

**PLEASE NOTE:** EPA is committed to advancing science to protect public health from the risks of exposure to certain PFAS, and to provide essential health protective information to regulators and the public. That is why EPA published interim Health Advisories for PFOA and PFOS in June 2022, based on a robust assessment of the best available science at that time. On March 14, 2023, EPA released a proposed national primary drinking water regulation (NPDWR) for PFOA and PFOS, as well as for four additional PFAS and their mixtures. This rule has considered additional updates to the science and is responsive to peer review feedback provided by EPA’s Science Advisory Board.

In the proposed rule, EPA presents updated noncancer toxicity values based on evaluating additional scientific information. These updated values are different from those used to calculate the 2022 interim HAs, which EPA based on the best available science at that time. EPA is accepting public comments on its proposed NPDWR, including on the proposed maximum contaminant level goals (MCLGs), other supporting information, and the draft 2023 toxicity values for PFOA and PFOS which are based on the best available science. Note that the MCLGs in the proposed rule are zero.

**The 2022 interim Health Advisories for PFOA and PFOS will continue to remain available as EPA finalizes a national primary drinking water regulation for those contaminants.**

# Technical Fact Sheet: Drinking Water Health Advisories for Four PFAS (PFOA, PFOS, GenX chemicals, and PFBS)

## Summary

As part of EPA's commitment to safeguard communities from per- and polyfluoroalkyl substances (PFAS), EPA has issued interim updated drinking water health advisories for perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS), and final health advisories for hexafluoropropylene oxide (HFPO) dimer acid and its ammonium salt (together referred to as "GenX chemicals") and perfluorobutane sulfonic acid and its related compound potassium perfluorobutane sulfonate (together referred to as "PFBS"). The interim health advisories for PFOA and PFOS are intended to provide information to states and public water systems until the National Primary Drinking Water regulation for PFAS takes effect. All four of these health advisories provide drinking water system operators, and state, tribal, and local officials who have the primary responsibility for overseeing these systems, with information on the health risks of these chemicals, so they can take the appropriate actions to protect their residents.

## Background

### *What Are PFAS?*

PFAS are synthetic chemicals that have been manufactured and used by a broad range of industries since the 1940s. PFAS are used in many applications because of their unique physical properties such as resistance to high and low temperatures, resistance to degradation, and nonstick characteristics. PFAS have been detected worldwide in the air, soil, and water. Due to their widespread use and persistence in the environment, most people in the United States have been exposed to PFAS. There is evidence that exposure above specific levels to certain PFAS may cause adverse health effects.

### *What Are Drinking Water Health Advisories?*

Drinking water health advisories (HAs) provide information on contaminants that can cause human health effects and are known or anticipated to occur in drinking water. EPA's HAs are non-enforceable and non-regulatory and provide technical information to drinking water system operators, as well as federal, state, tribal, and local officials on health effects, analytical methods, and treatment technologies associated with drinking water contamination.

### *Why is EPA Issuing These HAs?*

In 2016, EPA published HAs for PFOA and PFOS based on the evidence available at that time (U.S. EPA 2016, a,b). The science has evolved since then and EPA is now replacing the 2016 advisories with interim updated lifetime HAs for PFOA and PFOS that are based on new studies and draft toxicity values from EPA's 2021 draft PFOA and PFOS health effects documents. Fulfilling EPA's commitment in its October 2021 PFAS Strategic Roadmap, EPA has issued final lifetime HAs for GenX chemicals and PFBS.

### **How Does EPA Calculate HAs?**

The following equation is used to derive a lifetime noncancer health advisory. A lifetime noncancer health advisory is designed to be protective of noncancer effects over a lifetime of exposure, including sensitive populations and life stages, and is typically based on data from experimental animal toxicity and/or human studies.

$$\text{Lifetime HA} = \left( \frac{\text{RfD}}{\text{DWI-BW}} \right) * \text{RSC}$$

Where:

**RfD** = chronic reference dose—an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure of the human population to a substance that is likely to be without an appreciable risk of deleterious effects during a lifetime.

**DWI-BW** = drinking water intake rate adjusted for body weight—the 90th percentile DWI for the selected population or life stage, adjusted for body weight (BW), in units of L/kg bw-day. The DWI-BW considers both direct and indirect consumption of tap water (indirect water consumption encompasses water added in the preparation of foods or beverages, such as tea or coffee).

**RSC** = relative source contribution—the percentage of the total oral exposure attributed to drinking water sources (U.S. EPA, 2000) where the remainder of the exposure is allocated to all other routes or sources.

## **What Types of Health Outcomes are Associated with Exposure to These Four PFAS, and How Did EPA Develop the HAs?**

### ***PFOA and PFOS***

EPA is conducting extensive evaluations of human epidemiological and experimental animal study data to support the Safe Drinking Water Act (SDWA) National Primary Drinking Water Regulation for PFOA and PFOS. In November 2021, EPA released draft documents that summarize the updated health effects analyses for [EPA Science Advisory Board \(SAB\) review](#) (U.S. EPA, 2021a, b). EPA evaluated over 400 studies published since 2016 and used new human health risk assessment approaches, tools, and models. Human studies have found associations between PFOA and/or PFOS exposure and effects on the immune system, the cardiovascular system, development (e.g., decreased birth weight), and cancer. The new published peer-reviewed data and draft EPA analyses (U.S. EPA, 2021a, b) indicate that the levels at which negative health outcomes could occur are much lower than previously understood when the agency issued its 2016 HAs for PFOA and PFOS (70 parts per trillion or ppt). EPA's 2021 draft non-cancer reference doses (RfDs) based on human epidemiology studies for various effects (e.g., developmental/growth, cardiovascular health outcomes, immune health) range from  $\sim 10^{-7}$  to  $10^{-9}$  mg/kg/day. These draft RfDs are two to four orders of magnitude lower than EPA's 2016 RfDs of  $2 \times 10^{-5}$  mg/kg/day (U.S. EPA, 2021a, b).

The most sensitive non-cancer effect based on the draft EPA analyses, decreased immunity (i.e., decreased serum antibody concentrations after vaccination) in children in a human epidemiology study, was selected as the basis for the draft RfD (toxicity value) in the PFOA and PFOS health effects draft documents (U.S. EPA, 2021a, b). EPA used the draft RfD to derive the interim updated HAs for PFOA and PFOS. In the critical study, EPA selected the critical effect of decreased serum antibody concentration in children associated with increased serum PFOA and/or PFOS concentrations. EPA expects this critical effect to be protective of all other adverse health effects observed in humans because this adverse effect can reduce the protection afforded by vaccines after exposure to PFOA/PFOS during a sensitive developmental life stage and it yields the lowest point of departure (POD) (U.S. EPA, 2021a, b). For both PFOA and PFOS, an intraspecies uncertainty factor

(UF<sub>H</sub>) of 10 was applied to account for variability in the response within the human population (U.S. EPA, 2002). EPA identified children ages 0-5 years as a sensitive life stage, based on the critical study, and selected the corresponding DWI-BW. Based on a literature search of the available information on exposure sources and routes, EPA calculated the interim HAs for PFOA and PFOS using an RSC of 0.20, meaning that 20% of the exposure – equal to the RfD – is allocated to drinking water, and the remaining 80% is attributed to all other potential exposure sources (U.S. EPA, 2022a, b; U.S. EPA, 2000).

While there is evidence that PFOA is likely to be carcinogenic to humans, EPA has not derived a cancer risk concentration in water for PFOA at this time. For PFOS, there is suggestive evidence of carcinogenic potential in humans. Additional analyses of the cancer study data are ongoing for both PFOA and PFOS.

The underlying science that EPA used to develop the interim health advisories is currently undergoing SAB review, and therefore, these interim health advisories are subject to change. After receiving the SAB's final report, EPA will complete its revisions to address their feedback and recommendations, which could lead the agency to draw different conclusions than are reflected in the draft health effects analyses (U.S. EPA, 2021a, b). As a result, the interim health advisory levels for PFOA and PFOS (U.S. EPA, 2022a, b) could change. EPA may update or remove the interim health advisories for PFOA and PFOS upon finalization of the National Primary Drinking Water Regulation.

### ***GenX Chemicals and PFBS***

EPA's final health advisories for GenX chemicals and PFBS are based on animal toxicity studies following oral exposure to these chemicals. Studies of exposure to GenX chemicals have reported health effects in the liver, kidney, immune system, development, as well as cancer. The most sensitive non-cancer effect among the available data was an adverse liver effect (constellation of liver lesions) (U.S. EPA, 2021c). This critical effect was the basis for the final chronic RfD which EPA used to derive the final HA for GenX chemicals. To develop the final chronic RfD for GenX chemicals, EPA applied a composite UF of 3,000 (i.e., 10X for intraspecies variability (UF<sub>H</sub>), 3X for interspecies differences (UF<sub>A</sub>), 10X for extrapolation from a subchronic to a chronic dosing duration (UF<sub>S</sub>), and 10X for database deficiencies (UF<sub>D</sub>)) (U.S. EPA, 2021c). EPA identified lactating women as an adult life stage with the greatest potential exposure from drinking water, based on the critical study, and selected the corresponding DWI-BW. EPA calculated the final HA for GenX chemicals using an RSC of 0.20, meaning that 20% of the exposure -- equal to the RfD -- is allocated to drinking water, and the remaining 80% is attributed to all other potential exposure sources (U.S. EPA, 2022c). There is suggestive evidence of carcinogenic potential of oral exposure to GenX chemicals in humans and the available data are insufficient to derive a cancer risk concentration in water for GenX chemicals.

For PFBS, animal studies have reported health effects on the thyroid, reproductive system, development, and kidney following oral exposure. The most sensitive non-cancer effect was an adverse effect on the thyroid (i.e., decreased serum total thyroxine) in newborn mice in a study with exposure throughout gestation in the mothers. This critical effect was the basis for the final chronic RfD which EPA used to derive the final HA for PFBS (U.S. EPA, 2021d; U.S. EPA, 2022d). EPA applied a composite UF of 300 (i.e., 10X for intraspecies variability (UF<sub>H</sub>), 3X for interspecies differences (UF<sub>A</sub>), and 10X for database deficiencies (UF<sub>D</sub>)) (U.S. EPA, 2021d). EPA identified women of child-bearing age as a sensitive life stage, based on the critical study, and selected the corresponding DWI-BW. EPA calculated the final HA for PFBS using an RSC of 0.20, meaning that 20% of the exposure – equal to the RfD – is allocated to drinking water, and the remaining 80% is attributed to all other potential exposure sources (U.S. EPA, 2022d). There were no studies identified that evaluated potential cancer effects after PFBS exposure so the potential for cancer effects after PFBS exposure could not be evaluated.

## What are the HAs for the four PFAS?

PFOA Interim Updated Health Advisory – Input Parameters and HA Value			
Parameter	Value	Units	Source
Chronic RfD	1.5E-9	mg/kg/day	U.S. EPA, 2021a. <i>Draft</i> RfD based on developmental immune health outcome (suppression of tetanus vaccine response in 7-year-old children). Human epidemiological studies.
DWI-BW	0.0701	L/kg-day	U.S. EPA, 2019. 90th percentile direct and indirect consumption of community water, consumers-only population, two-day average, for children ages 0 to <5 years based on 2005–2010 National Health and Nutrition Examination Survey (NHANES).
RSC	0.2	N/A	U.S. EPA, 2021a. RSC based on a review of the current scientific literature.

**PFOA Interim Updated Lifetime Health Advisory = 4E-09 mg/L or 0.004 ppt (EPA 2022a)**

PFOS Interim Updated Health Advisory – Input Parameters and HA Value			
Parameter	Value	Units	Source
Chronic RfD	7.9E-09	mg/kg/day	U.S. EPA, 2021b. <i>Draft</i> RfD based on developmental immune health outcome (suppression of diphtheria vaccine response in 7-year-old children). Human epidemiological studies.
DWI-BW	0.0701	L/kg-day	U.S. EPA, 2019. 90th percentile direct and indirect consumption of community water, consumers-only population, two-day average, for children ages 0 to <5 years based on 2005–2010 NHANES.
RSC	0.2	N/A	U.S. EPA, 2021b. RSC based on a review of the current scientific literature.

**PFOS Interim Updated Lifetime Health Advisory = 2E-08 mg/L or 0.02 ppt (EPA 2022b)**

GenX Chemicals Final Health Advisory – Input Parameters and HA Value			
Parameter	Value	Units	Source
Chronic RfD	3E-06	mg/kg/day	U.S. EPA, 2021c. Final RfD based on critical liver effects (constellation of liver lesions as defined by the National Toxicology Program Pathology Working Group) in parental female mice exposed to HFPO dimer acid ammonium salt by gavage for 53–64 days.
DWI-BW	0.0469	L/kg-day	U.S. EPA, 2019. 90 <sup>th</sup> percentile two-day average, consumer only estimate of combined direct and indirect community water ingestion for lactating women (13 to <50 years) based on 2005–2010 NHANES.
RSC	0.2	N/A	U.S. EPA, 2021c. Based on a review of the current scientific literature.

**GenX Chemicals Final Lifetime Health Advisory = 0.00001 mg/L or 10 ppt (EPA 2022c)**

PFBS Final Health Advisory – Input Parameters and HA Value			
Parameter	Value	Units	Source
Chronic RfD	3E-04	mg/kg/day	U.S. EPA, 2021d: Final RfD based on critical effect of decreased serum total thyroxine (T4) in newborn (postnatal day (PND) 1) mice after gestational exposure to the mother.
DWI-BW	0.0354	L/kg-day	U.S. EPA, 2019. 90 <sup>th</sup> percentile two-day average, consumer only estimate of combined direct and indirect community water ingestion for women of childbearing age (13 to <50 years) based on 2005–2010 NHANES.
RSC	0.2	N/A	U.S. EPA, 2021d. Based on a review of the current scientific literature.

**PFBS Final Lifetime Health Advisory = 0.002 mg/L or 2,000 ppt (EPA 2022d)**

## Application of Health Advisories to Different Exposure Scenarios

Because the critical effects identified for PFOA, PFOS, and PFBS are developmental effects that can potentially result from short-term exposure to these PFAS during a critical period of development, EPA guidelines support applying the lifetime health advisories for these three PFAS to both short-term and chronic risk assessment scenarios (U.S. EPA, 1991).

The lifetime health advisory for GenX chemicals used a chronic RfD from the final EPA toxicity assessment (U.S. EPA, 2021c) based on the critical effect of adverse liver effects in adults (parental females) from a subchronic study (53–64 day exposure). In the assessment, a 10X UF<sub>s</sub> for subchronic to chronic exposure was applied to derive the chronic RfD (U.S. EPA, 2021c). Because the critical effect identified for GenX chemicals is in adults, the HA applies to chronic exposure scenarios. The HA was based on exposure to lactating women, an adult life stage with the greatest drinking water intake rate. Application of the GenX chemicals HA to a shorter-term risk assessment scenario would provide a conservative, health protective approach in the absence of other information.

## Consideration of Noncancer Health Risks from PFAS Mixtures

EPA recently released a *Draft Framework for Estimating Noncancer Health Risks Associated with Mixtures of Per- and Polyfluoroalkyl Substances (PFAS)* that is currently undergoing SAB review (U.S. EPA, 2021e). That draft document provides a flexible, data-driven framework that facilitates practical evaluation of two or more PFAS based on current, available EPA chemical mixtures approaches and methods. Examples are presented for three approaches—Hazard Index (HI), Relative Potency Factor (RPF), and Mixture BMD—to demonstrate application to PFAS mixtures. To use these approaches, specific input values and information for each PFAS are needed or can be developed.

The health advisory documents provide an example of how to use the HI approach to assess the potential noncancer risk of a mixture of PFOA, PFOS, GenX chemicals, and PFBS (U.S. EPA, 2022 a-d). A mixture PFAS HI can be calculated when health-based water concentrations (e.g., HAs, MCLGs) for a set of PFAS are available or can be calculated. In the example, hazard quotients (HQs) are calculated by dividing the measured component PFAS concentration in water (e.g., expressed as ng/L) by the relevant HA (e.g., expressed as ng/L), as shown in the equation below. Component HQs are then summed across the PFAS mixture to yield the mixture PFAS HI. A mixture PFAS HI greater than 1 indicates an exceedance of the health protective level and indicates potential human health risk for noncancer effects from the PFAS mixture in water. When component health-based water concentrations (in this case, HAs) are below the analytical method detection limit, as is the case for PFOA and PFOS, such individual component HQs exceed 1, meaning that any detectable level of PFOA or PFOS will result in an HI greater than 1 for the whole mixture. Further analysis could provide a refined assessment of the potential for health effects associated with the individual PFAS and their contributions to the potential joint toxicity associated with the mixture. For more details, please see U.S. EPA (2021e).

$$HI = \left( \frac{[PFOA_{water}]}{[PFOA_{HA}]} \right) + \left( \frac{[PFOS_{water}]}{[PFOS_{HA}]} \right) + \left( \frac{[GenX_{water}]}{[GenX_{HA}]} \right) + \left( \frac{[PFBS_{water}]}{[PFBS_{HA}]} \right)$$

Where:

**HI** = hazard index;

**[PFAS<sub>water</sub>]** = concentration for a given PFAS in water;

**[PFAS<sub>HA</sub>]** = the HA value for a given PFAS

## Where can I find more information?

To view the HA documents, go to: <https://www.epa.gov/sdwa/drinking-water-health-advisories-has>

To view the PFAS Strategic Roadmap: EPA's Commitments to Action 2021-2024, go to: <https://www.epa.gov/pfas/pfas-strategic-roadmap-epas-commitments-action-2021-2024>

For information on drinking water, go to: [www.epa.gov/safewater](http://www.epa.gov/safewater)

## References

- U.S. EPA (U.S. Environmental Protection Agency). 1991. *Guidelines for Developmental Toxicity Risk Assessment*. EPA-600-FR-91-001. EPA, Risk Assessment Forum, Washington, DC. Accessed April 2022. [https://www.epa.gov/sites/default/files/2014-11/documents/dev\\_tox.pdf](https://www.epa.gov/sites/default/files/2014-11/documents/dev_tox.pdf).
- U.S. EPA (U.S. Environmental Protection Agency). 2000. *Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000)*. EPA-822-B-00-004. EPA, Office of Water, Washington, DC. <https://www.epa.gov/sites/default/files/2018-10/documents/methodology-wqc-protection-hh-2000.pdf>.
- U.S. EPA (U.S. Environmental Protection Agency). 2002. *A Review of the Reference Dose and Reference Concentration Process*. EPA/630/P-02/002F. EPA, Risk Assessment Forum, Washington, DC. Accessed May 2022. <https://www.epa.gov/sites/default/files/2014-12/documents/rfd-final.pdf>.
- U.S. EPA (U.S. Environmental Protection Agency). 2016a. *Drinking Water Health Advisory for Perfluorooctanoic Acid (PFOA)*. EPA-822-R-16-005. EPA, Office of Water, Washington, DC. Accessed June 2022. [https://www.epa.gov/sites/production/files/2016-05/documents/pfoa\\_health\\_advisory\\_final\\_plain.pdf](https://www.epa.gov/sites/production/files/2016-05/documents/pfoa_health_advisory_final_plain.pdf).
- EPA (U.S. Environmental Protection Agency). 2016b. *Drinking Water Health Advisory for Perfluorooctane Sulfonate (PFOS)*. EPA-822-R-16-004. EPA, Office of Water, Washington, DC. Accessed June 2022. [https://www.epa.gov/sites/default/files/2016-05/documents/pfos\\_health\\_advisory\\_final\\_508.pdf](https://www.epa.gov/sites/default/files/2016-05/documents/pfos_health_advisory_final_508.pdf).
- U.S. EPA (U.S. Environmental Protection Agency). 2019. *Exposure Factors Handbook Chapter 3 (Update): Ingestion of Water and Other Select Liquids*. U.S. EPA Office of Research and Development, Washington, DC, EPA/600/R-18/259F. [https://www.epa.gov/sites/default/files/2019-02/documents/efh\\_-\\_chapter\\_3\\_update.pdf](https://www.epa.gov/sites/default/files/2019-02/documents/efh_-_chapter_3_update.pdf).
- U.S. EPA (U.S. Environmental Protection Agency). 2021a. *External Peer Review Draft: Proposed Approaches to the Derivation of a Draft Maximum Contaminant Level Goal for Perfluorooctanoic Acid (PFOA) (CASRN 335-67-1) in Drinking Water*. EPA-822-D-21-001. EPA, Office of Water, Washington, DC. Accessed April 2022. [https://sab.epa.gov/ords/sab/f?p=100:18:16490947993::RP,18:P18\\_ID:2601](https://sab.epa.gov/ords/sab/f?p=100:18:16490947993::RP,18:P18_ID:2601).
- U.S. EPA (U.S. Environmental Protection Agency). 2021b. *External Peer Review Draft: Proposed Approaches to the Derivation of a Draft Maximum Contaminant Level Goal for Perfluorooctane Sulfonic Acid (PFOS) CASRN 1763-23-1 in Drinking Water*. EPA-822-D-21-002. EPA, Office of Water, Washington, DC. Accessed April 2022. [https://sab.epa.gov/ords/sab/f?p=100:18:16490947993::RP,18:P18\\_ID:2601](https://sab.epa.gov/ords/sab/f?p=100:18:16490947993::RP,18:P18_ID:2601).
- U.S. EPA (U.S. Environmental Protection Agency). 2021c. *Human Health Toxicity Values for Hexafluoropropylene Oxide (HFPO) Dimer Acid and Its Ammonium Salt (CASRN 13252-13-6 and CASRN 62037-80-3)*. Also Known as "GenX Chemicals." EPA/822/R-21/010. EPA, Office of Water, Health and Ecological Criteria Division, Washington, DC. <https://www.epa.gov/chemical-research/human-health->

[toxicity-assessments-genx-chemicals](#)

- U.S. EPA (U.S. Environmental Protection Agency). 2021d. Human Health Toxicity Values for Perfluorobutane Sulfonic Acid (CASRN 375-73-5) and Related Compound Potassium Perfluorobutane Sulfonate (CASRN 29420-49-3). EPA/600/R-20/345F. EPA, Office of Research and Development, Washington, DC. <https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=350888>.
- U.S. EPA (U.S. Environmental Protection Agency). 2021e. Draft Framework for Estimating Noncancer Health Risks Associated with Mixtures of Per- and Polyfluoroalkyl Substances (PFAS). EPA-822-D-21-003. EPA, Office of Water, Washington, DC. <https://sab.epa.gov/ords/sab/f?p=100:18:16490947993:::RP,18:P18 ID:2601>
- U.S. EPA (U.S. Environmental Protection Agency). 2022a. Interim Drinking Water Health Advisory: Perfluorooctanoic Acid (PFOA) CASRN 335-67-1. EPA/822/R-22/003. EPA, Office of Water, Health and Ecological Criteria Division, Washington, DC. <https://www.epa.gov/sdwa/drinking-water-health-advisories-has>.
- U.S. EPA (U.S. Environmental Protection Agency). 2022b. Interim Drinking Water Health Advisory: Perfluorooctane Sulfonic Acid (PFOS) CASRN 1763-23-1. EPA/822/R-22/004. EPA, Office of Water, Health and Ecological Criteria Division, Washington, DC. <https://www.epa.gov/sdwa/drinking-water-health-advisories-has>.
- U.S. EPA (U.S. Environmental Protection Agency). 2022c. Drinking Water Health Advisory: Hexafluoropropylene Oxide (HFPO) Dimer Acid (CASRN 13252-13-6) and HFPO Dimer Acid Ammonium Salt (CASRN 62037-80-3), Also Known as “GenX Chemicals.” EPA/822/R-22/005. EPA, Office of Water, Health and Ecological Criteria Division, Washington, DC. <https://www.epa.gov/sdwa/drinking-water-health-advisories-has>.
- U.S. EPA (U.S. Environmental Protection Agency). 2022d. Drinking Water Health Advisory: Perfluorobutane Sulfonic Acid (CASRN 375-73-5) and Related Compound Potassium Perfluorobutane Sulfonate (CASRN 29420-49-3). EPA/822/R-22/006. EPA, Office of Water, Health and Ecological Criteria Division, Washington, DC. <https://www.epa.gov/sdwa/drinking-water-health-advisories-has>.