals.

Illinois EPA selected the ATSDR dose MRL of 0.000003 (3E-06) mg/kg-day, as the verified RfD for use in calculating the ADE. The ADE equals the product of multiplying the toxicity value by 70 kilograms (kg), which is the assumed average body weight of an adult human per Section 620:

$$ADE = 0.000003\, mg/kg\text{-}day \bullet 70\, kg = 0.00021\, mg/day$$

The next step in the development of the HTTAC is the evaluation of chemical-specific RSC data available for the chemical. Illinois EPA evaluated data from ATSDR, U.S. EPA Office of Water, and values developed by other states. There is little scientific consensus regarding the contribution of drinking water to the total amount of PFAS exposure to humans. Humans are exposed to PFOA through a variety of media, including, but not limited to air emissions, ingestion of fish or other animals exposed to PFOA, dermal exposure and incidental exposure from PFOA-containing consumer products, much of which varies on a site-specific basis. Due to this lack of consensus, Illinois EPA elected to use the conservative default value of 20% (0.20) for its HTTAC calculation.

Finally, the HTTAC is calculated by the product of the RSC and the ADE, divided by the per capita daily water consumption rate, specified in Appendix A as equal to 2 L/day:

$$HTTAC\ (mg/L) = \frac{0.20 \bullet 0.00021\, mg/day}{2\, L/day}$$

$$HTTAC\ (mg/L) = \frac{0.000042\, mg/day}{2\, L/day}$$

$$HTTAC = 0.000021\ mg/L$$

or:

21 ng/L or ppt

The calculated HNTAC is less than the calculated HTTAC. Therefore, the guidance level is equal to the carcinogen HNTAC of 0.0000006 mg/L or 0.6 ng/L.

The final step in ensuring a calculated guidance level is appropriate is to compare the guidance level to the chemical's practical quantitation limit (PQL), or minimum reporting level (MRL). U.S. EPA's Method 537.1 for analyses of PFAS drinking water samples states the PFOA MRL is 2 ng/L, which is above the calculated guidance level of 0.6 ng/L. Therefore, the MRL of 2 ng/L is the appropriate Health Advisory level.

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