PFAS Toxicological Profile Key messages
(Created collaboratively by the following agencies: ATSDR, EPA, DOD, NIH, NIEHS, FDA, USGS)

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Summary statement

The Agency for Toxic Substances and Disease Registry (ATSDR) publishes Toxicological Profiles (or Tox Profiles) as reference guides that provide information about contaminants. Tox Profiles include chemical and physical properties of the toxic substance, sources of exposure, routes of exposure, minimal risk levels (MRLs) (explained on page 8), health effects -- including those of children, and how the contaminant might interact in the environment. Although Tox Profiles are available to the general public, the primary users are expected to be researchers and health professionals, particularly health assessors at the regional and/or state level. Health assessors use MRLs as screening values to help identify exposures that could be potentially hazardous to human health.

ATSDR has worked collaboratively with the Environmental Protection Agency (EPA), the Food and Drug Administration (FDA), the National Institute of Health (NIH), the National Institute of Environmental Health Sciences (NIEHS), the US Geological Survey (USGS), and the Department of Defense (DOD) to create this set of talking points about a family of chemicals referred to as per- and polyfluoroalkyl substances (PFAS) and the Tox Profile for perfluoroalkyl substances (PFAS) a subset of the PFAS family. This is a living document and can be used by each agency for talking points, web content, community outreach, or other modes of communication to the general public.

What are PFAS?

PFAS are a large group of manmade chemicals that have been used in industry and consumer products worldwide since the 1950s. PFAS are resistant to grease, water, and oil, and have been used in products like carpet and fabric, as well as a coating for paper and cardboard packaging. These chemicals are also found in firefighting foam. Some chemicals that are in this group include:

- perfluorooctanoic acid (PFOA)
- perfluorooctane sulfonic acid (PFOS)
- perfluorononanoic acid (PFNA)
- perfluorohexane sulfonic acid (PFHxS)
- hexafluoropropylene oxide (HFPO)
- Perfluorobutane Sulfonate (PFBS)
- GenX

Historically, the two PFAS made in the largest amounts in the United States were PFOA and PFOS. In 2012, an initiative by the U.S. Food and Drug Administration (FDA) announced that manufacturers of some types of PFAS substances agreed to cease sale of all grease-proofing agents containing selected PFAS compounds into the marketplace. This means that the affected products will no longer be sold for application on paper or paperboard intended for food contact use.

Most companies have stopped making or reduced the use of PFOA and PFOS chemicals, but people and animals can still be exposed to the substances. Even though recent efforts to remove PFOA and PFOS have reduced the likelihood of exposure, many products might still contain these substances as well as other chemicals in the PFAS family. In addition, because many PFAS do not break down easily in air, soil, and water, the substances can persist in the environment for decades.

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Most people in the United States and in other industrialized countries have some amount of PFAS in their blood. However, these are usually at low levels. Because PFAS continues to be found in some foods and food packaging and are present in the environment (air, water, soil, etc.), completely eliminating exposure is unlikely.

How could people be exposed to PFAS?
People can be exposed to PFAS by:

- Drinking contaminated municipal water or private well water;
- Eating fish caught from water contaminated by PFAS (PFOS, in particular);
- Swallowing contaminated soil or dust;
- Breathing in contaminated dust particles or volatile PFAS;
- Eating food that was packaged in material that contains PFAS;
- Using some consumer products such as certain types of non-stick cookware, stain-resistant carpeting, and water-repellant clothing that contain PFAS or
- Absorbing PFAS through their skin (from contaminated water or soil).

Some specific groups, such as workers in facilities that make or use PFAS, can be exposed to higher amounts of these chemicals and have higher levels in their blood than the average person. In addition, people in some communities near factories that made or used PFAS might have been exposed to higher levels of these substances in their drinking water or soil. This is also true for people who worked or lived in areas that used certain types of firefighting foam that spread into the environment.

Infants might also be exposed *in utero* and through breastfeeding because these chemicals have been found in breast milk. Infants drinking formula made with water may be another route of exposure. In addition children can be exposed to PFAS in carpets that had been treated with PFAS for stain resistance. Children are more at risk from exposure to carpets because they are closer to the ground and often play on the floor or put things in their mouths.

Though there are multiple sources of PFAS exposure, research suggests that due to restricted use, exposure to PFOA and PFOS from today's consumer products is usually low.

What are the negative health effects of PFAS exposure?
Although a number of scientific studies have been completed, outcomes of these studies have not been consistent and additional factors still need to be considered. More research is needed to fully understand the possible negative health effects related to PFAS exposure. As of today, based on studies in humans and animals, scientists believe that some of the non-cancer health effects from PFAS exposure include:

- Increased cholesterol levels;
- Decrease in response from the body to some vaccines (immune system);
- Increased risk of thyroid disease;
- Decreased fertility in women;
- Increase in the risk of high blood pressure or pre-eclampsia in pregnant women; or
- Lower infant birth weights.

While numerous studies have examined possible relationships between levels of PFAS in blood and harmful health effects in people and animals, most of these studies analyzed only a small number of

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chemicals in the PFAS family. To date, scientists have learned that not all PFAS have the same health effects.

Some (but not all) PFAS build up in the human body. The levels of many PFAS go down slowly over time once exposure stops. Scientists across multiple federal agencies are studying how different amounts of PFAS in the body over time might affect human health. In addition, investigators are actively studying whether being exposed to multiple PFAS chemicals at the same time have health effects that are additive.

It is important to remember that the likelihood of adverse health effects depends on several factors, such as the concentration of PFAS, as well as the frequency and duration of exposure. More frequent exposure can increase risk. Higher concentration and length of time exposed can lead to increased risk.

How are animal studies used to predict PFAS health effects in people?
One way to learn about whether PFAS will harm people is to conduct studies in laboratory animals. It's important to note that humans and animals might react differently to PFAS, and not all effects observed in animals might occur in humans. To account for this difference, scientists use uncertainty factors to provide a conservative and health protective interpretation of the exposures in laboratory animal studies when extrapolating to human exposures.

PFOA and PFOS are the most studied members of the PFAS family. Most animal studies have tested doses of PFOA and PFOS that are **higher** than the levels found in the environment to which humans are exposed. The studies have found that PFOA and PFOS can cause damage to the liver, the testes, and the immune system, as well as producing changes in thyroid hormones and reproductive hormones. PFOA and PFOS have also caused birth defects, delayed development, and newborn deaths in lab animals.

If scientists do not have information about the health effects information in humans, ATSDR assumes that health effects observed in animals from exposure to the chemical could also cause similar health effects in humans exposed to the same chemical, if the health effects are biologically plausible (could happen) and relevant to humans.

What is an uncertainty factor?
Because the scientific information on a hazardous substance are often limited to animal studies and might not include human studies, uncertainty factors might be applied as part of the Minimal Risk Level (MRL) calculations resulting in lower, more conservative risk values. Uncertainty factors help us account for differences among what is observed in animals, as compared to humans; or when we don't know certain things about how a chemical might affect a sensitive population (for example, the very young, or people who might have other health problems); or when we do not have complete information about the exposure levels causing health effects. These uncertainty factors were used in deriving the MRLs for the four PFAS discussed below.

How do PFAS affect the immune system?
The National Toxicology Program (NTP) reviewed animal and human studies and concluded that both PFOA and PFOS could harm immune function in people. The conclusions are based on a high level of evidence that PFOA and PFOS suppressed the antibody response and affected multiple other aspects of the immune system. More information about the effect of PFAS on the immune system can be found here. (https://ntp.niehs.nih.gov/pubhealth/hat/noms/pfoa/index.html)

Can PFAS cause cancer?
The International Agency for Research on Cancer (IARC) has classified PFOA as possibly carcinogenic (possibly causing cancer) to humans; it has not evaluated whether other PFAS chemicals might also cause cancer. The Environmental Protection Agency (EPA) suggests that there is evidence that both PFOA and PFOS are possibly carcinogenic to humans (might have the potential to cause cancer). Scientists across multiple federal agencies are continuing studies to look more closely at this issue.

Studies do not clearly show whether all PFAS could cause cancer in people. Studies in humans suggest that people exposed to high levels of PFOA and PFOS might have increased risk of cancer, including kidney cancer and testicular cancer. However, these studies are not consistent and might not have looked at other factors, such as smoking.

Studies in animals have shown that PFOA and PFOS can cause cancer in the liver, testes, pancreas, and thyroid. However, some scientists believe that humans might not develop the same cancers as animals. Cancers typically take several years to decades to develop, and it can be difficult to link them directly to an environmental exposure.

What do we know about PFAS in people's blood?
Since 1999, CDC has measured several types of PFAS in the U.S. population as part of the National Health and Nutrition Examination Survey (NHANES). With a decrease in production and use of some PFAS, the national PFAS levels of those types studied have also gone down over time, while others have remained stable or increased. In particular, PFOS and PFOA are two PFAS that were widely used and have been measured through the survey.

According to NHANES data many Americans have detectable levels of PFAS in their blood.

- From 1999 to 2014, blood PFOA levels declined by more than 60%. (ref: www.cdc.gov/exposurereport)
- From 1999 to 2014, blood PFOS levels declined by more than 80%. (ref: www.cdc.gov/exposurereport)

Should I get my blood tested for PFAS?
According to NHANES data, many people in the United States have detectable levels of one or more types of PFAS in their blood, especially PFOS and PFOA. However, test results cannot tell you if you might have PFAS-related health problems or diseases now, or predict if you will have PFAS-related health problems in in the future. The test results will only tell you and your health care provider if you have been exposed[3] to PFAS. These are not tests that are regularly offered by doctors or public health departments.

Health care providers or other health professionals (for example, regional Pediatric and Environmental Health Specialty Units, or PEHSUs) are a good starting point if you want or need to know your PFAS levels.

When is blood testing for PFAS useful?
Blood tests for PFAS are most useful when they are part of either a scientific investigation or a health study.

A health study can show the levels of PFAS in people within a community that might have been exposed to the substances. For example, scientists can use the results to estimate the highest and

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lowest levels of PFAS levels in a specific community or PFAS levels in specific groups, such as children. Additional information can show other factors that might affect test results, like your age and job, where you get your drinking water, and how long you have lived in the area.

Scientists can compare investigation results to those in other communities, track trends in exposure over time, and use results to show the need for health studies or possible actions in the future.

How can I reduce my exposure to PFAS?
PFAS are present at low levels in some consumer products and food packaging, as well as the environment (air, water, soil, etc.), so you probably cannot prevent PFAS exposure altogether. However, there are steps you can take to reduce your exposure.

- If your drinking water contains PFOA or PFOS individually, or combined at a level above the EPA Lifetime Health Advisory level, consider using an alternative or treated water source for any activity in which you might swallow water, such as: drinking, food preparation and cooking, brushing teeth, and preparing infant formula.
- If you learn that your local surface water (e.g., lake or pond) is contaminated, and you rely on local fish as part of your diet, follow fish advisories that tell people to stop or limit eating fish from waters contaminated with PFAS or other compounds.
- Read consumer product labels; you can choose to avoid using products with PFAS if they are labeled.
- Consider vacuuming more frequently to help reduce the amount of indoor dust.

If you do not know about PFAS levels in your water, and you are concerned, you can ask your local health department or local water department about your water source. To provide Americans, including the most sensitive populations, with a margin of protection from a lifetime of exposure to PFOA and PFOS from drinking water, EPA has established the Lifetime Health Advisory levels at 70 parts per trillion. You can learn more by visiting: << https://www.epa.gov/ground-water-and-drinking-water/drinking-water-health-advisories-pfoa-and-pfos>>. Consult the EPA website for information about water filters in your home or in your community.

Consumers are encouraged to follow EPA recommendations to reduce personal exposure to PFAS. States may set levels for action at different levels or use other measures to estimate community risk or action.

Can a person drink tap water containing PFOA or PFOS at or below the level of the health advisory every day of their life and not expect adverse health effects from these chemicals?
Yes, the EPA health advisory level offers a margin of protection for all Americans from adverse health effects for a lifetime of exposure to PFOA and PFOS in drinking water at this level.

Can PFOA and/or PFOS be boiled out of my water?
No. PFOA and PFOS cannot be removed by heating or boiling water. However, there are steps you or your city water provider can take to reduce these contaminants. In some cases, drinking water systems might be able to reduce concentrations of PFAS, including PFOA and PFOS, by closing contaminated wells or changing rates of blending of water sources. Alternatively, public water systems can treat source water with activated carbon or high-pressure membrane systems (*e.g.*, reverse osmosis) to remove PFOA and PFOS from drinking water. Consult the EPA website for information about water

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filters in your home or in your community. For more information, visit the EPA or NSF websites (http://www.nsf.org/newsroom/nsf-international-certifies-first-water-filters-pfoa).

How is CDC/ATSDR involved in PFAS work?
CDC/ATSDR is involved in PFAS work either directly or by supporting local, territorial, tribal, state, and federal partners. CDC/ATSDR:

- Offers technical assistance to help state and local health departments learn more about PFAS and how to investigate PFAS exposure in their communities.
- Works with communities to understand how to reduce levels to below EPA's lifetime health advisory values.
- Is writing a Draft **Toxicological Profile** that will summarize what we know about PFAs that will offer an interpretation of the latest available published studies on PFAs. Toxicological Profiles (or Tox Profiles) are reference guides that provide information about a toxic substance, such as its chemical and physical properties, sources of exposure, routes of exposure, minimal risk levels (explained below), children's health, and general health effects, as well as how the substance might interact in the environment.

What is a Toxicological Profile?
Congress mandates that ATSDR produce Tox Profiles that include an examination, summary, and interpretation of available studies of the health effects of a hazardous substance. The primary users of these documents are expected to be researchers and health professionals, including health assessors at the regional and state level. Profiles go to peer review (shared with experts in the field) before they are released for public comment. If there are significant revisions as a result of the public comments, the profiles are again peer reviewed before releasing as a final.

Toxicology Profiles are developed in two stages:

1. ATSDR first produces a **draft** profile and announces the release of these draft profiles in the Federal Register for a 30-90 day public comment period.
2. After the comment period, ATSDR considers all input, revises the documents, and then finalizes the profile for posting on the ATSDR website.

The studies considered for review are held to the highest standards of data collection, and the peer-review process validates that they are scientifically accurate and reflect current scientific or laboratory best practice with consistent, factual results.

When are Toxicological Profiles made or revised?
By Congressional mandate, ATSDR produces toxicological profiles for hazardous substances found at National Priorities List (NPL) sites. These hazardous substances are ranked based on frequency of occurrence at NPL sites, toxicity, and potential for human exposure. Toxicological Profiles are developed from a priority list of 275 substances. ATSDR also prepares upon request Toxicological Profiles for the Department of Defense (DOD) and the Department of Energy (DOE) on substances related to Federal sites.

When new studies (scientific literature) are published that show new data or in some other way contribute new, significant understanding of the toxicology of the chemical, ATSDR decides if new toxicological profiles are warranted, or if existing profiles should be revised. ATSDR issues a notice in the Federal Register to request nominations and comments on the suggested substances for review.

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An internal ATSDR workgroup then reviews the literature and determines what can be updated and prioritized based upon new literature and public comment. ATSDR also sends letters to stakeholders, including other federal agencies, to request comments and/or nominations on the list of priority substances.

Which chemicals are included in the PFAS Tox Profile?
The chemicals in the current Tox Profile are referred to as perfluoroalkyls (PFAS). PFAS are a subset of the much larger family of PFAS that includes both per-and polyfluoroalkyl substances.

Four of the individual chemicals were targeted for Minimal Risk Level (MRL) development:

- Perfluorooctanoic acid (PFOA)
- Perfluorooctane sulfonic acid (PFOS)
- Perfluorononanoic acid (PFNA)
- Perfluorohexane sulfonic acid (PFHxS)

What is a Minimal Risk Level?
A Minimal Risk Level (MRL) is an estimate of the amount of a chemical a person can eat, drink, or breathe each day without a detectable risk to health. MRLs are intended to serve as a tool to help public health professionals determine areas and populations potentially at risk for health effects from exposure to a particular chemical.

It's important to note that MRLs are a screening tool that help identify exposures that could be *potentially* hazardous to human health. Exposure above the MRLs does not mean that health problems will occur. Instead, it may act as a signal to health assessors to look more closely at a particular site where exposures may be identified.

MRLs do not define regulatory or action levels for ATSDR. When health assessors find human exposures are occurring at higher than the set MRL, it means that they may want to look more closely at the human exposures. It does not mean that people will become sick from those exposures.

The way the MRL is calculated can change depending on type and quality of data available. MRLs can be set for 3 different time periods (the length of time people are exposed to the substance): acute (about 1 to 14 days), intermediate (from 15-364 days), and chronic (exposure for more than 365 days). ATSDR has developed over 400 human health minimal risk levels (MRLs). MRLs are developed for health effects other than cancer.

Proposed MRLs undergo a rigorous review process. They are reviewed by ATSDR's expert toxicologists, an expert panel of external peer reviewers, an interagency MRL workgroup, with participation from other federal agencies, including NCEH (CDC's National Center for Environmental Health), ATSDR, NTP (National Toxicology Program), NIOSH (National Institute of Occupational Safety and Health), and EPA; and are then submitted for public comment.

What are the MRLs for PFAS studied in the PFAS Tox Profile?
This PFAS Toxicological Profile contains both new and revised draft intermediate oral MRLs for specific PFAS substances (table below):

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Intermediate oral (15 to 364 days) MRLs	
REVISED level	**Previous level**
PFOA: $3x10^{-6}$ mg/kg/day	(previous level $2x10^{-5}$ mg/kg/day)
PFOS: 2×10^{-6} mg/kg/day	(previous level $3x10^{-5}$ mg/kg/day)

This version also offers new draft MRLs.

Intermediate oral (15 to 364 days) MRLs	
NEW level	**Previous level**
PFHxS: $2x10^{-5}$ mg/kg/day (no previous level set)	None
PFNA: $3x10^{-6}$ mg/kg/day(no previous level set)	None

All four MRLs in the updated version of the Tox Profile are considered draft until they have been finalized following the public comment period.

How are these MRLs calculated?
Scientists review data about the chemical, including:

- The ways that people could be exposed to the chemical (eating, drinking, breathing);
- How long people or animals are exposed the chemical, and any health effects;
- The concentration of the chemical the person is exposed to;
- How old the person is when they are exposed (a newborn? a child? an older person?).

All of these data are then reviewed to calculate MRLs. The calculations can change depending on several things, including:

- Who are we trying to protect by setting a level?
- Are there certain populations (such as infants) that might be more vulnerable to health effects?
- Do we know how people are being exposed, and for how long?
- What kinds of health problems do we think could happen with exposure?
- Are there similar chemicals that might cause health problems that we already know about?
- What is the quality of the data being reviewed, and do the studies show consistent health effects?

What has been revised in the MRLs?
The 2018 draft of the PFAs Tox Profile updates the current intermediate duration MRLs for two chemicals (i.e., PFOA and PFOS) and proposes new intermediate duration MRLs for two additional chemicals (i.e., PFHxS and PFNA) in response to the new and updated scientific data.

These newer draft MRLs are set lower than previously because they now take into consideration that immune effects might be an additional more sensitive health effect than developmental health effects alone. Exposure above the MRLs does not mean that health problems will happen.

MRLs listed in the PFAS Tox Profile are developed for health effects other than cancer. Scientists across multiple federal agencies are continuing studies to look more closely at health effects of these and other PFAS exposures and considering which risk management tools (e.g., health advisories, technical guidance, cleanup standards, or other enforceable regulations) are necessary to protect human health.

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What are the differences between ATSDR's MRL and EPA's Health Advisory?

Federal agencies have a variety of tools that provide federal, state, tribal, and local governments; health professionals; and the public with information about how a chemical might affect a person's health. All of them can be used together to create a more complete picture of how to assess health risks and protect people from future exposures.

ATSDR's MRLs and EPA's Health Advisories (HAs) are two different tools that are used in different situations. MRLs are intended to be used to help public health professionals determine areas and populations potentially at risk for health effects from exposure to a particular chemical. An MRL is an estimate of the amount of a chemical a person can eat, drink, or breathe each day without a detectable risk to health. MRLs are unique to each substance. These are used as screening levels by public health professionals. MRLs do not define regulatory or action levels for ATSDR, nor for other agencies. When health assessors find human exposures are occurring at higher than the set MRL, it means that they may want to look more closely at the human exposures. It does not mean that people will become sick from those exposures. ATSDR may work with EPA at a national or regional level to more fully examine these exposures. MRLs and HAs are presented in different units because MRLs are daily doses while HAs are concentrations. Mg/kg/day is a unit of daily dose, while ppt is a unit of concentration.

Drinking water HAs, on the other hand, provide information on contaminants that can cause human health effects and are known or anticipated to occur in drinking water. EPA uses reference doses (RfDs) to develop HAs. RfDs estimate a daily exposure to the human population (including sensitive subgroups, such as infants) that is likely to be without an appreciable risk of harmful effects *during a lifetime*. HAs are non-enforceable and provide technical guidance to states agencies and other public health officials who have the primary responsibility for overseeing drinking water systems, with information on the health risks of chemicals, so they can take the appropriate actions to protect their residents from harmful exposure.

Summary statement

The U.S. Government is working in a coordinated way to address PFAS contamination across the nation. In the past few years, researchers in state and federal agencies, in academia, and in industry have been working to develop new data to improve our understanding of the toxicity of these compounds in the environment and how often they might be found.

Different agencies play different roles in protecting public health, and the multiple tools and measures they develop are used for different purposes. It is important to note that the values that EPA and ATSDR develop are guidelines rather than mandates. All states have the authority to set their own limits for environmental contaminants and many states have already developed their own guidance values for PFAS.

Federal agencies have a variety of tools that provide other federal agencies, states, tribes, local governments, health professionals, and the public with information about how a chemical might impact a person's health. All of them might be used together to create a more complete picture of how to assess health risks and protect people from future exposures.

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