

Human Health Toxicity Assessment for GenX Chemicals

Summary

In October 2021, EPA published the final version of its human health toxicity assessment for hexafluoropropylene oxide (HFPO) dimer acid and its ammonium salt, referred to as “GenX chemicals.” The assessment provides hazard identification, dose-response information, and derives toxicity values called oral reference doses (RfDs) for chronic and subchronic exposures to GenX chemicals. The assessment also increases the available federal health information about the large chemical class of per- and polyfluoroalkyl substances (PFAS) of which GenX chemicals is a part and served as the basis for the drinking water health advisory for GenX chemicals, which the agency published in June 2022. Industry developed GenX chemicals to replace PFOA, a legacy PFAS. Policy makers can use the GenX chemicals toxicity assessment along with exposure information and other important considerations to determine if, and when, it is appropriate to take action to reduce exposure to GenX chemicals.

Background

What are PFAS?

PFAS are synthetic chemicals that have been manufactured and used by many different types of industries since the 1940s. PFAS are synthesized for many different uses including firefighting foams, coatings for clothes and furniture, and food contact substances. PFAS are also used in industrial processes and applications, such as manufacturing other chemicals and products. There are thousands of different PFAS, some of which have been more widely used and studied than others. PFOA and PFOS, for example, are two of the most widely used and studied chemicals in the PFAS group. These have been replaced in the United States with other PFAS, such as GenX chemicals, in recent years. Although PFAS chemical compositions vary, one common characteristic is that they break down very slowly and can accumulate over time in people, animals, and the environment. Because of their persistence, PFAS are sometimes referred to as “forever chemicals.”

What are GenX Chemicals?

GenX is a trade name for a processing aid technology used to make high-performance fluoropolymers without the use of PFOA. HFPO dimer acid and its ammonium salt are the major chemicals associated with the GenX processing aid technology. PFOA has eight carbon atoms and is considered a “longer chain” PFAS while GenX chemicals have six carbon atoms and are considered “shorter chain.” Because GenX chemicals can be used as a replacement for PFOA, they may be used in a similar fashion in the manufacture of the same or similar fluoropolymer end products. However, EPA does not have specific information from manufacturers on which commercial products rely on GenX chemicals as a processing aid. GenX chemicals have been found in surface water, groundwater, drinking water, rainwater, and air emissions.

How are people exposed to GenX chemicals?

People can be exposed to GenX chemicals through several different pathways, including drinking contaminated water and inhaling contaminated air. EPA’s final assessment for GenX chemicals focuses

solely on the potential human health effects associated with oral exposure (i.e., via drinking water). GenX chemicals have similar persistence in the environment as longer chain PFAS, such as PFOA and PFOS. They are also more mobile than longer chain PFAS, leading to the potential to result in exposure at greater distances than legacy PFAS in off-site transport or in ground water. GenX chemicals do not appear to accumulate as much in humans as longer chain PFAS, such as PFOA and PFOS. EPA's GenX toxicity assessment does not consider potential effects from exposure to GenX chemicals as part of a mixture (with different PFAS or other chemicals).

What health effects are associated with exposure to GenX chemicals?

Animal studies following oral exposure have shown health effects including on the liver, kidneys, the immune system, development of offspring, and an association with cancer. Based on available information across studies of different sexes, lifestyles, and durations of exposure, the liver appears to be particularly sensitive from oral exposure to GenX chemicals.

What is an EPA toxicity assessment?

A toxicity assessment is a written summary of the potential health effects associated with a chemical. The GenX chemicals toxicity assessment is similar to assessments developed under EPA's Integrated Risk Information System (IRIS) toxicological reviews (<https://www.epa.gov/iris>). The GenX chemicals toxicity assessment provides hazard identification, dose-response information, and derives toxicity values called oral reference doses (RfDs) for chronic and subchronic exposures. The GenX chemicals toxicity assessment draft underwent external peer review and public comment.

Toxicity assessments, along with exposure information and other important considerations to assess potential health risks, allow policy makers to determine if, and when, it is appropriate to take action to reduce exposure to a chemical. For example, in the future, EPA can gather information to characterize human exposure to GenX chemicals via drinking water, which will enable the agency to develop a drinking water health advisory. EPA has previously developed health advisories for two other PFAS: PFOA and PFOS (<https://www.epa.gov/ground-water-and-drinking-water/drinking-water-health-advisories-pfoa-and-pfos>).

EPA will continue to work with other federal, state, tribal, and local partners to provide technical assistance as they consider the final GenX chemicals toxicity values in their relevant exposure scenarios. All users of this toxicity assessment are advised to review the information provided in the document to ensure that the assessment is appropriate for the types of exposures and circumstances in question and that the risk management decisions would be supported by the assessment.

GenX Chemicals Toxicity Assessment

What are the reference doses for GenX chemicals?

As part of EPA's toxicity assessment, the agency has developed chronic and subchronic RfDs for GenX chemicals (Table 1). A reference dose is an estimate of the amount of a chemical a person can ingest daily over a lifetime (chronic RfD) or less (subchronic RfD) that is unlikely to lead to adverse health effects in humans. EPA will continue to work with state, tribal, and local partners to provide technical

assistance should they wish to use the final values with relevant exposure scenarios to support risk management decisions.

Table 1. Final GenX Chemicals Reference Doses (RfDs)

PFAS Chemical	Subchronic RfD (mg/kg-day)	Chronic RfD (mg/kg-day)
GenX Chemicals (EPA 2021)	0.00003 (3 x 10 ⁻⁵)	0.000003 (3 x 10 ⁻⁶)

To learn more about EPA’s human health risk assessment practices including the development of toxicity values, go to: <https://www.epa.gov/risk/conducting-human-health-risk-assessment>.

How does the final GenX chemicals assessment differ from the 2018 public draft version?

EPA’s final 2021 GenX chemicals assessment uses the state-of-the-art systematic review process established by EPA’s Office of Research and Development, incorporates new data available since 2018, and applies revised uncertainty factors. These changes resulted in the final chronic RfD for GenX chemicals of 0.000003 mg/kg-day which is lower than the 2018 draft chronic RfD (0.00008 mg/kg-day). The decrease in the chronic RfD occurred because EPA took into account new studies and analyses published after the completion of the 2018 draft assessment.

GenX Chemicals and Drinking Water

Can GenX chemicals affect my drinking water?

If you are concerned about GenX chemicals in your drinking water, EPA recommends you contact your local water utility to learn more about your drinking water and to see whether they have monitoring data for GenX chemicals or can provide any specific recommendations for your community. If you own a private well, EPA recommends learning more about how to protect and maintain your well for all contaminants of concern. For information on private wells visit: www.epa.gov/safewater.

Does EPA require public water systems to have drinking water samples analyzed for GenX chemicals?

Yes. On December 27, 2021, EPA issued a final rule requiring certain systems to monitor for 29 PFAS, including GenX chemicals, over the period of January 2023-December 2025 and report final results through 2026 (for more information, go to: <https://www.epa.gov/dwucmr/fifth-unregulated-contaminant-monitoring-rule>). This action will provide EPA, states, and communities with scientifically valid data on the national occurrence of these contaminants in drinking water.

Does EPA plan to issue a drinking water regulation for PFAS?

Yes, on March 14, 2023, EPA announced a proposed National Primary Drinking Water Regulation for six PFAS, including GenX chemicals. The agency expects to finalize the regulation by the end of 2023. For more information on the proposed regulation go to: <https://www.epa.gov/sdwa/and-polyfluoroalkyl-substances-pfas>.

Where can I find more information?

To view the final GenX chemicals toxicity assessment, EPA's response to public and peer review comments, and other related information on GenX chemicals, go to: <https://www.epa.gov/pfas/genx-toxicity-assessments-documents>.

To view the 2022 Drinking Water Health Advisory for GenX chemicals, go to: <https://www.epa.gov/sdwa/drinking-water-health-advisories-genx-chemicals-and-pfbs>

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