



# ILLINOIS ENVIRONMENTAL PROTECTION AGENCY

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## HEALTH ADVISORY UPDATE FOR PERFLUOROHEXANOIC ACID (PFHxA) CHEMICAL ABSTRACT SERVICES REGISTRY NUMBER (CASRN) 307-24-4

Prepared by:  
Office of Toxicity Assessment  
Illinois Environmental Protection Agency  
April 26, 2023

### REASON FOR ACTION

On January 28, 2021, Illinois Environmental Protection Agency (Illinois EPA) issued a health advisory for Perfluorohexanoic Acid (PFHxA) 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), PFHxA 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 PFHxA. 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 listed in the January 28, 2021, health advisory for PFHxA was 0.56 milligrams per liter (mg/L), or 560,000 nanograms per liter (ng/L) or parts per trillion (ppt). The health advisory guidance level was based on the State of Michigan Science Advisory Workgroup, published 2019.

On April 10, 2023, U.S. EPA's Integrated Risk Information System (IRIS) published its final toxicity assessment for PFHxA, resulting in Illinois EPA's issuance of an updated PFHxA health advisory guidance level of 0.0035 milligrams per liter (mg/L), or 3,500 nanograms per liter (ng/L) or parts per trillion (ppt).

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The updated 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://epa.illinois.gov/topics/water-quality/pfas/pfas-healthadvisory.html>

### **PURPOSE OF A HEALTH ADVISORY**

In accordance with 35 Ill. Adm. Code 620.601, the purpose 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 levels represent 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 PFHxA**

Through issuance of this updated Health Advisory, Illinois EPA is providing public notice of its updated guidance level for PFHxA in drinking water. For non-carcinogenic health effects, the updated guidance level is 0.0035 milligrams per liter (mg/L), or 3,500 nanograms per liter (ng/L) or parts per trillion (ppt).

Section 620.605 prescribes the methods for developing health advisories for carcinogens and non-carcinogens. PFHxA does not meet the definition of a "carcinogen", as defined in Section 620.110; therefore, the method for developing a health advisory for non-carcinogens was used. 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, or the human threshold toxicant advisory concentration (HTTAC) must be determined using the procedures contained in Appendix A of Section 620. U.S. EPA has not published an MCL or MCLG for PFHxA; therefore, Illinois EPA used the Appendix A procedures to calculate a HTTAC for PFHxA.

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) The 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 Assessment (OEHHA).
- 3) PPRTV “Appendix” Values.
- 4) Health Effects Assessment Summary Table (HEAST).

On April 10, 2023, U.S. EPA’s IRIS published a final peer reviewed toxicological profile titled, “*IRIS Toxicological Review of Perfluorohexanoic Acid [PFHxA, CASRN 307-24-4] and Related Salts.*” U.S. EPA’s IRIS is listed as a Tier 1 toxicity value source. The IRIS toxicological profile recommends a chronic oral reference dose (RfD) equal to 0.0005 (5E-04) mg/kg-day. The value is based on a critical effect of decreased offspring body weight in neonatal rats from exposure through gestation and lactation from a study by Loveless et. al., titled, “*Toxicological evaluation of sodium perfluorohexanoate,*” published in 2009. A benchmark dose 95% lower confidence limit at the 5% relative deviation response level (BMDL<sub>5RD</sub>) of 10.62 mg/kg-day was identified and used as the point of departure (POD). A human equivalent dose POD (POD<sub>HED</sub>) of 0.048 mg/kg-day was then derived by applying the ratio of the clearance between female rats and humans.

A total composite uncertainty factor (UF) of 100 (UF of 3 to account for toxicodynamic differences between humans and animals, UF of 10 to account for intrahuman variability, and UF of 3 to account for database uncertainties) was applied to the POD<sub>HED</sub>.

The overall RfD for PFHxA was calculated by dividing the POD<sub>HED</sub> by the composite uncertainty factor.

$$RfD = \frac{POD_{HED}}{UF}$$

$$RfD = \frac{0.048 \text{ mg/kg-day}}{100}$$

$$RfD = 0.00048 \text{ mg/kg-day}$$

Rounded to one significant digit:

$$RfD = 0.0005 \text{ mg/kg-day}$$

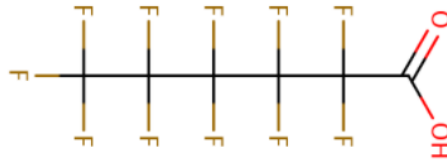
Using the RfD of 0.0005 (5E-4) mg/kg-day, and the procedures outlined in Section 620. Appendix A, the recommended guidance level for drinking water is 0.0035 milligrams per liter (mg/L), or 3,500 nanograms per liter (ng/L) or parts per trillion (ppt).

## **CHEMICAL CHARACTERISTICS** **AND** **POTENTIAL ADVERSE HEALTH EFFECTS**

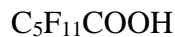
### General Description of PFHxA

Perfluorohexanoic Acid (PFHxA) (CASRN 307-24-4), also known as undecafluorohexanoic acid or PFHxA, 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 20<sup>th</sup> 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 and 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 PFHxA make it mobile, persistent and bioaccumulative, meaning fish and other animals may accumulate PFHxA in animal tissue when their food sources are contaminated with PFHxA. PFHxA is known to be persistent in the environment.

### **Structural Identifier**



### **Chemical Identifier**



### **Potential Adverse Health Effects of PFHxA**

Epidemiological studies on human health effects from exposure to PFHxA are limited in their ability to draw conclusions on the associations between health effects and exposure.

Information regarding health effects of PFHxA are primarily derived from animal studies, via the ingestion, or oral exposure, route. Laboratory studies observed the following effects in animals exposed to PFHxA:

- Increased liver weight
- Increased hepatocellular hypertrophy
- Increased perinatal mortality
- Decreased weight of offspring
- Reduced red blood cell count
- Decreased thyroid hormone

### **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 the World Health Organization's International Agency for Research on Cancer (IARC); 3) a "Human Carcinogen" or "Anticipated Human Carcinogen" by the United States 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 USEPA. PFHxA is not classified as a carcinogen by any of the above sources.

**ATTACHMENT TO HEALTH ADVISORY  
FOR  
PERFLUOROHEXANOIC ACID (PFHxA)  
CASRN 307-24-4**

**OVERVIEW OF KEY STUDIES**

For information regarding the studies used by IRIS for the derivation of its PFHxA RfD, refer to the IRIS Toxicological Review of Perfluorohexanoic Acid, located at:

[https://cfpub.epa.gov/ncea/iris\\_drafts/recordisplay.cfm?deid=357314](https://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=357314)

**DERIVATION OF THE HEALTH ADVISORY FOR PFHxA**

The first step in the derivation of a health advisory is to determine whether the chemical substance presents a carcinogenic risk to humans. PFHxA does not meet the definition of a carcinogen as specified in Section 620. Therefore, the guidance level will be based on non-carcinogenic effects of this chemical.

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 PFHxA; 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:

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

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 an RfD of 0.0005 (5E-4) 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:

$$ADE = 0.0005 \text{ mg/kg-day} \cdot 70 \text{ kg} = 0.035 \text{ mg/day}$$

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 PFHxA through a variety of media, including, but not limited to air emissions, ingestion of fish or other animals exposed to PFHxA, dermal exposure and incidental exposure from PFHxA-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 ingestion rate, specified in Appendix A as equal to 2 L/day:

$$HTTAC \text{ (mg/L)} = \frac{0.20 \cdot 0.035 \text{ mg/day}}{2 \text{ L/day}}$$

$$HTTAC \text{ (mg/L)} = \frac{0.007 \text{ mg/day}}{2 \text{ L/day}}$$

$$HTTAC = 0.0035 \text{ mg/L}$$

or:

$$3,500 \text{ ng/L or ppt}$$

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 PFHxA MRL is 2 ng/L, which is below the calculated guidance level of 3,500 ng/L. Therefore, the guidance level is appropriate.

## REFERENCES

IGA (Illinois General Assembly). Illinois Groundwater Protection Act (IGPA). 415 ILCS 55. Available at: <https://www.ilga.gov/legislation/ilcs/ilcs3.asp?ActID=1595&ChapterID=36>

Loveless, SE; Slezak, B; Serex, T; Lewis, J; Mukerji, P; O'Connor, JC; Donner, EM; Frame, , SR; Korzeniowski, SH; Buck, RC. 2009. Toxicological evaluation of sodium perfluorohexanoate. *Toxicology* 264: 32-44.

PCB (Pollution Control Board). Title 35: Environmental Protection: Subtitle F: Public Water Supplies: Chapter I: Pollution Control Board. Part 620: Groundwater Quality. Available at: <https://pcb.illinois.gov/SLR/PCBandIEPAEnvironmentalRegulationsTitle35>

U.S. EPA (United State Environmental Protection Agency) Office of Solid Waste and Emergency Response (OSWER). 2013. Tier 3 Toxicity Value White Paper. OSWER Document Number 9285.7-86. Available at: <https://www.epa.gov/sites/production/files/2015-11/documents/tier3-toxicityvalue-whitepaper.pdf>

U.S. EPA. Toxicological Review of Perfluorohexanoic Acid (PFHxA) and Related Salts (Final Report, 2023). U.S. Environmental Protection Agency, Washington, DC, EPA/635/R-23/027F, 2023. Available at: [https://cfpub.epa.gov/ncea/iris\\_drafts/recordisplay.cfm?deid=357314](https://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=357314)