PFAs Toxicological Profile Key messages

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The Agency for Toxic Substances and Disease Registry (ATSDR) publishes Toxicological Profiles (or Tox Profiles). 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, children's health, and general health effects, as well as how the substance might interact in the environment.

ATSDR has released a draft Tox Profile that will summarize what we know about PFAs and will offer an interpretation of the latest available published studies on PFAs. **To learn more about PFAS chemicals and potential health effects, click here.**

More about Tox Profiles

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.

Toxicological 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.

Creation of Tox Profiles

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. 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.

In the Tox Profiles**,** ATSDR develops comparison values to help identify chemicals that may be of concern at hazardous waste sites. One type of these values is called minimal risk levels (MRLs).

More about Minimal Risk Levels

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 this PFAS Tox Profile?

This PFAs Toxicological Profile contains both new and revised draft intermediate oral MRLs for specific PFAs substances (table below):

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.

What has been revised in the PFAs 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.

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, as well as 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.

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.

Government Agencies are Working Together to Protect Public Health

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.