Public health drinking water screening levels for PFAS

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Michigan PFAS Action Response Team Human Health Workgroup

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Executive Summary

The Michigan Department of Health and Human Services (MDHHS) serves to protect the health of the residents in our state. Our role extends beyond regulations to ensure the best available science is employed through in-depth risk assessments at all sites of contamination across the state, identifying who may be exposed, how they may be exposed, and what protections should be employed – be it mitigation or education – to ensure even the most vulnerable residents of our state are protected from harm from contaminants – regardless of source.

Providing public health perspectives and recommending protective actions at sites of contamination is a role MDHHS has been undertaking for decades with myriad chemicals at myriad sites. Although per- and polyfluoroalkyl substances (PFAS) are classified as an emerging contaminant, the method by which we determine screening levels, assess the risk, and recommend protective actions are tried, true, and recognized by state and federal agencies alike.

These screening levels provide a common well-studied baseline for our toxicologists to utilize as they conduct risk assessments and provide guidance to local health departments and/or implement public health actions directly at sites under investigation.

This document provides an in-depth look into the process that MDHHS employed to develop the public health drinking water screening levels for several PFAS, including the selection of the critical studies that were identified by the US Environmental Protection Agency, the Agency for Toxic Substances and Disease Registry, and several other states who are at the forefront with Michigan proactively responding to PFAS.

The following document is broken into nine sections as described below. A comprehensive Table of Contents follows.

- **Section 1: Risk Assessment 101**
  An overview of terms and methods used in this document.

- **Section 2: Selection of toxicity values**
  Discussion of state and federal agency values based on the available information and risk assessment approaches at the time of development, as well as a look into the sensitive toxicological endpoints with additional uncertainty factors added to protect all individuals and to protect for the additional health effects that may not be fully investigated at this time or are seen at higher exposure doses.

- **Section 3: Methodology, exposure scenario, and other parameters used to develop public health drinking water screening levels**
  A comprehensive review of state and federal agencies' levels and methods, identifying where differences exist as we select each decision point using health-protective and supportable scientific information and risk assessment approaches. This section also explains our use of the toxicokinetic model, the design of which is intended to prevent elevated PFAS exposure at all life stages and to future generations. This model was developed by Minnesota Department of Health and ensures that a child, at any time in their lifespan, including while breastfeeding (which will also be protective for formula-fed infants), will not have exposure that could increase

the risk of developing health effects. This model allows for protection of all life stages.

- **Section 4: Relative Source Contribution**
  An in-depth look at the Relative Source Contribution selected for this assessment. Relative Source Contribution (RSC) takes into account where else people may be exposed to a certain chemical in their everyday lives, excluding the source of concern for which the screening levels are being developed (in this case, drinking water).

- **Section 5: Summary of parameters selected for public health drinking water screening level development**
  An overview of MDHHS's decision points using health-protective and supportable scientific information and risk assessment approaches.

- **Section 6: Public Health Drinking Water Screening Levels for PFOA, PFOS, PFNA, PFHxS, PFBS**
  MDHHS's current public health drinking screening levels for PFOA, PFOS, PFNA, PFHxS, and PFBS can be found in this section. This public health drinking screening levels are based on current best available science. This body of science and knowledge is ever changing, which can lead to apparent discrepancies in screening levels across agencies and time. MDHHS will continue to remain abreast of the best available science and will update these screening levels and perhaps add additional public health drinking water screening levels as science dictates.

- **Section 7: References**

- **Section 8: Addendum - MPART Human Health Working Group Product**
  A summary of PFAS toxicological evaluations supporting health-based drinking water screening levels.

- **Section 9: Addendum - Matrix of Agency Screening Levels Worksheet**

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Section 1: Risk Assessment 101

Target Population Selection

The development of environmental chemical screening levels begins with determining the objectives for the levels, including the target population. For example, if the substances may be more harmful to children than adults than it would be important to use a child exposure scenario to protect that target population. The risk assessment describing the calculation of the screening levels would include decision points designed to achieve those objectives. Changing the objectives can result in changes in calculation methods and the resulting screening levels.

Components of Screening Levels

The risk assessment, describing the calculation of the screening levels, is made up of several components including the toxicity value, exposure scenario, and methodology. Each component needs to be critically evaluated with justifications for each input. Data-derived inputs are the most scientifically defensible. It is not uncommon to have inputs for which there is no data, and in those cases default risk assessment inputs are typically used.

Intent of Public Health Drinking Water Screening Levels

The MDHHS public health drinking water screening levels have a similar intent as the US EPA Maximum Contaminant Level Goal (MCLG), which are non-enforceable public health goals calculated to protect sensitive populations. The US EPA will set the MCLG to a value of zero when there is "evidence the chemical may cause cancer" or if "there is no dose below which the chemical is considered safe"[1] . Just like the MCLG, the MDHHS public health drinking water screening levels do not include feasibility concepts of cost or treatment technology.

The document describes the components that MDHHS considered when determining the screening levels for these PFAS, as well as the general assumptions that go into each of the calculations for the proposed MDHHS PFAS public health drinking water screening levels.

Unacceptable Risk

The MDHHS public health drinking water screening levels provide individuals who have PFAS in their drinking water a comparison to consider their level of risk tolerance compared to a health protective and science-based value. Individuals make choices each day that involve some degree of risk to them and their families. Similar to other risks, a person needs to decide how much risk is acceptable or unacceptable to them. MDHHS provides health education materials that are intended to allow everyone to understand they have a personal choice, there is science-based information that can help inform their choice, and there are options to limiting their exposure to the extent possible.

Critical Study & Co-critical Studies

When developing new toxicity values, toxicologists start by looking at scientific studies that have been conducted and published in journals that have high integrity. The studies are reviewed and one is selected to be the critical study for the purpose of developing the toxicity value. Sometimes, if multiple adverse health effects are identified, more than one study may be selected.

[1] https://www.epa.gov/dwregdev/how-epa-regulates-drinking-water-contaminants

- Critical study
    - Selected because it has the most sensitive health effect observed in all of the studies.
        - Typically, this is the health endpoint resulting from the lowest exposure dose.

- Multiple co-critical studies
    - Used when different health effect result from relatively similar exposures.
    - A toxicity value may be selected that represents an average of these exposures, if needed.

Laboratory animal studies are often selected as the critical study. Animal studies ensure exposure amounts to contaminants are controlled and adverse health effect have likely been caused by exposure to those controlled amounts. In some situations, humans have been exposed to a contaminant and health effects have been linked to exposure to that contaminant. In these cases, epidemiological studies can provide information on potential health effects in humans. This weight of evidence can provide additional support to adverse health effects seen in animal studies. In rare situations, a human epidemiological study can be used as the critical study, but only if information on the human exposure is very detailed.

If the study was conducted in laboratory animals, health effects identified in the critical study should be biologically relevant and plausible for humans. Using that critical study, a "point of departure" is identified.

Point of Departure (POD)

The point of departure (POD) may be the amount of an administered dose, a modeled dose, or a serum level. Per US Environmental Protection Agency (US EPA), a point of departure can be defined three ways:

- No Observed Adverse Effect Level (NOAEL)
    - The highest exposure level at which there are no biologically significant increases in the frequency or severity of adverse health effects in the exposed population compared to an appropriate unexposed comparison population; although some health effects may be seen at this level, they are not considered adverse or precursors of adverse effects.

- Lowest Observed Adverse Effect Level (LOAEL)
    - The lowest exposure level at which there are biologically significant increases in frequency or severity of adverse health effects in the exposed population compared to an appropriate unexposed comparison population.

- Benchmark Dose Lower Limit (BMDL)
    - The smallest quantity or concentration of a substance associated with a specified low (generally in the range of 1% to 10%) incidence of risk for a health effect or specified measure or change of a biological effect when compared to the background occurrence frequency of the effect.

To develop a toxicity value, the point of departure is divided by two types of factors:

- Uncertainty factor
    - Individual uncertainty factors range from 1 (greater certainty) to 10 (greater uncertainty)
    - Accounts for uncertainties due to the
        - potential variability among humans (intraspecies variability)
        - potential species differences between laboratory animals and humans (interspecies differences)
        - use of a point of departure in the critical study that resulted in adverse health effects being observed (LOAEL), instead of none observed (NOAEL)
        - use of a shorter time span than what would be considered chronic or a lifetime of exposure in the critical study

- Modifying factors
    - Individual modifying factors ranges from 1 (greater certainty) to 10 (greater uncertainty)
    - Accounts for uncertainties due to
        - gaps in the knowledge base, such as too few studies evaluating the development of a health endpoint (this may also be grouped with the uncertainty factors by different agencies)
        - other uncertainties identified but not otherwise addressed by the uncertainty factors

The factors are determined based on design of the critical study or studies, other toxicity or related information available, and the methods available to determine the toxicity value. The total uncertainty is the product of the individual uncertainty and modifying factors.

Toxicity values

Toxicity values can take myriad forms to serve many purposes, but the goal of all is to identify a number that can be used as a basis for toxicologists to determine how much exposure to a substance is unlikely to result in an unacceptable risk of developing health effects over a defined period of time, typically a lifetime. Toxicity values are based on a critical study or studies and determined by dividing the point of departure by the product of the uncertainty and modifying factors.

The types of toxicity values include:

- US EPA's Reference Doses (RfD)
    - An estimate (with uncertainty spanning up to an order of magnitude) of how much of a certain chemical humans (including the vulnerable populations) can be exposed to daily that is unlikely to cause an increased risk of harmful effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in US EPA's noncancer health assessments.

- Agency for Toxic Substances and Disease Registry's Minimal Risk Levels (MRL)
    - 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 developed for health effects other than cancer.

Toxicity values are used to develop screening levels.

Exposure assumptions or scenario

Since it is impossible for scientists to develop custom exposure assumptions for each of us individually, it is necessary for them to make certain assumptions about exposure pathways and lifestyles in general when calculating public health risk. The assumptions used by most toxicologists come from the *US EPA Exposure Factors Handbook*. This handbook is available at http://1.usa.gov/1Zx5wI2. These assumptions are developed through careful review of numerous scientific studies from a variety of sources and are widely used by toxicologists for this purpose.

- Populations at risk

  Screening level development typically requires selection of the appropriate population for exposure. To ensure these screening levels are sufficiently protective for everyone who consumes water, toxicologists considered PFAS exposures for:

    - infants that may be breast- or formula-fed
    - older children
    - adults

  Concerned about protecting the most vulnerable in the population, MDHHS evaluated toxicokinetic models that account for the transfer of PFAS to fetuses during pregnancy, along with exposure from breastmilk or reconstituted formula made with tap water.

- Because certain chemicals can remain in the body for a long time and chemical exposures that happened well in the past may be harmful to the fetus, MDHHS considered fetal exposure when calculating their screening levels.

- Relative Source Contribution

  Relative Source Contribution (RSC) takes into account where else people may be exposed to a certain chemical in their everyday lives, excluding the source of concern for which the screening levels are being developed (in this case, drinking water). RSCs typically vary between 20% and 80% to account for people's exposure through a source other than the environmental media being considered. For example, use of an RSC of 20% for a drinking water screening level indicates that 20% of an individual's total exposure is assumed to come from drinking water while 80% of the individual's total exposure is assumed to come from other non-drinking water sources.

- Knowing that PFAS comes from many sources besides water – including fish and game – MDHHS used RSCs when calculating their public health drinking water screening levels.

These are used to develop screening levels.

Screening levels

A screening level is the amount of a chemical in an environmental media, like drinking water or soil, for which there is minimal or no risk of developing a health effect for the populations exposed to that chemical.

- Calculations for screening levels and criteria consider the real-world circumstances that result in exposure, including the:
    - multiple ways people can be exposed to the chemical,
    - duration of exposure to the chemical
    - age(s) at time of exposure to the chemical

- The assumptions that toxicologists use to develop these numbers are also determined by:
    - the population(s) they are meant to protect
    - the amount of time this population needs protection (e.g.: is this a one-time exposure with limited impact or is there potential for long-term, exposure)
    - consideration for the life stage/age of population that needs protection
    - negative health effects they are meant to protect against - whether it's cancer or another health problem (aka non-cancer effects)

If people are exposed to levels of a substance above a screening level, that doesn't mean they will necessarily develop health effects. However, exposure to levels above a screening levels means that the margin of safety is reduced and additional evaluation is needed. These numbers are meant to be protective of the population as a whole, based on the available information and current understanding. It's important to note that there is no way to determine if health effects - cancer or not - will occur in any one individual if they are exposed to a chemical.

In many situations, because these screening levels are developed to be protective of all individuals, including formula- and breast-fed infants, when drinking water PFAS concentrations are below the public health drinking water screening levels, no further evaluation is typically required. When a source-specific release is the possible cause of the PFAS detections, a site-specific public health risk assessment may be needed to evaluate the mixture of PFAS and site-specific conditions. Drinking water PFAS concentrations above the screening level indicates further site-specific evaluation is needed, which can lead to public health recommendations. When multiple PFAS are detected, the Agency for Toxic Substances and Disease Registry recommends considering an evaluation of an individual's combined PFAS exposure.

Note, in locations where the source or groundwater plumes have been identified but have not been characterized by size or concentration, public health protective actions may be recommended at any detectable level of any PFAS.

Section 2: Selection of toxicity values

Toxicity values

The term "toxicity value" can refer to reference doses (RfD), Minimal Risk Levels (MRL), or a measure of the exposure to a substance (e.g. serum levels) that below which represents a minimal risk of developing health effects. Toxicity values are based on a "critical" study or studies where health effects are demonstrated with detailed exposure information. Lacking relevant human information, a laboratory animal study is often selected as the critical study as the exposure is well defined. In some cases, multiple co-critical studies are identified, with different health endpoints resulting from relatively similar exposures. Health endpoints identified in the critical study should be biologically relevant and plausible for humans, if the study was conducted in laboratory animals. The determination of biological relevance or plausibility can be made using information from epidemiological studies or from mechanistic data in laboratory animals and human and animal cell lines.[2] Typically, the critical study has the most sensitive health endpoint observed among all of the studies under consideration, i.e., the health endpoint resulting from the lowest exposure dose.

Using that critical study, a "point of departure" is identified. The point of departure (POD) is the dose-response point that marks the beginning of a low-dose extrapolation. This can be a no observed adverse effect level (NOAEL), lowest observed adverse effect level (LOAEL), or a lower limit on a benchmark dose (BMDL). The POD may be an administered dose, a modeled dose, or a serum level. When sufficient information is available on the way an individual PFAS moves into and out of human and laboratory animal's bodies, laboratory animal exposure doses can be converted to a human equivalent dose. The toxicokinetic parameters used to calculate a human equivalent dose include serum half-life and volume of distribution.

The POD is divided by uncertainty and modifying factors to derive the toxicity value. Uncertainty and modifying factor values typically range between one and ten, with higher numbers used when there is greater uncertainty. The uncertainty and modifying factors are multiplied together and the POD is divided by the product of these factors. Uncertainty factors are included to account for uncertainties due to the potential variability among humans (intraspecies variability), the potential differences between laboratory animals and humans (interspecies differences), the use of a point of departure that resulted in adverse health effects (i.e., LOAEL), and the use of a shorter than chronic exposure time[3]. A modifying factor is typically applied to account for gaps in the scientific knowledge base; for example, a minimal number of studies to identify the most sensitive health endpoint.[4]

In summary,

$$Toxicity\ value\ (i.e., RfD, MRL) = \frac{Point\ of\ Departure\ (e.g.,\ NOAEL, LOAEL, serum\ level)}{Uncertainty\ and\ modifying\ factors\ (e.g.,\ UF1\ x\ UF2)}$$

[2] Concepts from https://www.atsdr.cdc.gov/mrls/index.asp and https://www.epa.gov/iris/reference-dose-rfd-description-and-use-health-risk-assessments#1.2.1

[3] This uncertainty factor is not typically used by ATSDR as they develop values for acute (less than 14 days), intermediate (more than 14 days to one year), and chronic (over one year) exposures.

[4] https://www.epa.gov/sites/production/files/2015-09/documents/rags_a.pdf

PFAS evaluated

The following PFAS were those MDHHS considered for evaluation. For some, there is a sufficiently large dataset for the development of a public health drinking water screening level. For other PFAS, an exposure evaluation may be recommended, but there may not be sufficient information at this time to develop public health drinking water screening levels. See the PFAS groupings below.

- Public health drinking water screening levels are described and calculated in this document for the below PFAS.
    - PFOA (CAS Registry Number: 335-67-1)
    - PFOS (CAS Registry Number: 1763-23-1)
    - PFNA (CAS Registry Number: 375-95-1)
    - PFHxS (CAS Registry Number: 355-46-4)
    - PFBS (PFBuS; CAS Registry Number: 375-73-5)

- Public health drinking water recommendations might be possible for the below PFAS. An evaluation to determine public health recommendations for the below PFAS is in progress.
    - PFBA (CAS Registry Number: 375-22-4)
        - ATSDR (2018) identified a limited number of laboratory animals and human epidemiological studies.
    - PFOSA (CAS Registry Number: 754-91-6)
    - PFHpA (CAS Registry Number: 375-85-9)
        - ATSDR (2018) identified a limited number of human epidemiological studies.
    - PFHxA (CAS Registry Number: 307-24-4)
        - ATSDR (2018) identified a limited number of laboratory animal studies.
    - N-EtFOSAA (Et-PFOSA-AcOH;CAS Registry Number: 2991-50-6)
    - N-MeFOSAA (Me-PFOSA-AcOH; CAS Registry Number: 2355-31-9)

- Public health drinking water recommendations are unlikely for the below PFAS (Note, evaluation is still needed, and is underway, but there may not be sufficient information to provide recommendations.)
    - PFTeA (CAS Registry Number: 376-06-7)
    - PFTriA (CAS Registry Number: 72629-94-8)
    - PFDoA (CAS Registry Number: 307-55-1)
        - ATSDR (2018) identified a limited number of laboratory animal studies.
    - PFUnA (PFUA; CAS Registry Number: 2058-94-8)
        - ATSDR (2018) identified a limited number of laboratory animal studies.
    - PFDA (PFDeA; CAS Registry Number: 335-76-2)
        - ATSDR (2018) identified a limited number of laboratory animal and human epidemiological studies.
    - PFPeA (CAS Registry Number: 2706-90-3)
    - PFDS (CAS Registry Number: 335-77-3)
    - PFNS (CAS Registry Number: 68259-12-1)

- PFHpS (CAS Registry Number: 375-92-8)
- PFPeS (CAS Registry Number: 2706-91-4)
- FtS 8:2 (CAS Registry Number: 39108-34-4)
- FtS 6:2 (CAS Registry Number: 27619-97-2)
- FtS 4:2 (CAS Registry Number: 757124-72-4)

PFOA

The available PFOA toxicity values used by various agencies to develop drinking water screening levels were evaluated (See Section 8). The US Environmental Protection Agency, the Agency for Toxic Substances and Disease Registry, Minnesota Department of Health (MDH), and the New Jersey Department of Environmental Protection (NJ DEP).

US EPA restricted their candidate critical studies to those in which exposure spanned an adequate duration (with a preference for greater than seven weeks), multiple dose groups, use of a concurrent control, and with serum data amenable for modeling (US EPA 2016a). US EPA selected Lau et al. (2006) which included multiple doses, but no identified NOAEL. MDH selected Lau et al. (2006), and used the serum level estimated by US EPA.

ATSDR selected identical LOAELs from Onishchenko et al. (2011) and Koskela et al. (2016). Both studies used the same populations of laboratory animals and only evaluated a single dosing group. They did not identify a NOAEL, but they had a lower predicted serum concentration at the LOAEL than Lau et al. (2006) (8.29 micrograms per milliliter [µg/ml] versus 39.2 µg/ml for Lau et al. [2006] as modeled by ATSDR). The serum concentration at the LOAEL from Onishchenko et al. (2011) and Koskela et al. (2016) was also below the modeled serum concentrations from two immunotoxicity studies evaluated by ATSDR. This is important as immunotoxicity was considered to be the most sensitive effect in other PFAS evaluated by ATSDR.

NJ DEP selected a lower bound Benchmark Dose from Loveless et al. (2006). Loveless et al. (2006) was a 14-day exposure study in rats and mice, with liver weight changes being the critical effect identified (NJ DWQI 2017). In their final selections of studies, US EPA included a study with increased liver weight at double the average serum PFOA level from Lau et al. (2006). ATSDR identified a study with increased liver weight at an average serum PFOA level at more than 25 times the average serum PFOA level from Onishchenko et al. (2011) and Koskela et al. (2016). Additionally, when evaluating acute duration studies, ATSDR noted that the modeling approach they used for estimating human equivalent PFAS doses could not be used to estimate acute exposure in humans when the study exposure duration was 14 days as this duration represents 1% of the elimination half-life in humans (ATSDR 2018).

As a similar range of health endpoints were identified by all agencies, MDHHS selected the critical studies by ATSDR as the LOAEL from that study was well below the US EPA-selected study and also was protective for immunotoxicity. Below is a summary of the selected studies and ATSDR's evaluation and development of a provisional intermediate oral MRL.

Draft ATSDR PFOA MRL[5]

ATSDR has released four intermediate oral MRLs for PFAS, including PFOA, and uses those values in public health evaluations of environmental chemical exposure.[6] The information presented in the following table is a summary of the ATSDR MRL development for PFOA.

Critical study (these two studies used offspring from the same animals)	Onishchenko N, Fischer C, Wan Ibrahim WN, et al. 2011. Prenatal exposure to PFOS or PFOA alters motor function in mice in a sex-related manner. Neurotox Res 19(3):452-461.	Koskela A, Finnila MA, Korkalainen M, et al. 2016. Effects of developmental exposure to perfluorooctanoic acid (PFOA) on long bone morphology and bone cell differentiation. Toxicol Appl Pharmacol 301:14-21.
Description of the critical study	Pregnant mice were exposed to 0 or 0.3 mg PFOA/kg/day throughout pregnancy. Neurobehavioral effects (decreased number of inactive periods, altered novelty induced activity) were considered the critical effects.	Pregnant mice were exposed to PFOA mixed with food at the dose of 0 or 0.3 mg/kg/day throughout pregnancy. Group of five offspring (female) were sacrificed at either 13 or 17 months of age. The critical effects considered were skeletal alteration such as bone morphology and bone cell differentiation in the femurs and tibias.
Point of Departure	The average serum concentration was estimated in the mice (8.29 mg/L) using a three-compartment pharmacokinetic model (Wambaugh et al. 2013) using animal species-, strain-, sex-specific parameters.	
Human equivalent dose estimation	The relationship between external dose (mg/kg/day) and steady state serum concentration (mg/L) in humans was estimated assuming a single compartment first order model in which elimination kinetics are adequately represented by observed serum elimination $t_{1/2}$ value ($K_e = \ln(2)/t_{1/2}$), an assumed apparent volume of distribution (V_d, L/kg) and gastrointestinal absorption fraction (which is considered as 100%). The average serum concentration (8.29 mg/L) was multiplied by clearance factor of 0.000099 L/kg/day to derive a human equivalent dose of 0.000821 mg/kg/day which is defined as the continuous ingestion dose (mg/kg/day) that would result in steady-state serum concentration (8.29 mg/L).	
Uncertainty and modifying factors	A total uncertainty factor of 300: 10 for use of a LOAEL 3 for animal to human variability 10 for human variability	
Toxicity Value	Intermediate oral MRL of 0.000003 mg/kg/day (3 ng/kg/day)	

[5] https://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=1117&tid=237, Agency for Toxic Substances and Disease Registry. 2014. Exposure Dose Guidance for Water Ingestion. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. November 2014., and Agency for Toxic Substances and Disease Registry. Drinking Water Comparison Values. Atlanta, GA. [updated 2018 July 26; accessed 2018 August 21]. Available from ATSDR's Sequoia Database.

[6] More details on the ATSDR Public Health Assessment process can be found in the Public Health Assessment Guidance Manual (https://www.atsdr.cdc.gov/hac/PHAManual/toc.html).

During MDHHS' evaluation of the ATSDR MRL for PFOA, the toxicokinetic model inputs used to calculate a human equivalent dose were also evaluated. The ATSDR selected a serum half-life of 1,400 days (3.8 years) from an occupationally-exposed group of retired fluorochemicals production workers (24 men, 2 women) (Olsen et al. 2007a). Participants were followed for up to 5.3 years. The PFOA serum half-life ranged from 561 to 3,334 days (1.5 to 9.1 years) in the individual participants with an arithmetic mean of 3.8 years. ATSDR stated that it selected the Olsen et al. (2007a) serum half-life because participants were followed for a longer time than those in the Bartell et al. (2010) study (ATSDR 2018).

The US EPA selected a different serum half-life for PFOA in their evaluation (EPA 2016a): a serum half-life of 840 days (2.3 years) from a study following 200 individuals (100 men, 100 women) exposed by drinking PFOA-contaminated water. Participants provided blood samples six times: one, two, three, six, and twelve months after the initial blood donation. The mean PFOA half-life was 840 days (2.3 years). US EPA stated that they selected this study (Bartell et al. 2010) because exposure through PFOA-contaminated water was relevant to the general population (EPA 2016a).

Additionally, ATSDR noted that a serum half-life would be most applicable to serum concentrations falling within the ranges identified in the studies and that serum concentrations "substantially below or above" these ranges would result in less certain half-lives (ATSDR 2018). Olsen et al. (2007) provided the initial arithmetic mean of 691 ng/ml (ppb) (0.691 mg/L) for PFOA with a range of 72 to 5,100 ng/ml (0.072 to 5.1 mg/L). Bartell et al. (2010) provided an initial mean serum PFOA concentration of 180 ± 209 (standard deviation) ng/ml. Steenland et al. (2009) reported a mean serum PFOA of 80 ng/ml (0.08 mg/L), with a range of 0.25 to 17,556 ng/ml (0.00025 to 17.556 mg/L) for the 46,294 community residents participating in the C8 Health Project in 2005-2006.

MDHHS selected the PFOA serum half-life of 840 days (2.3 years) as more relevant for exposure to the general population as this half-life corresponds to data from Bartell et al. (2010) in which 200 individuals (100 men, 100 women) were exposed by drinking PFOA-contaminated water. Although this selection of serum half-life, based on Bartell et al. (2010), was made after careful consideration of external validity and applicability to Michigan residents, it is important to note that any serum half-life estimation can be influenced by background levels of PFAS to which individuals are exposed (Bartell 2012). The impact of background exposures can increase with extended follow-up durations, meaning, with protracted follow-up samples serum half-life estimates can become more susceptible to bias from background exposure.

PFOS

The available PFOS toxicity values used by various agencies to develop drinking water screening levels were evaluated (See Section 8). US EPA, ATSDR, and MDH selected the same critical study, Luebker et al. (2005b), however each applied distinct parameters (i.e. different physiologically based pharmacokinetic [toxicokinetic] modeling approaches, different uncertainly and/or modifying factors) that significantly affected their derived toxicity values. US EPA and ATSDR calculated different average serum PFOS concentrations associated with the Luekker et al. (2005) NOAEL. US EPA calculated 6.26 mg/L, which the MDH used, while ATSDR calculated 7.43 mg/L. Both US EPA and ATSDR used the same first order one compartment model to extrapolate average serum PFOS concentrations, however, different software and modeling runs were used, resulting in small differences. Although the serum concentrations used as the POD were different, the greater difference was in the total uncertainty factors selected by each agency: US EPA used a total uncertainty factor of 30, MDH used a total uncertainty factor of 100, and ATSDR used a combined total uncertainty and modifying factor of 300. There were also minor differences in the clearance rates used by these agencies to calculate the human equivalent doses (HED).[7] However, the HEDs were almost identical (0.00051 mg/kg/day for US EPA and MDH versus 0.000515 mg/kg/day for ATSDR.

The NJ DEP selected Dong et al. (2009), a study using a 60-day exposure and that measured immunotoxicity endpoints, as their critical study. No time weighted average serum concentration was available, but NJ DEP used the mean serum concentration measured at the end of the dosing (NJ DWQI 2018). This study (Dong et al. 2009), along with other immunotoxicity studies, was evaluated by both US EPA and ATSDR. ATSDR did not select it, or any other immunotoxicity study, as a critical study but did develop a "candidate MRL" using an immunotoxicity study (Dong et al. 2011). Note, Dong et al. (2011) reported the highest NOAEL among all immunotoxicity studies. The US EPA, however, noted that immunological effects were seen at doses that also increased liver weight, and "based on limited evidence, neither response appeared more sensitive than the other" (US EPA 2016b).

MDHHS selected the average serum PFOS concentration associated with the Luekker et al. (2005) NOAEL calculated by ATSDR. Below is a summary of the selected study and ATSDR's evaluation and development of a provisional intermediate oral MRL. The additional modifying factor that ATSDR used in developing their MRL for PFOS is also discussed below.

[7] The relationship between external dose (mg/kg/day) and steady state serum concentration (mg/L) in humans was estimated assuming a one compartment first order model in which elimination kinetics are adequately represented by observed serum elimination $t_{1/2}$ value ($K_e = \ln(2)/t_{1/2}$), an assumed apparent volume of distribution (Vd, L/kg), and gastrointestinal absorption fraction (which is considered as 100%). US EPA multiplied the average serum concentration (6.26 mg/L) by clearance factor of 0.000081 L/kg/day (K_e x Vd) to derive a human equivalent dose of 0.00051 mg/kg/day and ATSDR multiplied the average serum concentration (7.43 mg/L) by clearance factor of 0.000069 L/kg/day (K_e x Vd) to derive a human equivalent dose of 0.000515 mg/kg/day.

Draft ATSDR PFOS MRL[8]

ATSDR has released four intermediate oral MRLs for PFAS, including PFOS, and uses those values in public health evaluations of environmental chemical exposure.[9] The information presented in the following table is a summary of the ATSDR MRL development for PFOS.

Critical study	Luebker DJ, Case MT, York RG, et al. 2005. Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats. Toxicology 215(1-2):126-148.
Description of the critical study	Male and female rats were given 0, 0.1, 0.4, 1.6 and 3.2 mg/kg/day PFOS by oral gavage for 6 weeks prior to and during mating. Females were treated through gestation and lactation and across two generation.
Point of Departure	For the F1 generation, a NOAEL of 0.1 mg/kg/day and LOAEL of 0.4 mg/kg/day were identified for delayed eye opening. For the F2 generation, a NOAEL of 0.1 mg/kg/day and LOAEL of 0.4 mg/kg/day were identified based on decreased mean pup body weight.
Human equivalent dose estimation	The average serum concentration for the NOAEL (0.1 mg/kg/day) was estimated (7.43 mg/L) using a three-compartment pharmacokinetic model (Wambaugh et al. 2013). The relationship between external dose (mg/kg/day) and steady state serum concentration (mg/L) in human was estimated assuming a single compartment first order model in which elimination kinetics are adequately represented by observed serum elimination $t_{1/2}$ value ($K_e = \ln(2)/t_{1/2}$), an assumed apparent volume of distribution (V_d, L/kg) and gastrointestinal absorption fraction (which is considered as 100%). The average serum concentration (7.43 mg/L) was multiplied by a clearance factor of 0.000069 L/kg/day ($K_e * V_d$) to derive a human equivalent dose of 0.000515 mg/kg/day which is defined as the continuous ingestion dose (mg/kg/day) that would result in a steady-state serum concentration (7.43 mg/L).
Uncertainty and modifying factors	A total uncertainty and modifying factor of 300. A total uncertainty factor of 30 (applied to the human equivalent dose): 3 for animal to human variability 10 for human variability Additionally, a modifying factor of 10 was also included for the concern that immunotoxicity may be more sensitive than developmental toxicity.
Toxicity value	Intermediate Oral MRL of 0.000002 mg/kg/day (2 ng/kg/day)

[8] https://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=1117&tid=237, Agency for Toxic Substances and Disease Registry. 2014. Exposure Dose Guidance for Water Ingestion. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. November 2014., and Agency for Toxic Substances and Disease Registry. Drinking Water Comparison Values. Atlanta, GA. [updated 2018 July 26; accessed 2018 August 21]. Available from ATSDR's Sequoia Database.

[9] More details on the ATSDR Public Health Assessment process can be found in the Public Health Assessment Guidance Manual (https://www.atsdr.cdc.gov/hac/PHAManual/toc.html).

Evaluation of the 10-fold modifying factor added to PFOS for immune effects in ATSDR's MRL derivation

PFOS is the only ATSDR MRL with a 10-fold modifying factor to account for "the concern that immunotoxicity may be a more sensitive endpoint of PFOS toxicity than developmental toxicity" (ATSDR 2018). PFNA and PFHxS also have a modifying factor of 10 applied, with the rationale of accounting for 'database limitations' related to no or limited immunotoxicity literature for these chemicals. Note, US EPA did not apply modifying factors to account for immunotoxicological endpoints or database uncertainties (US EPA only applied uncertainty factors for intra- and interspecies variability, and LOAEL to NOAEL extrapolation in the case of PFOA).

MDHHS evaluated the inclusion of a full 10-fold modifying factor for limitations relating to immunotoxicological endpoints resulting from PFOS exposure.

ATSDR noted that there was data supporting immunosuppression as a potentially more sensitive endpoint than developmental effects following PFOS (oral, intermediate duration) exposure. Laboratory animal studies, particularly studies in mice, provide strong evidence of the immunotoxicity of PFOS. These data are consistent with human epidemiological studies. A number of epidemiological studies have examined the association between serum PFOS levels and decreased immune response. PFOS has been found to be associated with decreased response to vaccines, especially the tetanus vaccine (Grandjean et al. 2017, ATSDR 2018). The ATSDR (2018) concluded that the weight of the epidemiological evidence suggests associations between exposure to PFOS and decreased vaccine response. This conclusion was based upon consistency of findings across studies, quality of studies, dose-response relationships, and the plausibility of the association. The conclusion is also supported by the National Toxicology Program's examination of the available immunotoxicity literature on PFOS and PFOA, which stated in summary that, based on human studies, there is moderate evidence that exposure to PFOS is associated with suppression of antibody response (NTP 2016). This same NTP Monograph also made note of the consistency of findings across studies, stating that "The data are considered a consistent pattern of findings for PFOA and PFOS-associated antibody suppression in humans."

ATSDR evaluated laboratory animal studies reporting impaired antibody responses resulting from oral exposure to relatively low doses of PFOS. However, ATSDR did not consider these data as a POD MRL development because time-weighted average (TWA) serum PFOS values were not predicted due to a lack of pharmacokinetic model parameters for the two mouse strains tested (i.e. no models approved by ATSDR). Note, also, these are acute or intermediate exposures, and studies evaluating immune effects following chronic PFOS exposure are not available.

Comparing dose-response curves between mouse strains (which has limitations) for developmental versus immunological effects shows there are significantly lower LOAELs from the immunosuppression literature than from the developmental literature. LOAELs for developmental endpoints range from 0.3 to 2 milligrams per kilogram per day (mg/kg/day) while immunological endpoint LOAELs range from 0.00166 to 0.083 mg/kg/day (ATSDR 2018, Table A-14).

ATSDR also calculated a candidate MRL using the NOAEL of 0.0167 mg/kg/day identified in the Dong et al. (2011) paper as part of their justification for the modifying factor addition. A TWA concentration was estimated using a similar approach described for PFHxS and PFNA in the MRL approach section. The

estimated TWA concentration was 1.2 µg/mL for the 0.0167 mg/kg/day; this estimated TWA concentration was used to calculate a human equivalent dose (HED) of 0.000083 mg/kg/day.

A total uncertainty factor of 30 (3 for extrapolation from animals to humans using dosimetric adjustments and 10 for human variability) was applied to the HED resulting in the candidate MRL of 3 ng/kg/day. No modifying factor was added.

This MRL is similar to the MRL calculated (2 ng/kg/day) from the selected critical study (Luebker et al. 2005), based on developmental endpoints, and "lends support to using the additional uncertainty factor of 10 to account for the lack of pharmacokinetic modeling parameters for the mouse strains tested for immunotoxicity". Effectively, the candidate MRL estimated for immunological effects is nearly identical to that of the MRL for developmental effects inclusive of the 10-fold modifying factor.

MDHHS determined that it was appropriate to retain the 10-fold modifying factor included by ATSDR because: it matches the ATSDR approach, other immune studies have lower LOAELs than the immune study used in ATSDR's candidate MRL calculation, a 10-fold uncertainty factory may be required on a *de novo* calculation of a toxicity value using one of the immune studies due to the subchronic (and not chronic) duration of exposure.

PFNA

The available PFNA toxicity values used by various agencies to develop drinking water screening levels were evaluated (See Section 8). ATSDR and NJ DEP developed PFNA toxicity values using the same critical study, Das et al. (2015), but using different methods. NJ DEP calculated a lower limit on a Benchmark Dose as their point of departure. The PFNA serum concentrations from Das et al. (2015) were collected on gestational day 17, and NJ DEP noted that that value represents the maximum serum concentration and that the average serum concentration, which could have led to the liver weight effects, may have been lower throughout the whole exposure period. NJ DEP used their lower limit on a Benchmark Dose serum level, applied uncertainty factors, and calculated a water value using an estimated serum to drinking water ratio (NJ DWQI 2015).

ATSDR estimate a TWA serum PFNA concentration associated with the NOAEL using an empirical clearance model. Then, using that TWA serum PFNA concentration, calculated a human equivalent dose from the average serum PFNA level and applied uncertainty factors.

MDHHS selected the TWA serum PFNA concentration estimated by ATSDR. Below is a summary of the selected study and ATSDR's evaluation and development of a provisional intermediate oral MRL.

Draft ATSDR PFNA MRL[10]

ATSDR has released four intermediate oral Minimal Risk Levels for PFAS, including PFNA, and uses those values in public health evaluations of environmental chemical exposure.[11]

Critical Study	Das KP, Grey BE, Rosen MB, et al. 2015. Developmental toxicity of perfluorononanoic acid in mice. Reproductive Toxicology 51:133-144.
Description of the Critical Study	Timed-pregnant mice were given 0, 1, 3, 5 or 10 mg/kg PFNA by oral gavage daily from gestational day (GD) 1 to 17 and control received an equivalent amount of water i.e. 10 ml/kg body weight. *Body weight endpoints* – Decreased body weight *Developmental endpoints* – Developmental delays in mice
Point of Departure	A NOAEL of 1 mg/kg/day was identified for developmental effects.

[10] https://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=1117&tid=237, Agency for Toxic Substances and Disease Registry. 2014. Exposure Dose Guidance for Water Ingestion. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. November 2014., and Agency for Toxic Substances and Disease Registry. Drinking Water Comparison Values. Atlanta, GA. [updated 2018 July 26; accessed 2018 August 21]. Available from ATSDR's Sequoia Database.

[11] More details on the ATSDR Public Health Assessment process can be found in the Public Health Assessment Guidance Manual (https://www.atsdr.cdc.gov/hac/PHAManual/toc.html).

Human Equivalent Dose Estimation	The average serum concentration for NOAEL (1 mg/kg/day) was estimated (8.91 µg/mL) in dams using an empirical clearance model. The estimated time-weighted average serum concentration corresponding to the NOAEL was 6.8 µg/mL. ATSDR was provided the serum concentrations by the study authors. ATSDR used a serum elimination rate constant (k_e) of 7.59×10^{-4} /day and an estimated volume of distribution for PFNA in humans of 0.2 L/kg. ATSDR assumed that PFNA is well absorbed after oral exposure, and used an absorbance factor (AF) of 1, based on animal studies of PFNA and other perfluorocarboxylic acid analogs. $NOAEL_{HED}$ = (TWA serum x k_e x V_d)/AF = 0.001 mg/kg/day
Uncertainty and Modifying Factors	A total uncertainty and modifying factor of 300. A total uncertainty factor of 30: 3 for extrapolation from animals to humans with dosimetric adjustments 10 for human variability Additionally, a modifying factor of 10 was also included for database deficiencies.
Toxicity Value	Provisional Intermediate oral MRL of 0.000003 mg/kg/day (3 ng/kg/day)

PFHxS

The available PFHxS toxicity values used by various agencies to develop drinking water screening levels were evaluated (See Section 8). ATSDR and the Texas Commission of Environmental Quality (CEQ) selected the same study (Hoberman and York 2003) for PFHxS toxicity value development. ATSDR also included a peer-reviewed publication of the research report, which was available in 2009 (Butenhoff et al. 2009), listed as the critical study along with the research report. Texas CEQ used the LOAEL of 0.3 mg/kg/day with a toxicokinetics extrapolation factor while ATSDR estimated an average PFHxS serum concentration.

MDHHS selected the ATSDR estimated serum concentration for developing a public health drinking water screening level. Below is a summary of the critical and supporting studies and ATSDR's evaluation and development of a provisional intermediate oral MRL for PFHxS.

Draft ATSDR PFHxS MRL[12]

ATSDR has released four oral intermediate Minimal Risk Levels for PFAS, including PFHxS, and uses those values in public health evaluations of environmental chemical exposure.[13]

Critical Study	Butenhoff JL, Chang S, Ehresman DJ, et al. 2009. Evaluation of potential reproductive and developmental toxicity of potassium perfluorohexanesulfonate in Sprague Dawley rats. Reprod Toxicol 27:331-341. Hoberman AM, York RG. 2003. Oral (gavage) combined repeated dose toxicity study of T-7706 with the reproduction/developmental toxicity screening test. Argus Research.
Description of the Critical Study	Sprague-Dawley rats were given 0.3, 1, 3, or 10 mg/kg PFHxS by oral gavage one time daily for 42-56 days (intermediate exposure). Control group animals (0 mg/kg) received an equivalent volume of water (10 ml/kg). Two major health endpoint categories were identified: *Hepatic endpoints* – Increased liver weight; centrilobular hepatocellular hypertrophy *Thyroid endpoints* – Hypertrophy and hyperplasia of thyroid follicular cells
Point of Departure	a NOAEL of 1 mg/kg/day was identified for thyroid effects (noted as the most sensitive endpoint)

[12] https://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=1117&tid=237, Agency for Toxic Substances and Disease Registry. 2014. Exposure Dose Guidance for Water Ingestion. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. November 2014., and Agency for Toxic Substances and Disease Registry. Drinking Water Comparison Values. Atlanta, GA. [updated 2018 July 26; accessed 2018 August 21]. Available from ATSDR's Sequoia Database.

[13] More details on the ATSDR Public Health Assessment process can be found in the Public Health Assessment Guidance Manual (https://www.atsdr.cdc.gov/hac/PHAManual/toc.html).

Human Equivalent Dose (HED)	The average serum concentration for the NOAEL (1 mg/kg/day) was estimated (89.12 µg/mL) using an empirical clearance model. As a pharmacokinetic model for predicting the time-weighted average (TWA) serum concentrations was not identified for PFHxS, a TWA serum concentration of 73.22 µg/mL was estimated from measured serum concentrations of adult males exposed to 1 mg/kg/day. ATSDR also used a serum elimination rate constant (k_e) of 0.000223/day, a volume of distribution (V_d) of 0.287 L/kg and an absorption fraction (AF) of 1 based on published studies. $NOAEL_{HED}$ = (TWA serum x k_e x V_d)/AF = 0.0047 mg/kg/day
Uncertainty and Modifying Factors	A total uncertainty and modifying factor of 300. A total uncertainty factor of 30: 3 for extrapolation from animals to humans with dosimetric adjustments 10 for human variability Additionally, a modifying factor of 10 was also included for database limitations.
Toxicity Value	Intermediate oral MRL of 0.00002 mg/kg/day (20 ng/kg/day)

One additional PFHxS study, Chang et al. (2018), was published after ATSDR gathered studies for evaluation. MDHHS evaluated this study to determine if information available in the study would be a more appropriate critical study.

Chang et al. (2018) utilize a very similar experimental design, and are the same primary authors, as the critical study cited by ATSDR for the PFHxS MRL derivation. The key differences are the use of mice (rats were the species used in the critical study) and dosing continued after birth with observations made in the F1 generation. Measured thyroid effects did not occur in the F0 generation even at the doses observed to cause changes in rats and equivocal effects occurred at a similar dose in the F1 generation (thyroid gland weights were increased but no corresponding change in histology was observed). Chang et al. (2018) reports no significant thyroid effects following exposure to 0.03, 1 or 3 mg/kg/day potassium PFHxS. They did report an equivocal decrease in live litter size at 1 and 3 mg/kg/day, but the pup-born-to-implant ratio was unaffected. Adaptive hepatocellular hypertrophy was observed, and in 3 mg/kg/day F0 males, it was accompanied by concomitant decreased serum cholesterol and increased alkaline phosphatase.

Serum levels in the ATSDR critical study (Butenhoff et al. 2009) were estimated to be 73 µg/mL for adult male rats exposed to 1 mg/kg/day PFHxS. That is comparable to the measured serum levels of 77.9 µg/mL in adult male mice used in the Chang et al. (2018) study following the same dose (1 mg/kg/day) of PFHxS. MDHHS determined that the information from the Change et al. (2018) study warranted no change in the critical study selection.

PFBS

The available PFBS toxicity values used by various agencies to develop drinking water screening levels were evaluated (see Section 8). Two critical studies were the basis of the PFBS toxicity values developed by US EPA and MDH: Lieder et al. (2009a) and Lieder et al. (2009b). Both studies identified kidney hyperplasia as the critical effect. Lieder et al. (2009a) was a 90-day rat oral gavage study with potassium PFBS (K+PFBS). Rats were dosed with K+PFBS at doses of 0, 60, 200, and 600 mg/kg/day. Lieder et al. (2009a) identified a NOAEL for female rats in this study of 600 mg/kg/day (highest dose of study) and a NOAEL for the male rat of 60 mg/kg/day based on hematological effects. The US EPA identified a NOAEL of 200 mg/kg/day for both female and male rats. US EPA noted that the hematological changes in male rats were not dose-dependent and not observed in female rats. US EPA used their Benchmark Dose Software (BMDS version 2.3) and a modeled the lower limit on a Benchmark Dose associated with a benchmark response of 10% ($BMDL_{10}$). The health endpoint selected for the modeling was the kidney hyperplasia data. The US EPA selected a $BMDL_{10}$ of 78.7 mg/kg/day as a point of departure for development of subchronic and chronic provisional RfDs.

Lieder et al. (2009b) conducted a two-generation reproductive study in Sprague-Dawley rats orally dosed with 0, 30, 100, 300, or 1000 mg/kg/day K+PFBS, with 30 rats per sex per group. Parental (F0) generation rats were treated 10 weeks prior to mating, which continued through mating for male rats and through mating, gestation, and lactation for female rats. F1 generation rats were weaned and treated as described for the parental generation. F2 generation rats were only exposed to K+PFBS through placental transfer and during nursing. The study authors noted that the NOAEL was 100 mg/kg/day due to the liver and kidney effects observed in the parental and F1 generation rats. Body weight effects were noted in the F1 generation, with a NOAEL of 300 mg/kg/day. No effects on reproductive function were noted in the parental or F1 generations. MDH estimated a $BMDL_{10}$ of 45 mg/kg/day for the epithelial hyperplasia in kidneys of F0 females from the Lieder et al. (2009b) data (MDH 2017a). The US EPA also modeled kidney hyperplasia data from the two-generational Lieder et al (2009b) study. The $BMDL_{10}$ for that study was 26.6 mg/kg/day for F0 generation female rats and 52.4 mg/kg/day for F1 generation female rats. However, the US EPA noted that these are less reliable estimates as there is no data point near the benchmark response, which is recommended for Benchmark Dose modeling (US EPA 2014).

Given the similarity of health endpoints identified in both studies and the differences in $BMDL_{10}$ compared to the identified NOAEL of each study, the US EPA $BMDL_{10}$ was selected by MDHHS. Below is a summary of the selected studies and US EPA's evaluation and development of a provisional chronic Reference Dose.

US EPA PFBS RfD[14]

The US EPA developed the chronic PFBS RfDs as provisional peer-reviewed toxicity values (PPRTVs). PPRTVs are toxicity values developed for use in the Superfund Program and are internally reviewed by a

[14] Additional information on these values can be found in the "Provisional Peer-Reviewed Toxicity Values for Perfluorobutane Sulfonate (CASRN 375-73-5) and Related Compound Potassium Perfluorobutane Sulfonate (CASRN 29420-49-3)" document located at https://cfpub.epa.gov/ncea/pprtv/documents/PotassiumPerfluorobutaneSulfonate.pdf.

standing National Center for Environmental Assessment scientist panel and also by three external scientific experts. These PPRTV values were finalized in 2014.

Critical Study	Lieder PH, SC Chang, RG York, JL Butenhoff. 2009a. Toxicological evaluation of potassium perfluorobutanesulfonate in a 90-day oral gavage study with Sprague-Dawley rats. Toxicology 255:45-52.
Description	A 90-day rat oral gavage study was conducted with potassium PFBS (K+PFBS). Rats were dosed with K+PFBS at doses of 0, 60, 200, and 600 milligrams per kilogram per day (mg/kg/day). No treatment-related mortality, body weight, or neurological effects were noted. Histopathological changes were observed in the kidneys. The changes observed were minimal-to-mild hyperplasia of the epithelial cells of the medullary and papillary tubules and the ducts in the inner medullary region. There were no corresponding changes in kidney weights. Clinical chemistry parameters related to kidney function were unchanged. The US EPA identified a NOAEL of 200 mg/kg/day for both female and male rats.
Point of Departure	Subchronic and chronic: $BMDL_{10}$ of 78.7 mg/kg-day based on increased incidence of kidney hyperplasia in female rats is selected as the point of departure
Human Equivalent Dose Estimation	18.9 mg/kg/day calculated using dosimetric adjustment factor (based on body weight scaling)
Uncertainty and Modifying Factors	Chronic – a total uncertainty factor of 1000: 3 for animal to human toxicodynamic differences 10 for human to human variability 3 for a database gap 10 for extrapolation of a subchronic study to a chronic duration
Toxicity Value	Chronic provisional RfD: 0.02 mg/kg/day (20,000 ng/kg/day)

The US EPA included an assessment of the confidence in the study (high), the database (medium), and overall confidence in the subchronic and chronic provisional RfDs (medium). The overall confidence determined by the US EPA cannot be higher than the lowest designation of confidence in the assessment.

MDHHS evaluated the calculation of both US EPA's and MDH toxicity values. While US EPA used a dosimetric adjustment factor based on body weight scaling to estimate a human equivalent dose, MDH converted their selection of a point of departure to a human equivalent dose using toxicokinetic adjustment based on serum half-life of PFBS in humans (665 hours) and female Sprague-Dawley rats (1.9 hours). The half-life for female Sprague-Dawley rats used by MDH is similar to the half-lives presented in the draft ATSDR *Toxicological Profile for Perfluoroalkyls*, Table 1-1 and Table 3-5 (ATSDR 2018). MDHHS applied the MDH toxicokinetic adjustment to the US EPA chronic pRfD in place of the dosimetric adjustment factor and retained US EPA's uncertaintiy factor. This results an RfD of 0.00023 mg/kg/day.

Section 3: Methodology, exposure scenario, and other parameters used to develop public health drinking water screening levels

Screening level development typically requires selection of the appropriate population for exposure. For drinking water, evaluation of infants that may be breast- or formula-fed is needed along with evaluation of older children and adults to ensure that any screening levels are sufficiently protective for all populations. Infants have an approximately seven-fold higher water intake rate than older children and adults and may be more sensitive to specific chemicals (Goeden 2018). Various approaches used by MDH, including a toxicokinetic model that predicts the prenatal transfer of PFAS to fetuses during pregnancy along with postnatal exposure from breastmilk or reconstituted formula made with tap water, were evaluated. The MDH's toxicokinetic model is described below.

Among the parameters included in the evaluation is relative source contribution, water intake (amount of water per day), and body weight. Relative Source Contributions (RSC) are discussed in the section below. Water intake rates (water intake divided by body weight) used by most agencies are recommendations of upper percentile drinking water ingestion from the US EPA. These are currently compiled in the US EPA Exposure Factors Handbook (US EPA 2011) and are occasionally updated. There are two provided, per capita and consumer only water intake rates. Per capita water intake rates are intakes averaged over the entire population, which includes people who do not directly drink water. Consumer only intake is calculated from survey participants that reported drinking water (US EPA 2011). Consumer only water intake rates are a more conservative value and are more protective for water consumers.

Minnesota Department of Health Toxicokinetic Model[15]

Toxicity value derivation and drinking water screening level development for a given PFAS chemical depend on several factors and assumptions including:

- Critical study used to derive toxicity value
- Toxicokinetic model used to estimate a human equivalent dose
- Uncertainty factors/modifying factor applied
- Exposure scenario selected
- Drinking water intake rate assumption
- Relative source contribution assumption

US EPA and MDH considered the same developmental studies (Lau et al. 2006; Luebker et al. 2005;) to derive a health-based drinking water screening value for PFOA (from mice study) and PFOS (from rat study), respectively. Paired maternal-serum, umbilical cord blood and breast milk studies have shown that PFOA and PFOS cross the placenta and are excreted through breast milk. Maternal serum, cord blood and breast milk concentrations of different PFAS chemicals are summarized in Table 1.

[15] MDH. 2017b. Background Document: Toxicokinetic Model for PFOS and PFOA and Its Use in the Derivation of Human Health-based Water Guidance Values. Minnesota Department of Health.

MDH determined that the traditional approach, using equations to calculate a drinking water screening level based on body weight, water intake rate, and RSC, to derive a drinking water screening level would not be adequate to address the bioaccumulative nature and developmental toxicity of PFOA and PFOS. The traditional equations do not include the body-burden at birth or any transfer of chemicals through breastmilk. To account for the above and also high early-life intake rates, MDH developed a simple one-compartment toxicokinetic model.

MDH's one compartment toxicokinetic model assumes the body as one homogeneous volume in which the chemicals mix uniformly between blood and various tissues of the body relative to the rate of elimination.

To derive health-based drinking water screening values, MDH used a reasonable maximum exposure (RME) approach to ensure that the most heavily exposed individuals within the population will be protected. This does not represent a worst case scenario, rather it is intended to be protective of the majority of the population. The two RME scenarios considered for water intake are:

1. An infant-fed formula reconstituted with contaminated water starting at birth and continuing ingestion of contaminated water through life.

2. An infant exclusively breast-fed for 12 months, followed by drinking contaminated water through life.

The model predicts daily serum concentrations over a lifetime of exposure to a constant PFOA or PFOS concentration in drinking water. The daily maternal serum concentration is adjusted for PFAS loss via transfer to the infant and excretion represented by the clearance rate. For breast-fed infants, the daily intake (excretion route for the mother) was calculated from the breast milk intake rate and the breast milk concentration (breast milk to maternal serum ratio). The infant is assumed to be exposed to PFOA and PFOS in utero and serum concentration was estimated using maternal serum concentration at delivery (assumed to be at steady-state concentration) and a placental transfer factor (cord blood to maternal serum ratio).

The following age-specific parameters were incorporated in the toxicokinetic model:

1. 95th percentile drinking water intake rate, consumers only, from birth to over 21 years old (US EPA Exposure Factors Handbook: MDH 2017b)
2. Upper percentile (mean plus two standard deviations) breast milk intake rate (US EPA Exposure Factors Handbook: MDH 2017b)
3. Body weight
4. Volume of distribution (chemical-specific; age-adjusted based on information on extracellular water content as a percent of body weight)
5. Time-weighted average of 95th percentile water ingestion rate from birth to 30-35 years of age (to calculate maternal serum concentration at delivery) (MDH 2017b)

A chemical –specific serum half-life was also included in the model. MDH evaluated available information on infant serum half-life and the adult estimate was retained based on the limitations of the infant data. No age adjustments were made to the serum half-live values.

MDH used the average serum concentration of the LOAEL level for PFOA (1 mg/kg/day: pup developmental effect and maternal liver weight) and NOAEL for PFOS (0.1 mg/kg/day: decreased mean pup body weight, maternal food consumption and body weight change) that was estimated using a three-compartment pharmacokinetic model.

MDH assumed that serum concentration is the best measure of internal dose (PFOS: 0.063 mg/L and PFOA: 0.13 mg/L) and the most appropriate basis for deriving an RfD that is protective of potential health effects. The exposure contributed from non-water sources was addressed using the relative source contribution (RSC) factor. MDH used the US EPA exposure decision tree process along with recent national and local biomonitoring data to identify an RSC of 50% for PFOS (0.063 mg/L x 0.5 = 0.0315 mg/L) and PFOA (0.13 x 0.5 = 0.065 mg/L). An iterative approach was used to identify the water concentration that maintains the serum concertation at or below an RSC of 50% throughout life.

Based on all of the MDH selected inputs to the model:

- the water concentrations that maintains PFOS and PFOA concentration at or below an RSC of 50% are 60 ng/L and 150 ng/L, respectively, for the formula-fed infant exposure scenario.
- the water concentrations that maintains PFOS and PFOA concentration at or below an RSC of 50% are 27 ng/L and 35 ng/L, respectively, for the breastfed infant scenario.

Because of the bioaccumulative nature of PFOS and PFOA, chronic exposure to the mothers and the subsequent transfer through breastmilk result in higher exposure to breastfed infants. Based on this, the breast-fed exposure scenario was more protective for all segments of the population and hence was selected by MDH as the basis for their health-based screening values for PFOS (27 ng/L) and PFOA (35 ng/L).

MDH evaluated their model with maternal and infant serum and breastmilk PFOA and PFOS concentrations collected in two different studies. The ratio of modeled to measured values for maternal and infant serum ranged from 0.40 to 1.7 under various inputs to the model. Based on the available information,

MDH also had the model reviewed by six academic, government, and private industry experts (MDH 2017b).

Selection of methodologies to calculate public health drinking water screening levels

MDHHS selected the MDH toxicokinetic model as the current, most appropriate method to calculate public health drinking water screening levels. While MDH used the model for PFOA and PFOS, MDHHS evaluated the available information to determine whether the model could be used for additional PFAS. As much of the needed information for PFNA and PFHxS was already evaluated by ATSDR, the focus was on the available information used to develop the placental and breast-milk transfer rates. Tables 1 through 4 present summaries of the concurrent measurement of maternal serum, cord blood, and breast-milk concentrations that were available to calculate placental and breast-milk transfer rates. PFOA and PFOS information is presented as a comparison to the information on PFNA and PFHxS.

Table 1: Maternal serum, cord blood, and breast milk concentration of PFOS.

Maternal serum concentration (ng/ml)			Cord blood concentration (ng/ml)			Breast milk concentration (ng/ml)			References
Mean	Median	95th or Max	Mean	Median	95th or Max	Mean	Median	95th or Max	
3.67	3.065	24.5	1.28	1.115	8.04	0.04	<LOD	0.376	Cariou et al. 20115
29.9	NA	NA	11.0	NA	NA	NA	NA	NA	Fei et al. 2007
5.6	NA	9.4	2.0	NA	3.6	0.061	NA	0.13	Kim et al. 2011
36.9	NA	NA	16.7	NA	NA	NA	NA	NA	Tittlemier et al. 2004
16.19	14.54	20.22	7.19	6.08	9.11	NA	NA	NA	Monroy et al. 2008
12.1	NA	NA	7.2	NA	NA	NA	NA	NA	Midasch et al. 2007
3.5	3.2	9.4	1.1	1.0	2.8	NA	0.04	0.11	Formme et al. 2010
3.184	2.922	13.188	1.686	1.47	6.674	0.056	0.042	0.198	Liu et al. 2011
20.7	18.7	48	NA	NA	NA	0.201	0.166	0.470	Kärrman et al. 2007
NA: not available; LOD: limit of detection.									

Table 2: Maternal serum, cord blood, and breast milk concentration of PFOA.

Maternal serum concentration (ng/ml)			Cord blood concentration (ng/ml)			Breast milk concentration (ng/ml)			References
Mean	Median	95th or Max	Mean	Median	95th or Max	Mean	Median	95th or Max	
1.22	1.045	7.31	0.919	0.860	7.06	0.041	<LOQ	0.308	Cariou et al. 20115
NA	NA	NA	NA	NA	NA	0.054	0.026	0.211	Motas et al. 2016
3.8	3.8	5.3	NA	NA	NA	NA	NA	NA	Kärrman et al. 2007
4.5	NA	NA	3.7	NA	NA	NA	NA	NA	Fei et al. 2007
2.2	NA	NA	3.4	NA	NA	NA	NA	NA	Tittlemier et al. 2004
2.24	1.81	2.64	1.94	1.58	2.37	NA	NA	NA	Monroy et al. 2008
2.3	1.9	8.7	1.7	1.4	4.2	NA	NA	0.25	Formme et al. 2010
2.75	NA	NA	3.41	NA	NA	NA	NA	NA	Midasch et al. 2007
1.6	NA	3.2	1.1	NA	2.7	0.041	NA	0.077	Kim et al. 2011
1.655	1.264	5.879	1.50	1.115	6.442	0.181	0.121	1.44	Liu et al. 2011
NA: not available; LOQ: limit of quantitation.									

Table 3: Maternal serum, cord blood, and breast milk concentration of PFHxS.

Maternal serum concentration (ng/ml)			Cord blood concentration (ng/ml)			Breast milk concentration (ng/ml)			References
Mean	Median	95th or Max	Mean	Median	95th or Max	Mean	Median	95th or Max	
2.28	0.619	31	1.19	0.342	16	0.026	<LOD	0.217	Cariou et al. 20115
4.7	4.0	11.8	NA	NA	NA	0.085	0.07	0.172	Kärrman et al. 2007
0.89	NA	1.4	0.58	NA	1.1	0.0072	NA	0.016	Kim et al. 2011
4.053	1.62	2.66	5.05	2.07	2.77	NA	NA	NA	Monroy et al. 2008
0.081	0.068	0.36	0.064	0.055	0.277	NA	NA	NA	Liu et al 2011
NA: not available; LOD: limit of detection.									

Table 4: Maternal serum, cord blood, and breast milk concentration of PFNA. NA: not available; LOD: limit of detection; LOQ: limit of quantitation.

Maternal serum concentration (ng/ml)			Cord blood concentration (ng/ml)			Breast milk concentration (ng/ml)			References
Mean	Median	95th or Max	Mean	Median	95th or Max	Mean	Median	95th or Max	
0.519	0.43	3.29	0.266	<LOQ	2.25	0.014	<LOD	<LOQ	Cariou et al. 20115
NA	NA	NA	NA	NA	NA	0.041	0.04	0.07	Motas et al. 2016
0.8	0.63	2.5	NA	NA	NA	0.017	NA	0.02	Kärrman et al. 2007
0.79	NA	1.3	0.37	NA	0.77	<LOQ	NA	NA	Kim et al. 2011
0.80	0.69	0.87	0.94	0.72	0.80	NA	NA	NA	Monroy et al. 2008
0.546	0.483	1.145	0.332	0.315	0.966	0.026	0.019	0.095	Liu et al. 2011
NA: not available; LOD: limit of detection.									

Based on the above data, MDHHS estimated a placental transfer factor and breast milk transfer factor from paired maternal serum-cord blood and breast milk studies (Table 5).

Table 5: Placental and breast milk transfer factor for PFOA, PFOS, PFHxS and PFNA.

List of PFAS chemical	Placental transfer factor[1, 3]	Breast milk transfer factor[2, 3]
PFOA	0.87	0.052
PFOS	0.42	0.013
PFHxS	0.8	0.012
PFNA	0.69	0.032

1 = The placental transfer factor is calculated by taking the ratio of cord blood concertation to maternal serum concertation.
2 = The breast milk transfer factor is calculated by taking the ratio of breastmilk concentration to maternal serum concertation.
3 = The transfer factors were calculated from a minimum of three paired maternal serum-cord blood and maternal serum-breast milk studies.

Limitation of Toxicokinetic Model: In general, while the use of toxicokinetic model is one step ahead from the traditional way of calculating the drinking water screening level, modeling (both the classical and physiologically based approach) is an oversimplification of the reality. The classical one compartment toxicokinetic model assumes the whole body as one homogenous volume and the change that occurs in the plasma reflects the change in the tissue, which is not necessarily true for PFAS.

For this specific model and inputs used there are additional limitations. One being the values used for the serum half-life and volume of distribution. The adult serum half-life was used for all age groups. There is limited information on infant serum half-lives and use of an adult value for infants and children may not accurately represent age-related differences.

The volume of distribution for PFOA and PFOS is thought to be a representation of extracellular fluid volume. Infants and younger children have a higher water content than older children and adults. While the adult volume of distribution was age-adjusted based on extracellular water content as a percentage of body weight, this may not fully account for the potential difference in infants and younger children versus adults.

Additional information may become available that assists in addressing these limitations. That information should be evaluated and parameters updated as needed.

MDH Equation for PFBS

As maternal serum, cord blood, and breastmilk levels for PFBS were not available, a more traditional approach to calculating a drinking water screening level was used. MDHHS selected the MDH equation for PFBS as it averaged a water intake rate throughout a person's lifetime, from infancy to adulthood (MDH 2017a).

MDH uses the following equation to derive their non-cancer Health Based Values (nHBVs):

$$nHBV = \frac{(Reference\ Dose)x(relative\ source\ contribution)x\ (Conversion\ Factor)}{Water\ intake\ rate}$$

MDH a water ingestion rate of 0.044 L/kg/day (time-weighted average 95th percentile water intake over a lifetime of approximately 70 years of age) (chronic exposure).

MDH used a relative source contribution (RSC) factor of 20% (chronic exposure).
MDH uses the above default RSC for chemicals that are not highly volatile. This RSCs was selected based on a US EPA decision tree. See the Relative Source section for more discussion

The Conversion factor is 1000 µg/mg.

Section 4: Relative Source Contribution

Relative Source Contribution (RSC) is the percentage of a person's exposure to a chemical that comes from drinking water. An RSC of 20% assumes that the other 80% of a person's exposure to a chemical comes from a non-drinking water source.

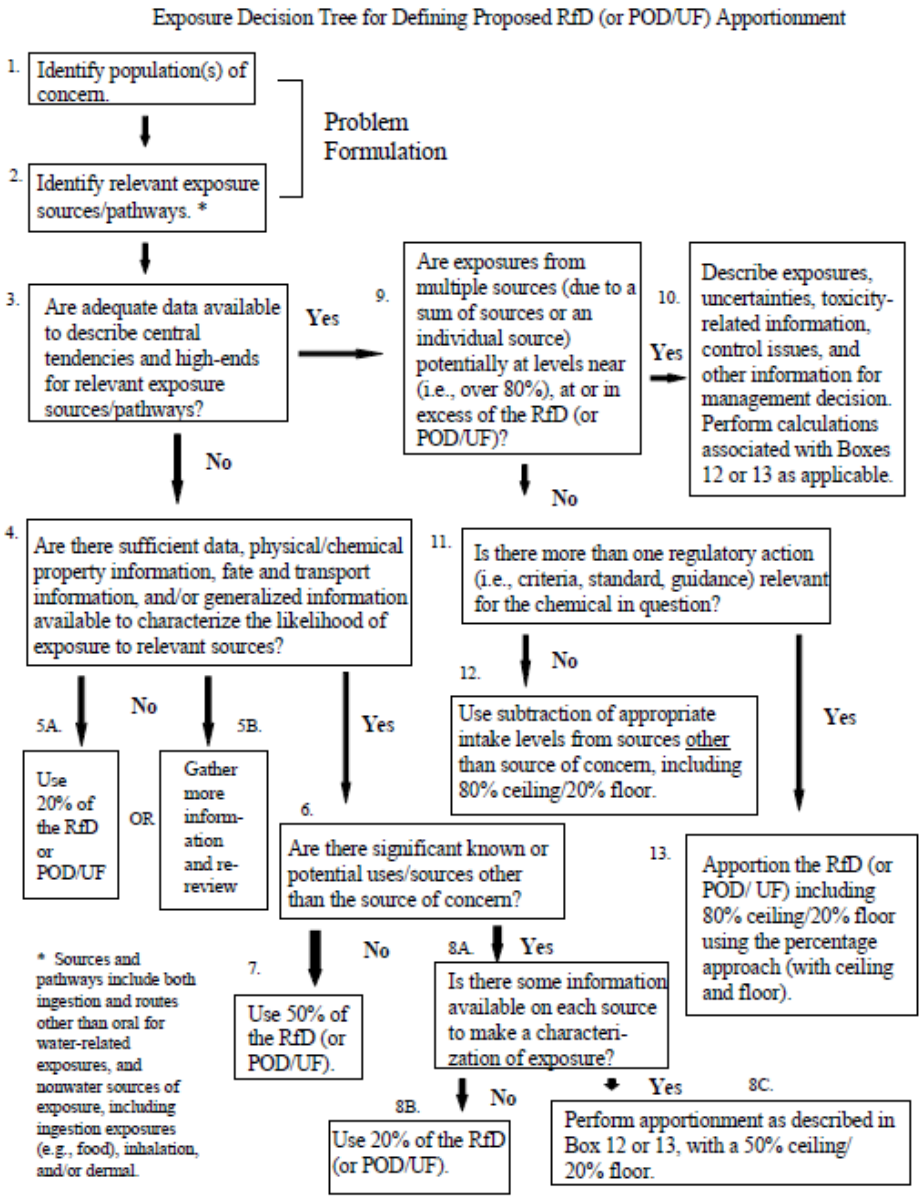
General use of RSCs

The US EPA provides guidance on the selection of a Relative Source Contribution value and also uses specific ones for various screening levels. There is an Exposure Decision Tree that takes into account specific populations of concern, whether these populations are experiencing exposure from multiple sources, and whether levels of exposure or other circumstances make apportionment of the RfD or POD/UF desirable. The most conservative RSC is established at 20%, and the RSC can reach a ceiling of 80% as more information is available about exposure pathways and the source of exposure (See Figure 1).

One other exposure route that is included in the RSC is consumption of fish. When selecting an RSC for use in a dietary intake, marine fish are included as a source of exposure. Freshwater and estuarine fish species consumption is included in the drinking water RSC. Freshwater or estuarine fish may come from waters used as sources of drinking water exposure and the substances present in the water may also be present in the fish. (US EPA 2015)

For US EPA's drinking water screening levels there are several default RSCs selected. For the one- and 10-day health advisories for children, there is no RSC (i.e., assumes 100% of the exposure is from drinking water). For the US EPA's Lifetime Health Advisories, which are typically calculated for a 70-kg adult drinking 2 L of water per day, there is a default RSC of 20% (US EPA 2018). US EPA Maximum Contaminant Limit Goals (MCLGs) also incorporate a default RSC of 20% for non-carcinogens if there isn't sufficient chemical-specific information on other sources of exposure (US EPA 2002).

Figure 1: Exposure Decision Tree for selecting a Relative Source Contribution (US EPA 2000, Figure 4-1)



The US EPA also suggested that when sufficient information is available the subtraction method could be used. The subtraction method allocates the entire RfD to the known sources of exposure by subtracting the known non-target sources of exposure and allocating the remainder of the RfD to the target (i.e. drinking water) in cases where the total estimated exposure is less than the RfD (US EPA 2000).

- To calculate the RSC using the subtraction method:
    - Subtract all non-drinking water exposures (i.e. background) from the RfD to determine the amount of the RfD available for drinking water exposure
    - Determine what percentage of the RfD that remainder represents

- Apply the resulting percentage as the RSC in the health reference level equation

Other agencies have also developed default RSC values using guidance from US EPA. The Minnesota Pollution Control Agency has selected a default RSC of 20% for their Human Health-Based Water Quality Standards. This RSC was selected to account for incidental ingestion during recreational activities, such as swimming and wading, and the consumption of fish. When chemical-specific data is available and sufficient to describe other sources and routes of exposure, a substance-specific RSC can be developed, but would no higher than 80% (MPCA 2014).

The MDEQ defaults to an RSC of 20% in their Part 201 Residential and Non-residential Drinking Water Criteria. MDEQ Rule 57 surface water values for human health include a default RSC of 80%[16].

ATSDR has a variety of screening levels that it calculates with agency-developed MRLs, US EPA RfDs, and US EPA CSF. None of ATSDR's drinking water screening levels (also known as comparison values) incorporate an RSC (ATSDR 2005).

PFAS-specific RSCs

Other agencies have selected RSCs for PFOA, PFOS, PFNA, and PFBS. Their selections are described below.

PFOA

The US EPA's Lifetime HA for PFOA includes a default RSC of 20%. This is due to a lack of information on other exposure. (US EPA 2016a).

MDH used the US EPA exposure decision tree process along with recent national (CDC's 2013-2014 National Health and Nutrition Examination Survey [NHANES] for participants 12 and older) and local biomonitoring data to identify an RSC of 50% for PFOA (MDH 2017b).

NJ DEP used a 20% RSC as there was insufficient data to develop a chemical-specific RSC for PFOA. NJ DEP noted that the default 20% used to at least partially account for higher PFOA exposures in infants (NJ DWQI 2017).

PFOS

The US EPA selected a 20% for use in the Lifetime HA due to a variety of uncertainties. These include a lack of data on other exposure routes, commercial food levels of PFOS, and potential transformation of PFOSA precursors to PFOS (US EPA 2016b).

MDH used the US EPA exposure decision tree process along with recent national (2013-2014 NHANES for participants 12 and older) and local biomonitoring data to identify an RSC of 50% for PFOS (MDH 2017b).

NJ DEP used 20% (default used to at least partially account for higher PFOS exposures in infants (NJ DWQI 2018).

[16] http://dmbinternet.state.mi.us/DMB/ORRDocs/AdminCode/302_10280_AdminCode.pdf

PFNA

NJ DEP selected an RSC of 50% using the subtraction method. Their background PFNA data was the 95th percentile from the 2011-2012 NHANES, which was PFNA serum levels measured in participant 12 years and older (NJ DWQI 2015)

PFBS

MDH selected a default RSC of 20% as there was insufficient data supporting an alternate RSC (MDH 2017a).

Selection of RSCs for PFOA, PFOS, PFNA, PFHxS, and PFBS

MDHHS used the subtraction method to select the appropriate relative source contribution for exposure for the development of PFAS public health drinking water screening levels using the latest data available from NHANES (2013-2014 which included PFAS serum levels from 3- to 11-year-olds along with participants 12 years and older) (CDC 2018). See Table 6 for the 3- to 11-year-olds and Table 7 for participants 12 and older.

Table 6: Percentage of serum level that could be apportioned due to ingestion of contaminated water for 3- to 11-year-olds.

List of PFAS chemical	Serum concentration of RfD (mg/L)	Background (95th Percentile NHANES in mg/L)	Serum level that could be apportioned due to water ingestion (mg/L)	Percentage of serum that could be apportioned to water ingestion (%)
PFOA	0.028	0.00419	0.02381	85
PFOS	0.0248	0.011	0.0138	56
PFHxS	0.2442	0.00312	0.24108	99
PFNA	0.0227	0.00326	0.01944	86
The serum level that could be allocated due to water ingestion is estimated by subtracting the background which is 2013-2014 NHANES 95th Percentile serum levels for children 3 to 11 years old from serum concentration at RfD, and the percentage is calculated by dividing the serum level due to water ingestion to the serum concentration at RfD.				

Table 7: Percentage of serum level that could be apportioned to ingestion of contaminated water for greater than 12 years old.

List of PFAS chemical	Serum concentration of RfD (mg/L)	Background (95th Percentile NHANES in mg/L)	Serum level that could be apportioned due to water ingestion (mg/L)	Percentage of serum that could be apportioned to water ingestion (%)
PFOA	0.028	0.00557	0.02243	80
PFOS	0.0248	0.0185	0.0063	25
PFHxS	0.2442	0.0056	0.2386	98
PFNA	0.0227	0.002	0.0207	91
The serum level that could be allocated due to water ingestion is estimated by subtracting the background which is 2013-2014 NHANES 95th Percentile serum levels for general population, greater than 12 years old from serum concentration at RfD, and the percentage is calculated by dividing the serum level due to water ingestion to the serum concentration at RfD.				

Although MDHHS selected the RSC of 50% for PFOA, PFOS, PFHxS, and PFNA based on the best available information, there are several limitations inherent in this evaluation. For one, the "background" of NHANES doesn't take into account other potentially elevated exposures possible from site-specific contamination, such as fish consumption from waterbodies with elevated PFOS, home-produced foods irrigated with and/or animals watered with PFAS-contaminated water from site-specific contamination.

The "background" values used are from 2013-2014 NHANES data, which is the latest available, and may be outdated by now. They are intended to represent nationwide background and are not Michigan specific. In the future, if the data allows, the North Kent County Exposure Assessment's low stratum (i.e. households with less than 70 ppt total PFAS) may provide additional data.

As there is no NHANES data for PFBS, MDHHS selected a RSC of 20% for PFBS.

Section 5: Summary of parameters selected for public health drinking water screening level development

Serum levels used in development of these screening levels are not meant to indicate a level where health effects are likely. These serum levels are calculated to be at a point where no or minimal risk exists for people drinking water with a certain PFAS.

PFOA

Critical Studies (ATSDR)	Onishchenko N, Fischer C, Wan Ibrahim WN, et al. 2011. Prenatal exposure to PFOS or PFOA alters motor function in mice in a sex-related manner. Neurotox Res 19(3):452-461.
Point of Departure (calculated by ATSDR)	8.29 mg/L serum PFOA
Uncertainty and modifying factors (ATSDR)	A total uncertainty factor of 300 (10 for use of a lowest observed adverse effect level (LOAEL), 3 for animal to human variability and 10 for human variability)
Toxicity value (ATSDR)	average serum concentration of 0.028 mg/L
Methodology for drinking water screening level development (MDH)	MDH toxicokinetic model
Exposure scenario (model parameters, water intake)	Breast-fed infant, which is also protective of a formula-fed infant Placental transfer = 0.87 (MDH 2017b) Breastmilk transfer = 0.052 (MDH 2017b) Half-life = 840 days (US EPA 2016a: Bartell et al. 2010) Volume of distribution = 0.2 L/kg (ATSDR 2018) 95th percentile drinking water intake, consumers only, from birth to more than 21 years old (MDH 2017b: US EPA 2011) Upper percentile (mean plus two standard deviations) breast milk intake rate (MDH 2017b: US EPA 2011) Time-weighted average of water ingestion rate from birth to 30-35 years of age (to calculate maternal serum concentration at delivery) (MDH 2017b)
Relative Source Contribution (MDHHS)	50% (0.5) Based on 2013-2014 NHANES 95th percentiles for 3-11 and over 12 years old participants (CDC 2018)
Public Health Drinking Water Screening Level (MDHHS)	9 ng/L (ppt)

Description of the Public Health Drinking Water Screening Level (MDHHS)	Protective of breast-feeding infants, both from exposure they may receive prenatally and while breast-feeding (higher levels in drinking water may cause maternal serum and breast-milk to result in elevated infant exposure)

See Figure 1.

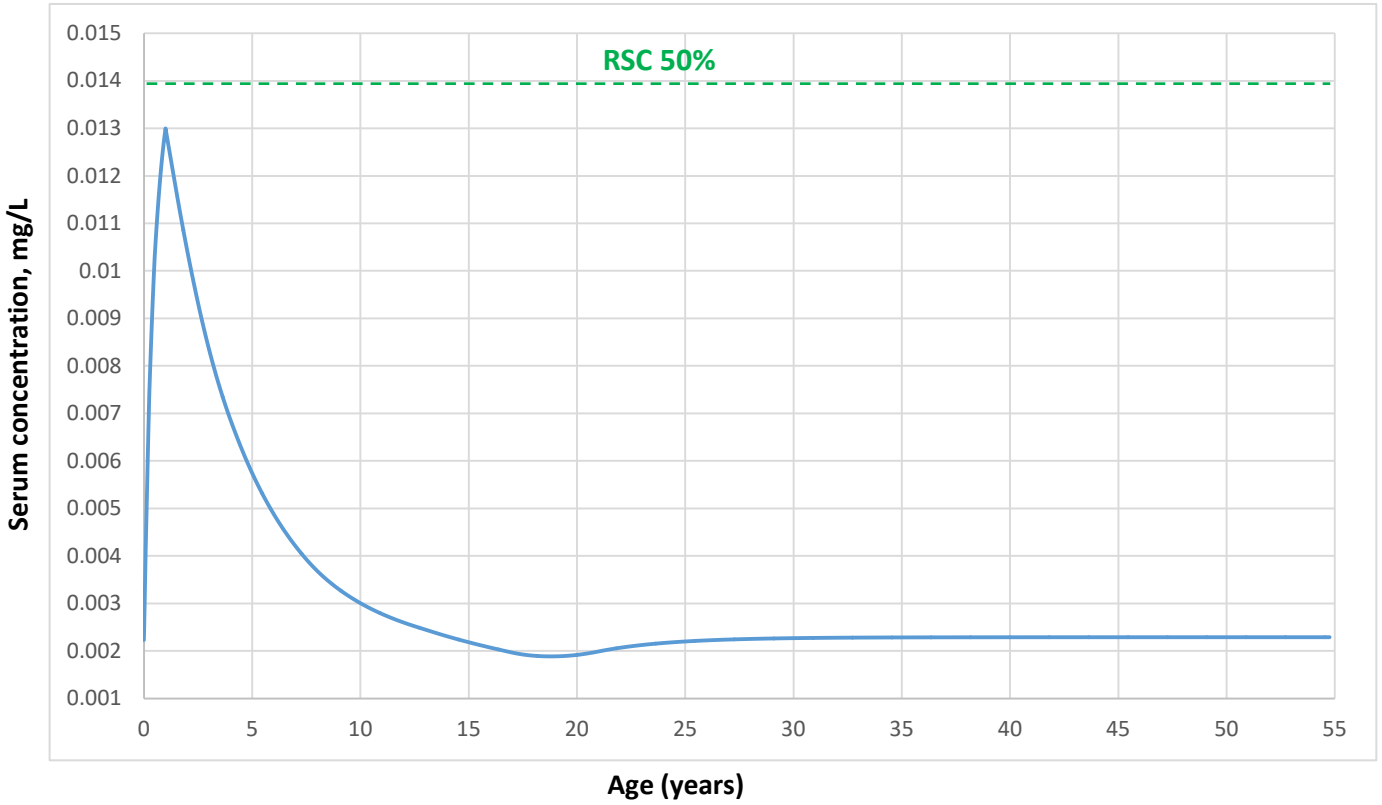


Figure 1. PFOA serum concentration for an infant exclusively breast-fed for 12 months, followed by drinking contaminated water through life (RSC of 50% [0.014 mg/L = 50% of the serum equivalent at the RfD] and a water concentration of 9 ng/L).

PFOS

Critical Study	Luebker DJ, Case MT, York RG, et al. 2005. Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats. Toxicology 215(1-2):126-148.
Point of Departure	7.43 mg/L serum PFOS
Uncertainty and modifying factors	A total uncertainty and modifying factors of 300 (3 for animal to human variability and 10 for human variability) and modifying factor of 10 (for concern that immunotoxicity may be more sensitive than developmental toxicity)
Toxicity value	average serum concentration of 0.0248 mg/L
Methodology for drinking water screening level development	MDH toxicokinetic model
Exposure scenario (model parameters, water intake)	Breast-fed infant, which is also protective of a formula-fed infant Placental transfer = 0.43 (MDH 2017b) Breastmilk transfer = 0.013 (MDH 2017b) Half-life = 2000 days (ATSDR 2018: Olsen et al. 2007) Volume of distribution = 0.2 L/kg (ATSDR 2018) 95th percentile drinking water intake, consumers only, from birth to more than 21 years old (MDH 2017b: US EPA 2011) Upper percentile (mean plus two standard deviations) breast milk intake rate (MDH 2017b: US EPA 2011) Time-weighted average water ingestion rate from birth to 30-35 years old (to calculate maternal serum concentration at delivery) (MDH 2017b)
Relative Source Contribution	50% (0.5) Based on 2013-2014 NHANES 95th percentiles for 3- to 11-year-old participants (CDC 2018) (Based on 2013-2014 NHANES 95th percentiles for 12 and older, use of a 50% RSC for infants results in an modeled serum level for adults that is lower than the serum level equivalent with an RSC of 27%)
Public Health Drinking Water Screening Level	8 ng/L (ppt)
Description of the Public Health Drinking Water Screening Level	Protective of breast-feeding infants, both from exposure they may receive prenatally and while breast-feeding (higher levels in drinking water may cause maternal serum and breast-milk to result in elevated infant exposure)

See Figure 2.

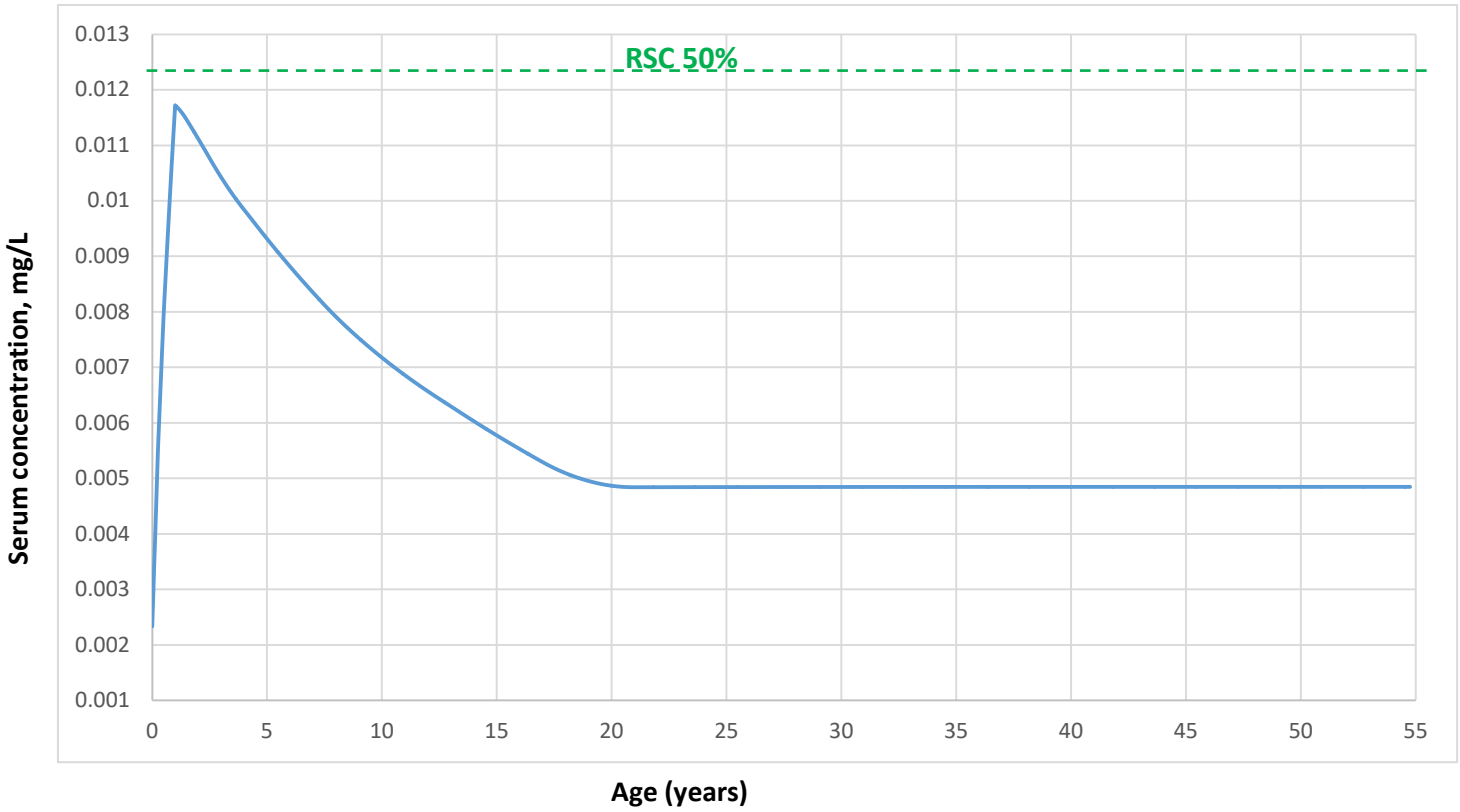


Figure 2. PFOS serum concentration for an infant exclusively breast-fed for 12 months, followed by drinking contaminated water through life (RSC of 50% [0.0124 mg/L = 50% of the serum equivalent at the RfD] and a water concentration of 8 ng/L).

PFNA

Toxicity value/studies/health endpoints	Das KP, Grey BE, Rosen MB, et al. 2015. Developmental toxicity of perfluorononanoic acid in mice. Reprod Toxicol 51:133-144.
Point of Departure	6.8 mg/L serum PFNA
Uncertainty and modifying factors	A total uncertainty factor of 300 (3 for animal to human variability and 10 for human variability and 10 for database limitation)
Toxicity value	average serum concentration of 0.0227 mg/L
Methodology for drinking water screening level development	MDH toxicokinetic model
Exposure scenario (model parameters, water intake)	Breast-fed infant, which is also protective of a formula-fed infant Placental transfer = 0.69 Breastmilk transfer = 0.032 Half-life = 900 days (ATSDR 2018: Zhang et al. 2013) Volume of distribution = 0.2 L/kg (ATSDR 2018) 95th percentile drinking water intake, consumers only, from birth to more than 21 years old (MDH 2017b: US EPA 2011) Upper percentile (mean plus two standard deviations) breast milk intake rate (MDH 2017b: US EPA 2011) Time-weighted average water ingestion rate from birth to 30-35 years of age (to calculate maternal serum concentration at delivery) (MDH 2017b)
Relative Source Contribution	50% (0.5) Based on 2013-2014 NHANES 95th percentiles for 3-11 and over 12 years old participants (CDC 2018)
Public Health Drinking Water Screening Level	9 ng/L (ppt)
Description of the Public Health Drinking Water Screening Level	Protective of breast-feeding infants, both from exposure they may receive prenatally and while breast-feeding (higher levels in drinking water may cause maternal serum and breast-milk to result in elevated infant exposure)

See Figure 3.

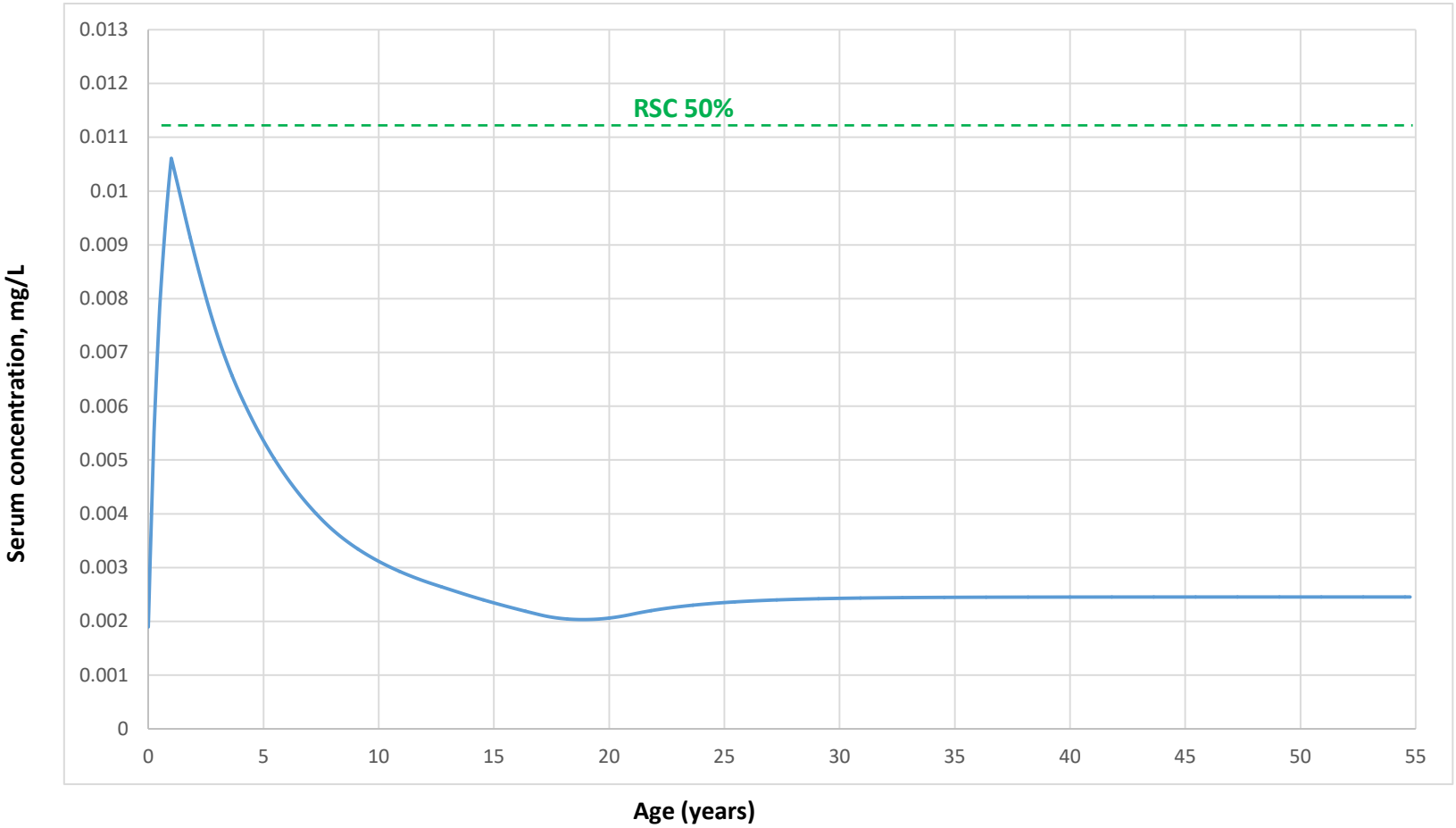


Figure 3. PFNA serum concentration for an infant exclusively breast-fed for 12 months, followed by drinking contaminated water through life (RSC of 50% [0.01135 mg/L = 50% of the serum equivalent at the RfD] and a water concentration of 9 ng/L).

PFHxS

Toxicity value/studies/health endpoints	Butenhoff JL, Chang S, Ehresman DJ, et al. 2009. Evaluation of potential reproductive and developmental toxicity of potassium perfluorohexanesulfonate in Sprague Dawley rats. Reprod Toxicol 27:331-341.
Point of Departure	73.22 mg/L serum PFHxS
Uncertainty and modifying factors	A total uncertainty factor of 300 (3 for animal to human variability and 10 for human variability and 10 for database limitation)
Toxicity value	average serum concentration of 0.2441 mg/L
Methodology for drinking water screening level development	MDH toxicokinetic model
Exposure scenario (model parameters, water intake)	Breast-fed infant, which is also protective of a formula-fed infant Placental transfer = 0.8 Breastmilk transfer = 0.012 Half-life = 3100 days (ATSDR 2018: Olsen et al. 2007) Volume of distribution = 0.287 L/kg (ATSDR 2018) 95th percentile drinking water intake, consumers only, from birth to more than 21 years old (MDH 2017b: US EPA 2011) Upper percentile (mean plus two standard deviations) breast milk intake rate (MDH 2017b: US EPA 2011) Time-weighted average water ingestion rate from birth to 30-35 years of age (to calculate maternal serum concentration at delivery) (MDH 2017b)
Relative Source Contribution	50% (0.5) Based on 2013-2014 NHANES 95th percentiles for 3-11 and over 12 years old participants (CDC 2018)
Public Health Drinking Water Screening Level	84 ng/L (ppt)
Description of the Public Health Drinking Water Screening Level	Protective of breast-feeding infants, both from exposure they may receive prenatally and while breast-feeding (higher levels in drinking water may cause maternal serum and breast-milk to result in elevated infant exposure)

See Figure 4.

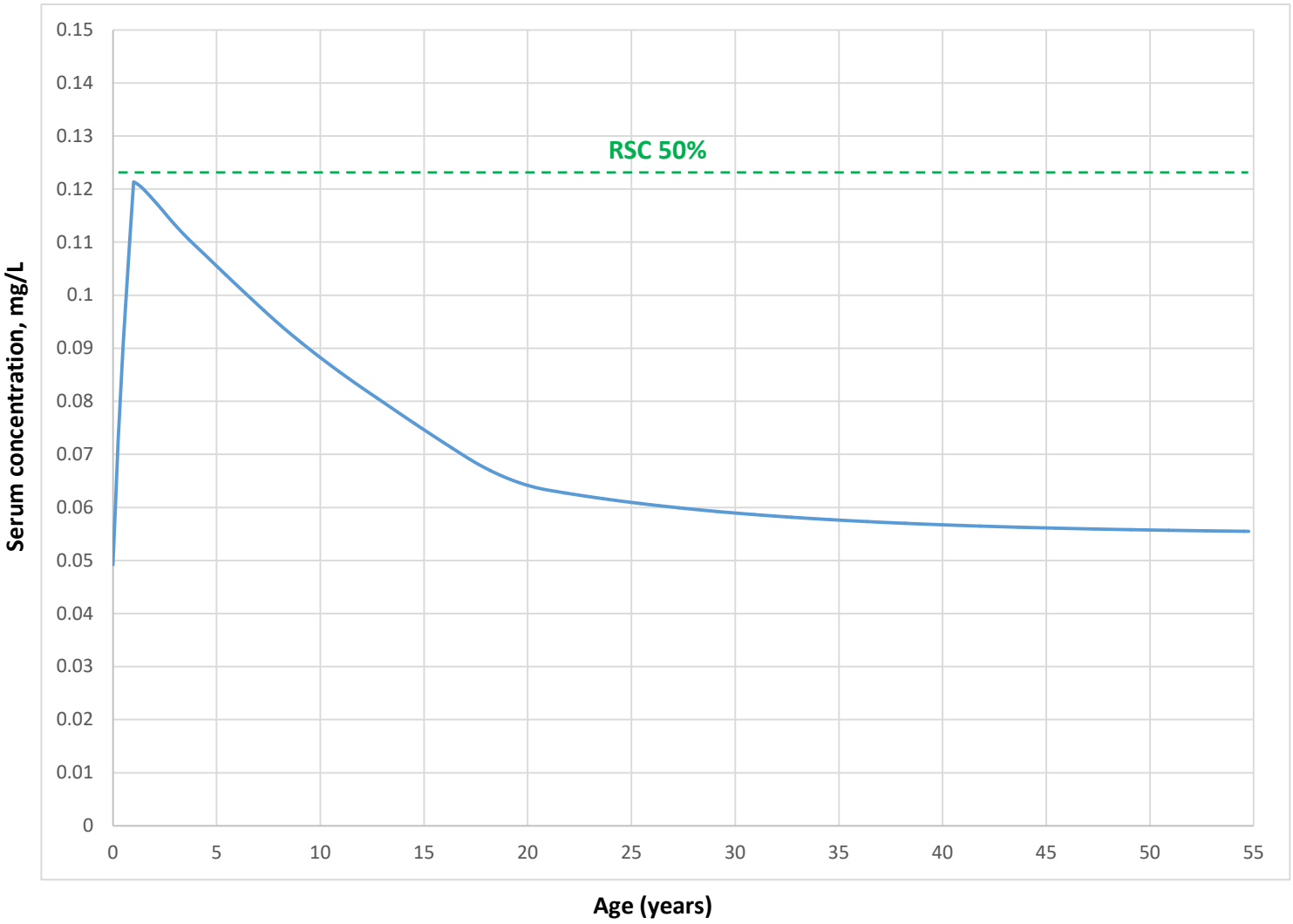


Figure 4. PFHxS serum concentration for an infant exclusively breast-fed for 12 months, followed by drinking contaminated water through life (RSC of 50% [0.1221 mg/L = 50% of the serum equivalent at the RfD] and a water concentration of 84 ng/L).

PFBS

Toxicity value/studies/health endpoints	Lieder PH, Chang SC, York RG, et al. 2009a. Toxicological evaluation of potassium perfluorobutanesulfonate in a 90-day oral gavage study with Sprague-Dawley rats. Toxicology 255:45-52.
Point of Departure	78.7 mg/kg/day ($BMDL^{10}$) divided by 350 for a human equivalent dose of 0.225 mg/kg/day
Uncertainty and modifying factors	Total uncertainty factor of 1,000: • A 3 for toxicodynamic differences in rats and humans • A 3 for database gap as no developmental toxicity study has been conducted • A 10 for human to human variability • A 10 for less than chronic duration
Toxicity value	230 ng/kg/day
Methodology for drinking water screening level development	MDH drinking water screening level equation (see above)
Exposure scenario (model parameters, water intake)	Water ingestion rate (chronic) = 0.044 L/kg/day (time-weighted average of the 95th percentile of consumers only over a lifetime of approximately 70 years of age).
Relative Source Contribution	20% (default)
Public Health Drinking Water Screening Level	1000 ng/L (ppt)
Description of the Public Health Drinking Water Screening Level	Protective for exposure throughout a lifetime (infant to adult)

Equation for PFBS

$$Public\ health\ drinking\ water\ screening\ level = \frac{(Reference\ Dose)x(relative\ source\ contribution)x\ (Conversion\ Factor)}{Water\ intake\ rate}$$

Along with the RfDs described above inputs were used:

- Water intake rate: 0.044 L/kg/day (time-weighted average over a lifetime of approximately 70 years of age).
- RSC = 20%
- Conversion factor = 1000 µg/mg.

Section 6: Public Health Drinking Water Screening Levels for PFOA, PFOS, PFNA, PFHxS, PFBS

Use of the public health drinking water screening levels

Environmental media screening levels, such as those for drinking water, are developed using multiple pieces of information, including toxicity values and exposure parameters.

The US EPA defines toxicity values as:

- "A numerical expression of a substance's dose-response relationship used in risk assessments".[17]

ATSDR has a similar definition for their minimal risk levels (MRLs):

- "An estimate of the daily human exposure to a substance that is likely to be without appreciable risk of adverse health effects during a specified duration of exposure".[18]

Oral toxicity values include:

- US EPA reference doses (RfDs),)
- US EPA cancer slope factors, and
- ATSDR MRLs.

Variance of Screening Levels

Because of various assumptions and the selection of exposure parameters, drinking water screening levels developed by different agencies often vary. Many of the differences are driven by:

- Identification of the most sensitive population
- Scenario used to describe that population's exposure
- Assumption of body weights
- Assumption of water intake rates
- Relative Source Contribution (RSC)

About Relative Source Contribution

Relative Source Contribution (RSC) is the amount of the total exposure to the chemical allocated to the exposure pathway being assessed (e.g., drinking water) after accounting for the assumed background exposure amount for any given population. RSCs vary typically between 20% and 80% of assumed exposures when people could have potential or known exposure to the chemical through media other than the source of concern. For example, use of an RSC of 20% for a drinking water screening level indicates that 20% of an individual's total exposure assumed to come from drinking water and 80% of the individual's total exposure is assumed to come from other sources.

[17] US EPA RAGS A https://www.epa.gov/sites/production/files/2015-09/documents/rags_a.pdf
[18] https://www.atsdr.cdc.gov/hac/phamanual/appf.html

This document and subsequent attachments describe the available toxicity values, methodology for developing screening levels, and a description of the selection criteria for each PFAS.

Public Health Drinking Water Screening Levels

Table 8 presents recommended public health drinking water screening levels. The PFOA, PFOS, PFNA, and PFHxS public health drinking water screening levels were developed using a toxicokinetic model[19] to be protective for the population of most concern: bottle- and breast-fed infants. Toxicokinetic models are used to predict chemical absorption, distribution, metabolism, and elimination in humans and animals based on what is known from animal and human studies. Much of the human information used for these specific models were from studies of occupational exposed adults and adults exposed to PFOA-contaminated drinking water.

PFBS public health drinking water screening levels are calculated using a methodology different than the other four PFAS because the necessary model inputs are not available. Instead, the PFBS screening level was developed using typical drinking water screening level equations. PFBS is one of the PFAS measured in participants of the Center for Disease Control and Prevention's National Health and Nutrition Examination Survey (NHANES). Almost all of the NHANES participants in the 2003-2010 and 2011-2014 survey years did not have detectable PFBS in their serum. Participants in the 2013-2014 survey years included children ages 3 to 11. One reason why PFBS may not be detected in humans is the relatively short serum half-life of PFBS compared to other PFAS. In occupationally exposed humans, PFBS had a serum half-life of approximately 665 hours (about 28 days), which is much shorter than serum half-lives estimated for PFOA, PFOS, PFHxS, and PFNA. As PFBS is not detectable in serum and has a shorter half-life than the other PFAS included here, public health drinking water screening levels developed using the typical drinking water screening level equations are assumed to be adequately protective. The PFBS public health drinking water screening level is calculated to be protective of exposure for children as well as adults.

Comparison of drinking water PFAS concentrations to the public health drinking water screening levels:

- **Below Screening Levels: Further Action Not Typically Required**

  In many situations, because these screening levels are developed to be protective of all individuals, including formula- and breast-fed infants, when drinking water PFAS concentrations are below the public health drinking water screening levels, no further evaluation is typically required. When a source-specific release is the possible cause of the PFAS detections, a site-specific public health risk assessment can occur to account of mixtures of PFAS and site-specific conditions.

- **Above Screening Levels: May Require Mitigation and Additional Evaluation**

  Drinking water PFAS concentrations above the screening level indicates further site-specific evaluation is needed, which can lead to public health recommendations. When multiple

[19] The toxicokinetic model was developed by the Minnesota Department of Health (Minnesota Department of Health Background Document: Toxicokinetic Model for PFOS and PFOA and Its Use in the Derivation of Human Health-based Water Guidance Values.).

PFAS are detected, the Agency for Toxic Substances and Disease Registry recommends considering an evaluation of an individual's combined PFAS exposure.

Note, in locations where the source or groundwater plumes have been identified but have not been characterized by size or concentration, public health protective actions may be recommended at any detectable level of any PFAS.

These public health drinking water screening levels will be periodically evaluated, likely on a multi-year schedule, and additional or revised screening levels for other PFAS will be developed as relevant information becomes available.

Table 8: Recommended public health drinking water screening levels (in nanograms per Liter [ng/L] or parts per trillion [ppt]) for various PFAS.

PFAS	Public Health Drinking Water Screening Level	Description of protectiveness of the screening level
PFOA	9 ng/L (parts per trillion [ppt])	Protective of breast-feeding infants, both from exposure they may receive prenatally and while breast-feeding (higher levels in drinking water may cause maternal serum and breast-milk to result in elevated infant exposure). This screening level is also protective of formula-fed infants and other ages (older child and adult exposure).
PFOS	8 ng/L (ppt)	
PFNA	9 ng/L (ppt)	
PFHxS	84 ng/L (ppt)	
PFBS	1000 ng/L (ppt)	Protective of a lifetime of exposure, from infancy to adulthood

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Section 8: Addendum - MPART Human Health Working Group Product

Section 9: Addendum - Matrix of Agency Screening Levels Worksheet

Section 8: Addendum- MPART Human Health Working Group Product

Summary of PFAS toxicological evaluations supporting health-based drinking water screening levels

Michigan Department of Health and Human Services

Michigan PFAS Action Response Team Human Health Workgroup

November 5, 2018

Summary

While the knowledge regarding perfluoroalkyl substances (PFAS) toxicity is expanding daily, there are still data gaps that limit the development of toxicity values and drinking water screening levels[1]. Several federal and state agencies have developed PFAS toxicity values over the past decade, however, these are primarily on a limited subset of PFAS. Both the toxicity values and drinking water screening levels vary due to critical study selection that serves as the basis of the toxicity value, the exposure scenario for the drinking water screening levels, the selection of uncertainty or modifying factors and a relative source contribution factor, and incorporation of toxicokinetic information both in the calculation of a toxicity value and drinking water screening levels.

Multiple health-based drinking water screening levels were calculated by these states and federal agencies as a result of varying toxicity values, exposure scenarios, and drinking water screening level equations. The original calculated drinking water values are described. In addition, to minimize the influence of inter-agency variability, with drinking water screening levels calculated by holding either the toxicity values or exposure scenarios constant are also presented for comparison. These latter calculations demonstrate the range of health-based drinking water screening levels that could be derived through application of a single toxicity value across different screening level development practices. (Note that this comparison may not part of the standard policies and procedures by the agencies developing the values.) These findings indicate that the range of drinking water values can vary by one to two orders of magnitude (10 to 100 times).

The Agency for Toxic Substances and Disease Registry (ATSDR) has provided guidance for assessing people's exposure to chemicals in drinking water and other media. As stated in their Public Health Assessment Guidance Manual[2], health-based drinking water screening levels, which can also be called comparison values,

"…serve only as guidelines to provide an initial screen of human exposure to substances. Although concentrations at or below the relevant comparison value may reasonably be considered safe, it does not automatically follow that any environmental concentration that exceeds a comparison value would be expected to produce adverse health effects."

Many decisions must be made by public health professionals in the derivation of health-based drinking water screening levels. Scientific consensus on the selection of the most appropriate PFAS toxicity values could reduce some of the variability observed among the many reported screening levels. However, as demonstrated by the program summaries in this document, agency-specific science policy decisions represent a significant contribution to the range of reported screening levels. The selected exposure scenario determines which assumptions, such as infant or adult receptor, respective drinking water intake rates, and length of exposure, are evaluated. These assumptions, in turn, are represented by a range of possible values, leading to further variability in decision making.

[1] The term "drinking water screening level is used generically as many agencies have specific names for their screening values for drinking water or groundwater used as a source of drinking water.
[2] The ATSDR Public Health Assessment Guidance Manual (2005 Update) is at https://www.atsdr.cdc.gov/hac/PHAManual/toc.html.

Key findings included in this document:

- The approaches used to develop drinking water screening levels vary based on health endpoints identified or programmatic decisions. These findings in this document indicate that the range of drinking water values can vary by one to two orders of magnitude (10 to 100 times).
- Twelve state agencies, including the Michigan Department of Environmental Quality, use the US Environmental Protection Agency's PFOA+PFOS Lifetime Health Advisory. One additional state will be proposing use of Lifetime Health Advisory to replace their current value.
- Three state agencies use the PFOA+PFOS Lifetime Health Advisory, but include additional PFAS beyond PFOA and PFOS.
- An additional two state agencies use the US Environmental Protection Agency PFOA and PFOS toxicity values (reference doses) in their own drinking water screening level equations.
- While various approaches are used, several agencies evaluate multiple PFAS together:
    - the US Environmental Protection Agency has combined PFOA and PFOS in their Lifetime Health Advisory,
    - the Agency for Toxic Substances and Disease Registry recommends that when multiple PFAS are present, they be evaluated together, and
    - the Minnesota Department of Health recommends concurrent evaluation of multiple chemicals using an additive approach.

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Purpose

The purpose of this document is to provide a short description of existing poly- and perfluoroalkyl substances (PFAS) toxicity values used by various state and federal agencies and a side-by-side comparison of drinking water screening levels that could result from those toxicity values using a consistent set of equations.

Background

Environmental media screening levels, such as those for drinking water, are developed using multiple pieces of information including toxicity values and exposure parameters. The US EPA defines toxicity values as, "a numerical expression of a substance's dose-response relationship used in risk assessments".[3] ATSDR has a similar definition for their minimal risk levels – "an estimate of the daily human exposure to a substance that is likely to be without appreciable risk of adverse health effects during a specified duration of exposure".[4] Oral toxicity values include EPA reference doses (RfDs) and cancer slope factors and ATSDR minimal risk levels (MRLs).

The development of toxicity values protective of noncancer health effects, such as the RfDs or MRLs, begins with a review of the available toxicity and epidemiology literature and identification of a critical study or studies. Adequate human data is typically selected over laboratory animal data; however, adequate human data is often unavailable. Laboratory animal studies are often selected as the critical study. In some cases, multiple co-critical studies are identified, with different health endpoints resulting from relatively similar exposures. Health endpoints identified in the critical study should be biologically relevant and plausible for humans, if the study was conducted in laboratory animals. The determination of biological relevance or plausibility can use information from epidemiological studies or from mechanistic data in laboratory animals and human and animal cell lines.[5]

Using that critical study, a "point of departure" is identified. This can be a no observed adverse effect level (NOAEL), lowest observed adverse effect level (LOAEL), or a lower limit on a benchmark dose (BMDL). The point of departure (POD) may be an administered dose, a modeled dose, or a serum level. When sufficient information is available on the way an individual PFAS moves into and out of human and laboratory animal's bodies, laboratory animal serum levels can be converted to a human equivalent serum level.

The point of departure is divided by uncertainty and modifying factors to derive the toxicity value. Uncertainty and modifying factor values typically range between one and ten, with higher numbers used when there is greater uncertainty. The uncertainty and modifying factors are multiplied together and the point of departure is divided by the product of these factors. Uncertainty factors are included to account for uncertainties due to the potential intraspecies variability among humans, the potential interspecies differences between laboratory animals and humans, the use of a point of departure that

[3] US EPA RAGS A https://www.epa.gov/sites/production/files/2015-09/documents/rags_a.pdf
[4] https://www.atsdr.cdc.gov/hac/phamanual/appf.html
[5] Concepts from https://www.atsdr.cdc.gov/mrls/index.asp and https://www.epa.gov/iris/reference-dose-rfd-description-and-use-health-risk-assessments#1.2.1

resulted in adverse health effects (i.e., LOAEL), and the use of a shorter than chronic exposure time[6]. A modifying factor is typically applied to account for gaps in the knowledge base; for example, a minimal number of studies evaluating the development of a health endpoint.[7]

Typically, the critical study has the most sensitive health endpoint observed in all of the studies, i.e., the health endpoint resulting from the lowest exposure dose. There may be an RfD selected that represents an average when there are multiple health endpoints resulting from a similar range of doses.

These toxicity values are then used to develop screening levels for environmental media, including drinking water. ATSDR uses their MRLs to develop environmental media evaluation guides for drinking water, air, and soil. ATSDR also develops screening levels using US EPA's RfDs and cancer slope factors.

As an overview of the variability in exposure scenarios and inputs, ATSDR's Environmental Media Evaluation Guides (EMEGs), Reference Dose Media Evaluation Guides (RMEGs), Cancer Risk Evaluation Guides (CREGs); US EPA's Tapwater Regional Screening Levels (RSL), Drinking Water Equivalent Levels (DWELs), Lifetime Health Advisories (HA); and MDEQ's Part 201 Residential Drinking Water Criteria are briefly summarized below.

Table 1: Exposure scenario and inputs to various drinking water screening levels used by the Agency for Toxic Substances and Disease Registry (ATSDR), US Environmental Protection Agency (US EPA), and Michigan Department of Environmental Quality (MDEQ) Remediation and Redevelopment Division (RRD).

	ATSDR[1]	US EPA[2]	MDEQ[3]
Exposure route included	EMEG, RMEG, CREG - Ingestion	DWEL, Lifetime HA - Ingestion Tapwater RSL - Ingestion, inhalation, dermal contact	Ingestion
Toxicity value	EMEG – Minimal Risk Level (MRL) RMEG – US EPA's Reference Dose (RfD) CREG – US EPA's Cancer Slope Factor (CSF)	DWEL, Lifetime HA - EPA's RfD Tapwater RSL – US EPA's RfDs and CSFs, ATSDR's MRLs or California EPA's CSF	US EPA's RfDs and CSFs, ATSDR's MRLs or California EPA's CSF
Body weight	EMEG, RMEG - 7.8 kg child; 80 kg adult CREG – age-specific body weight for a 78 year lifetime (child and adult)	DWEL, Lifetime HA - 70 kg adult Tapwater RSL - 15 kg for a child and 80 kg for an adult (Age-adjusted for carcinogens)	Age-adjusted using a 15 kg child and 80 kg adult

[6] This uncertainty factor is not typically used by ATSDR as they develop values for acute (less than 14 days), intermediate (more than 14 days to one year), and chronic (over one year) exposures.
[7] https://www.epa.gov/sites/production/files/2015-09/documents/rags_a.pdf

	ATSDR[1]	US EPA[2]	MDEQ[3]
Water ingestion rate	EMEG, RMEG - 1.113 Liters (L)/day child; 3.092 L/day adult CREG – age-specific rate for a 78 year lifetime (child and adult)	DWEL, Lifetime HA - 2 L/day adult Tapwater RSL - 0.78 L/day for a child and 2.5 L/day for an adult (Age-adjusted for carcinogens)	Age-adjusted using 0.78 L/day for a child and 2.5 L/day for an adult
Relative Source Contribution	None used (all exposure is assumed to be from water)	DWEL - 100% (all exposure is assumed to be from water) Lifetime HA - 20% (non-water sources of exposure are 80% of total exposure)	20% (non-water sources of exposure are 80% of total exposure)

1 = There are no additional exposure parameters or inputs for these calculations. The equation and a more detailed description can be found at https://www.atsdr.cdc.gov/hac/phamanual/appf.html. EMEG = Environmental Media Evaluation; RMEG = Reference Dose Media Evaluation Guides; CREG = Cancer Risk Evaluation Guides

2 = For the Tapwater Regional Screening Level (RSL), other inputs are used to address days of exposure (350 out of 365 days), the target hazard quotient or cancer risk, dermal contact and inhalation routes of exposure along with a conversion factor for differences in the units used. The full equation and exposure parameters can be found at https://www.epa.gov/risk/regional-screening-levels-rsls-equations. For the Drinking Water Equivalent Level (DWEL) and Lifetime Health Advisories (HA), the equation uses a daily exposure for a lifetime.

3 = For the Residential Drinking Water Criteria, other inputs are used to address days of exposure (350 out of 365 days) and the target hazard quotient or cancer risk. The proposed Part 201 criteria include consideration of developmental toxicants; equations for an exposure to a child only or a pregnant woman are also available.

As presented in Table 1, there are multiple areas of difference in the drinking water screening levels developed by different agencies. Many of the differences are driven by the population considered most sensitive, and the appropriate body weights and water ingestion rates will vary accordingly. Relative Source Contributions (RSC) are used, typically between 20 and 80%, when people have potential or known exposure to the chemical through media other than drinking water. For example, use of an RSC of 20% for a drinking water screening level indicates that 20% of an individual's total exposure is assumed to come from drinking water while 80% of the individual's total exposure is assumed to come from other sources.

Major PFAS identified at Michigan sites of groundwater contamination

Four residential well data sets were assessed at PFAS contamination sites – Wurtsmith Air Force Base and Oscoda area, North Kent County Disposal Investigations area, Grayling area, and Alpena Combat Readiness Training Center area. Data received by MDHHS by June 14, 2018 was included in this summary. For all four data sets, between 96 and 99% of the mass of PFAS detected was composed of

nine individual chemicals,[8] as shown in Figure 1. The sum of PFOS and PFOA ("Group 1", which are included in the US EPA Lifetime HA) concentrations ranged from 16 to 73% of total PFAS at each site, while the sum of PFOA, PFOS, PFNA, and PFHxS (Groups 1 and 2; the four chemicals for which ATSDR developed provisional intermediate oral MRLs) accounted for between 31 and 84% of total PFAS at each site.[9]

The six chemicals (PFBA, PFBS, PFHpA, PFHxA, PFPeA, and 6:2 FTS) which account for the majority of remaining PFAS at these sites (which are not included in the US EPA Lifetime HA or have no available ATSDR MRLs) are designated as "Group 3" in Figure 2 and represent between 13 and 68% of total PFAS observed at each site. The sum of Groups 1, 2, and 3 together account for more than 96% of the mass of PFAS detected at these sites. Of the remaining chemicals ("Group 4"), 15 comprised the remaining 1.5 to 3.2% of PFAS mass observed at these sites, while five further chemicals were not detected in any sample at these sites.[10]

For the PFAS listed in this section, various federal agency and other states toxicity values have been compiled and described below. Toxicity values for additional PFAS are included in Appendix 1 for reference.

[8] PFOA, PFOS, PFHxS, PFBA, PFBS, PFHxA, PFHpA, PFPeA, and 6:2 FTS

[9] PFNA concentrations were negligible, accounting for less than 1% (ranging from 0.1 to 0.5%) of total PFAS at each site.

[10] The suite of chemicals analyzed varied by site and sample, which will likely have caused a degree of bias in these reported proportions.

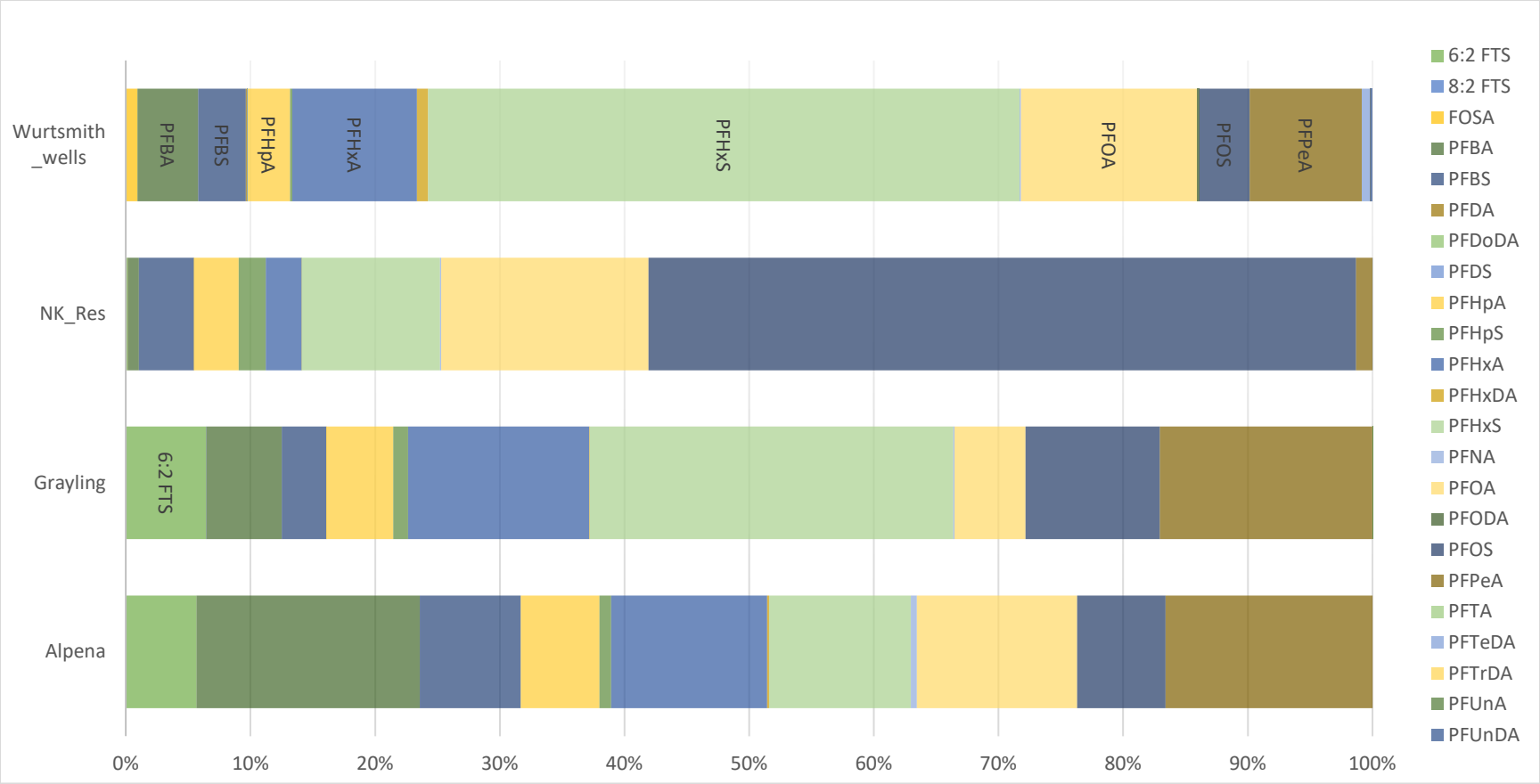

Figure 1: Sum of PFAS detections by chemical by mass as a proportion of site total (Wurtsmith_wells = Wurtsmith Air Force Base and Oscoda area, NK_Res = North Kent County Disposal Investigations area, Grayling = Grayling area , and Alpena = Alpena Combat Readiness Training Center area).

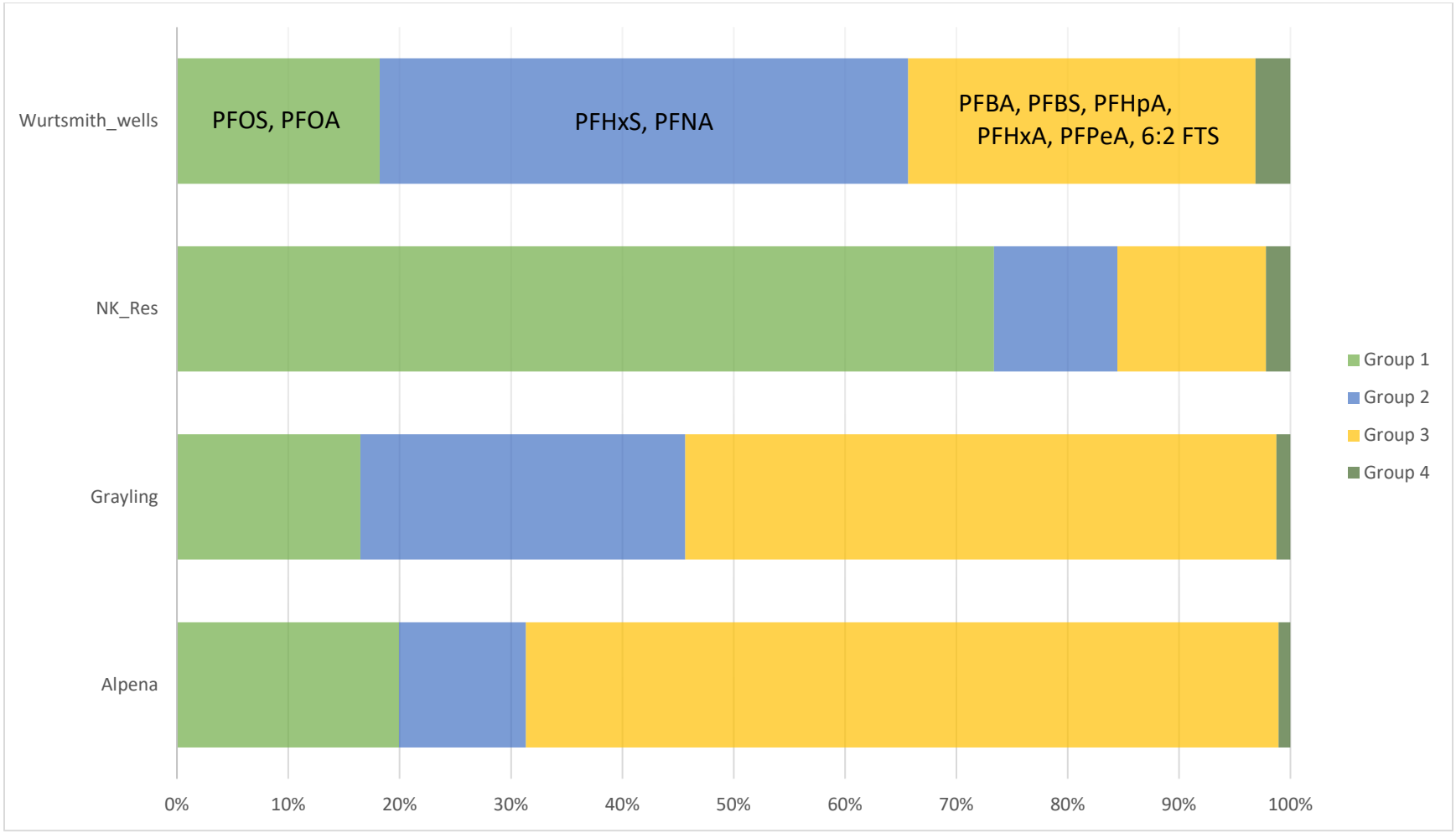

Figure 2: Sum of PFAS detections by chemical groups by mass as a proportion of site total. Group 1 represents PFOS+PFOA, Group 2 represents PFHxS and PFNA, Group 3 represents PFBA, PFBS, PFHpA, PFHxA, and 6:2 FTS, and Group 4 represents the remaining PFAS with generally minor contributions to total PFAS at these sites (Wurtsmith_wells = Wurtsmith Air Force Base and Oscoda area, NK_Res = North Kent County Disposal Investigations area, Grayling = Grayling area , and Alpena = Alpena Combat Readiness Training Center area).

A description of the health endpoint(s), toxicity values, and drinking water calculations used for existing federal and other states' PFAS values

Available toxicity values for PFOA, PFOS, PFHxS, PFBA, PFBS, PFHxA, PFHpA, PFPeA, and 6:2 FTS developed by federal agencies and other states are described in this section. State agency values were selected for presentation based on identification of state- or federal agency-derived toxicity values. This was not meant to be a complete and comprehensive identification of all state-used values. This is a presentation of the development of the toxicity values but does not include discussion of possible adjustments based on professional assessments by State of Michigan toxicologists.

The information in this section is organized in tables. See below for description of each entry.

Critical study	Citation for the study or studies used by the agency for development of a toxicity value
Description of the critical study	Brief summary of the critical study
Point of Departure	The dose-response point (No Observed Adverse Effect Level [NOAEL], Lowest Observed Adverse Effect Level [LOAEL], or Lower Limit of a Benchmark Dose [BMDL]) used as the basis of the calculation for the toxicity value.
Human equivalent dose	A dose of a chemical estimated from a dose used in an animal study thought to potentially produce the same level of effect in humans. For example, if a NOAEL from an animal study was used, this is the equivalent dose for humans. The human equivalent dose may incorporate information on toxicokinetic differences from the animal species used in the study to humans (half-life or clearance rates for chemicals). In lieu of any specific toxicokinetic information, the human equivalent dose may be scaled using body weight and body surface area differences.
Uncertainty and modifying factors	These factors are included to account for uncertainty inherent in the development of a toxicity value. Individual uncertainty factors, between 1 and 10, are used to account for variability among humans, variability between animals and humans, use of data from a study with a shorter than chronic duration, use of a LOAEL instead of a NOAEL, and uncertainty due to missing investigations into certain health endpoints. Modifying factors are used when there are additional uncertainties not accounted for with the standard uncertainty factors.
Toxicity value	This is the health-based value developed by the agency. It can be used to calculate drinking water screening levels.
Exposure parameters for drinking water screening level	These are the exposure parameters and inputs used in the development of the drinking water screening levels. Water intake and body weights may vary based on the population considered most sensitive. Use of an RSC (consideration of other exposure sources) varies as well.
Drinking water screening level	Drinking water levels calculated using the particular toxicity value and exposure parameters.

There are a number of supporting studies that US EPA and state agencies have reviewed for development of their toxicity values. However, only the critical studies used to derive health-based values for drinking water are briefly described below. The US EPA health effects support documents[11] and the ATSDR Toxicological Profile for Perfluoroalkyls, draft for public comment[12], describe a majority of the existing published information in greater detail. See the additional studies section for a description of several other recent toxicological and epidemiological studies not included in the ATSDR Toxicological Profile for Perfluoroalkyls, draft for public comment.

There are several states that address mixtures of PFAS in a combined manner. Many of the states start with the US EPA Lifetime Health Advisory for PFOA+PFOS and, using the same number, add in other PFAS. See Appendix 2 for more details. International values are included in Appendix 3.

Perfluorooctanoic acid (PFOA)

US EPA PFOA[13]

Because of similar developmental effects and identical RfDs, USEPA used a conservative and health protective approach and hence recommended the Lifetime Health Advisory (HA) value of 70 nanograms per Liter (ng/L) be applied to both PFOA and PFOS individually (when only one is present) or in combination for both short-term and lifetime application. The US EPA also evaluated potential screening levels based on the carcinogenic effects of PFOA. A cancer slope factor based on testicular tumor development in rats was estimated. The potential drinking screening level based on carcinogenic effects using a cancer risk of development of cancer in one individual out of 1,000,000 exposed was higher than the Lifetime Health Advisory described below. Therefore, the Lifetime HA is also protective against carcinogenic effects.

Critical study	Lau, C., J.R. Thibodeaux, R.G. Hanson, M.G. Narotsky, J.M. Rogers, A.B. Lindstrom, and M.J. Strynar. 2006. Effects of perfluorooctanoic acid exposure during pregnancy in the mouse. *Toxicological Science* 90:510–518.
Description of the critical study	Timed-pregnant mice were given 0, 1, 3, 5, 10, 20 or 40 milligrams per kilogram (mg/kg) PFOA by oral gavage daily from gestational day (GD) 1 to 17. Mice in the control group (no PFOA) received an equivalent volume of water (10 milliliters [ml]/kg). The critical effects were reduced ossification of proximal phalanges (forelimb and hindlimb) in male and female pups and accelerated puberty in male pups. Maternal liver weight also significantly increased in the 1 mg/kg treatment group.
Point of Departure	A LOAEL of 1 mg/kg/day was identified for both the pup developmental effects and maternal liver weight as all doses used in the study resulted in observable effects.

[11] https://www.epa.gov/ground-water-and-drinking-water/drinking-water-health-advisories-pfoa-and-pfos
[12] https://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=1117&tid=237
[13] https://www.epa.gov/sites/production/files/2016-05/documents/pfoa_health_advisory_final_508.pdf and https://www.epa.gov/sites/production/files/2016-05/documents/pfoa_hesd_final_508.pdf

Human equivalent dose	The average serum concentration for LOAEL (1 mg/kg/day) was estimated as 38 mg/L using a three-compartment pharmacokinetic model (Wambaugh et al. 2013)[A]. The estimated mouse serum concentration (38 mg/L) was considered to be at steady-state and was converted to a human oral equivalent dose using linear human kinetics information. Human elimination kinetics were considered adequately represented by observed serum elimination half-lives ($t_{1/2}$ value ($K_e = \ln(2)/t_{1/2}$)). Assumed apparent volume of distribution (V_d, L/kg) and gastrointestinal absorption fraction (which is considered as 100%) were also included. The average serum concentration (38 mg/L) was multiplied by a clearance factor of 0.00014 L/kg/day (K_e * V_d) to calculate a human equivalent dose of 0.0053 mg/kg/day. The human equivalent dose is defined as the continuous ingestion dose (mg/kg/day) that would result in the steady-state serum concentration associated with the LOAEL (38 mg/L).
Uncertainty and modifying factors	A total uncertainty factor of 300: 10 for human variability 3 for animal to human toxicodynamic difference 10 for LOAEL to NOAEL extrapolation
Toxicity value	RfD of 0.00002 mg/kg/day (20 ng/kg/day)
Exposure parameters for drinking water screening level	A water ingestion rate for lactating women (0.054 L/kg/day) and a relative source contribution (RSC) of 20% were used to calculate the lifetime HA.
Drinking water screening level	Lifetime HA of 70 ng/L (parts per trillion [ppt]) The Lifetime HA should also be used for short-term (weeks to months) exposure.
A = Wambaugh JF, Setzer RW, Pitruzzello AM, Liu J, Reif DM, Kleinstreuer NC, Wang NC, Sipes N, Martin M, Das K, DeWitt JC, Strynar M, Judson R, Houck KA, Lau C. 2013. Dosimetric anchoring of in vivo and in vitro studies for perfluorooctanoate and perfluorooctanesulfonate. Toxicol Sci. 136(2):308-327.	

Draft ATSDR PFOA[14]

ATSDR has released four Minimal Risk Levels for PFAS, including PFOA, and uses those values in public health evaluations of environmental chemical exposure.[15]

[14] https://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=1117&tid=237, Agency for Toxic Substances and Disease Registry. 2014. Exposure Dose Guidance for Water Ingestion. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. November 2014., and Agency for Toxic Substances and Disease Registry. Drinking Water Comparison Values. Atlanta, GA. [updated 2018 July 26; accessed 2018 August 21]. Available from ATSDR's Sequoia Database.

[15] More details on the ATSDR Public Health Assessment process can be found in the Public Health Assessment Guidance Manual (https://www.atsdr.cdc.gov/hac/PHAManual/toc.html).

Critical study (these two studies used offspring from the same animals)	Onishchenko N, Fischer C, Wan Ibrahim WN, Negri S, Spulber S, Cottica D, Ceccatelli S. 2011. Prenatal exposure to PFOS or PFOA alters motor function in mice in a sex-related manner. Neurotox Res. 19(3):452-61.	Koskela A, Finnilä MA, Korkalainen M, Spulber S, Koponen J, Håkansson H, Tuukkanen J, Viluksela M. 2016. Effects of developmental exposure to perfluorooctanoic acid (PFOA) on long bone morphology and bone cell differentiation. Toxicol Appl Pharmacol. 301:14-21.
Description of the critical study	Pregnant mice were exposed to 0 or 0.3 mg PFOA/kg/day throughout pregnancy. Neurobehavioral effects (decreased number of inactive periods, altered novelty induced activity) were considered the critical effects.	Pregnant mice were exposed to PFOA mixed with food at the dose of 0 or 0.3 mg/kg/day throughout pregnancy. Group of five offspring (female) were sacrificed at either 13 or 17 months of age. The critical effects considered were skeletal alteration such as bone morphology and bone cell differentiation in the femurs and tibias.
Point of Departure	The average serum concentration was estimated in the mice (8.29 mg/L) using a three-compartment pharmacokinetic model (Wambaugh et al. 2013)[A] using animal species-, strain-, sex-specific parameters.	
Human equivalent dose	The relationship between external dose (mg/kg/day) and steady state serum concentration (mg/L) in humans was estimated assuming a single compartment first order model in which elimination kinetics are adequately represented by observed serum elimination $t_{1/2}$ value ($K_e = \ln(2)/t_{1/2}$), an assumed apparent volume of distribution (V_d, L/kg) and gastrointestinal absorption fraction (which is considered as 100%). The average serum concentration (8.29 mg/L) was multiplied by clearance factor of 0.000099 L/kg/day to derive a human equivalent dose of 0.000821 mg/kg/day which is defined as the continuous ingestion dose (mg/kg/day) that would result in steady-state serum concentration (8.29 mg/L).	
Uncertainty and modifying factors	A total uncertainty factor of 300: 10 for use of a LOAEL 3 for animal to human variability 10 for human variability	
Toxicity Value	Provisional Intermediate oral MRL of 0.000003 mg/kg/day (3 ng/kg/day)	
Exposure parameters for drinking water screening level	Environmental Media Evaluation Guides (EMEGs) for drinking water: Adult body weight of 80 kg and water ingestion rate of 3.092 L/day Child body weight of 7.8 kg and water ingestion rate of 1.113 L/day	
Drinking water screening level	Intermediate EMEGs: Adult – 78 ng/L (ppt) Child – 21 ng/L (ppt)	

A = Wambaugh JF, Setzer RW, Pitruzzello AM, Liu J, Reif DM, Kleinstreuer NC, Wang NC, Sipes N, Martin M, Das K, DeWitt JC, Strynar M, Judson R, Houck KA, Lau C. 2013. Dosimetric anchoring of in vivo and in vitro studies for perfluorooctanoate and perfluorooctanesulfonate. Toxicol Sci. 136(2):308-327.

ATSDR also has a CREG (Cancer Risk Evaluation Guide) of 350 ng/L (ppt) based on US EPA's cancer slope factor.[16]

Alaska Department of Environmental Conservation PFOA[17]

The PFOA groundwater cleanup value uses the U.S. EPA RfD for PFOA described above.

Critical study	See US EPA PFOA
Description of the critical study	See US EPA PFOA
Point of Departure	See US EPA PFOA
Human equivalent dose	See US EPA PFOA
Uncertainty and modifying factors	See US EPA PFOA
Toxicity Value	See US EPA PFOA
Exposure parameters for drinking water screening level	For ingestion, a child's body weight of 15 kilograms and a daily drinking water intake rate of 0.78 liters were used. The groundwater cleanup levels also incorporate dermal exposure, and inhalation, when appropriate. A Relative Source Contribution of 100% was used.
Drinking water screening level	Groundwater cleanup level of 400 ng/L (ppt)

The Alaska Department of Health and Human Services has recommended an alternate water supply when PFOS and PFOA levels are higher than the US EPA's Lifetime HA of 70 ng/L.[18]

[16] Agency for Toxic Substances and Disease Registry. Drinking Water Comparison Values. Atlanta, GA. [updated 2018 July 26; accessed 2018 August 21]. Available from ATSDR's Sequoia Database.

[17] https://dec.alaska.gov/spar/csp/pfas-contaminants, http://dec.alaska.gov/spar/csp/guidance_forms/docs/pccl%20sept%2015,%202016%20final.pdf, and https://dec.alaska.gov/spar/csp/guidance_forms/docs/Interim%20Tech%20Memo%20-%20DEC%20cleanup%20levels%20and%20EPA%20HAs%20for%20PFOS%20and%20PFOA%20August%202016%20Final.pdf, https://dec.alaska.gov/spar/csp/guidance_forms/docs/Interim%20Tech%20Memo%20-%20DEC%20cleanup%20levels%20and%20EPA%20HAs%20for%20PFOS%20and%20PFOA%20August%202016%20Final.pdf, https://dec.alaska.gov/spar/csp/guidance_forms/docs/Interim%20Tech%20Memo%20-%20DEC%20cleanup%20levels%20and%20EPA%20HAs%20for%20PFOS%20and%20PFOA%20August%202016%20Final.pdf

[18] http://dhss.alaska.gov/dph/Epi/eph/Documents/PFCs/2017_12_14%20FAI%20PFAS%20Fact%20Sheet.pdf

California Environmental Protection Agency State Water Resources Control Board Division of Drinking Water PFOA – Notification Level[19]

The California Environmental Protection Agency (CA EPA) establishes both "notification levels" and "response levels" for chemicals that lack a Maximum Contaminant Limit. There are certain requirements and recommendations that apply when chemicals are found at concentrations greater than their respective notification level. CA EPA adopted the NJ DEP PFOA value as a notification level. There are additional recommendations that apply when chemicals are present above their respective response levels. For PFOA, the response level is five times the notification level. See the discussion below for the CA EPA PFOA response level.

Critical study	See NJ DEP PFOA
Description of the critical study	See NJ DEP PFOA
Point of Departure	See NJ DEP PFOA
Human equivalent dose	See NJ DEP PFOA
Uncertainty and modifying factors	See NJ DEP PFOA
Toxicity Value	See NJ DEP PFOA
Exposure parameters for drinking water screening level	See NJ DEP PFOA
Drinking water screening level	Notification level of 14 ng/L (ppt)

California Environmental Protection Agency State Water Resources Control Board Division of Drinking Water PFOA – Response Level[20]

The California Environmental Protection Agency (CA EPA) establishes both "notification levels" and "response levels" for chemicals that lack a Maximum Contaminant Limit. There are certain requirements and recommendations that apply when chemicals are found at concentrations greater than their respective notification level. CA EPA adopted the NJ DEP PFOA value as a notification level. See the discussion above for the CA EPA PFOA notification level. There are additional recommendations that apply when chemicals are present above their respective response levels. For PFOA, the response level is five times the notification level. CA EPA adopted the US EPA PFOA value as a response level.

[19] https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/NotificationLevels.html, https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/documents/notificationlevels/notification_levels_response_levels_overview.pdf, https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/documents/pfos_and_pfoa/OEHHA_Recommended_Int_NL_Jun_26_2018.pdf, and https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/PFOA_PFOS.html

[20] https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/NotificationLevels.html, https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/documents/notificationlevels/notification_levels_response_levels_overview.pdf, https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/documents/pfos_and_pfoa/OEHHA_Recommended_Int_NL_Jun_26_2018.pdf, and https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/PFOA_PFOS.html

Critical study	See US EPA PFOA
Description of the critical study	See US EPA PFOA
Point of Departure	See US EPA PFOA
Human equivalent dose	See US EPA PFOA
Uncertainty and modifying factors	See US EPA PFOA
Toxicity Value	See US EPA PFOA
Exposure parameters for drinking water screening level	See US EPA PFOA
Drinking water screening level	Response level of 70 ng/L (ppt) (total concentration of PFOA and PFOS)

Minnesota Department of Health PFOA[21] - Short-term, Subchronic, Chronic (Subchronic and Chronic set to the Short-term value)

The Minnesota Department of Health (MDH) developed health-based values and limits for as guidance for evaluation of human health risks of chemicals in groundwater or drinking water.[22]

MDH selected a single PFOA health-based value for short-term, subchronic, and chronic exposures, as short-term exposures may potentially stay in the body for an extended period of time. The PFOA health based values were developed using a toxicokinetics model to predict serum concentrations in infants exposed from birth to steady-state serum levels. The model incorporates the infant's preexisting body burden from transfer through the placenta using a maternal body burden at steady-state serum levels.[23]

Critical study	Lau, C., JR Thibodeaux, RG Hanson, MG Narotsky, JM Rogers, AB Lindstrom, MJ Strynar. (2006). "Effects of Perfluorooctanoic Acid Exposure during Pregnancy in the Mouse." Toxicological Sciences 90(2): 510-518.

[21] http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfoa.pdf
[22] http://www.health.state.mn.us/divs/eh/risk/guidance/gw/index.html
[23] Minnesota Department of Health. May 2017. Background Document Toxicokinetic Model for Perfluorooctane Sulfonate (PFOS) and Perfluorooctanoic Acid (PFOA) and Its Use in the Derivation of Human Health-Based Water Guidance Values

Description of the critical study	Timed-pregnant mice were given 1, 3, 5, 10, 20, or 40 milligrams per kilogram (mg/kg) PFOA by oral gavage daily from gestational day (GD) 1 to 17. Mice in the control group (no PFOA) received an equivalent volume of water (10 milliliters [ml]/kg). The critical effects identified were delayed ossification, accelerated preputial separation in male offspring, a trend for decreased pup body weight, and increased maternal liver weight. In offspring exposed during development, co-critical effects were changes in liver weight, histology, and triglycerides, and delayed mammary gland development. In adult animals exposed, co-critical effects were liver weight changes accompanied by changes in liver enzyme levels, changes in triglyceride and cholesterol levels, and microscopic evidence of cellular damage, decreased spleen weight, decreased spleen lymphocytes, and decreased IgM response, and kidney weight changes.
Point of Departure	The average mouse maternal serum concentration (38 mg/L) corresponding to the LOAEL was selected as the POD, as estimated by the US EPA using a pharmacokinetic model.
Human equivalent dose	The POD was multiplied by a clearance rate of 0.00014 L/kg/day, resulting in 0.0053 mg/kg/day.
Uncertainty and modifying factors	A total uncertainty factor of 300: 3 for LOAEL to NOAEL extrapolation 10 for human to human variability 3 for animal to human difference 3 for database deficiency
Toxicity Value	An RfD of 0.000018 mg/kg/day (18 ng/kg/day) The serum concentration associated with the RfD is 0.13 mg/L, however, it was noted that this value is inappropriate to use for individual assessment.
Exposure parameters for drinking water screening level	Two exposure scenarios for water intake were considered (1: an infant fed formula reconstituted with contaminated water starting at birth and continuing ingestion of contaminated water through life, and, 2: an infant exclusively breast-fed for 12 months, followed by drinking contaminated water through life). The more protective exposure scenario for a breast-fed infant was selected to use as the water intake rate. A placental transfer factor of 87% (percent of maternal serum level) and a breastmilk transfer factor of 5.2% (percent of maternal serum level) were used in the calculation of the health-based drinking water value. An RSC of 50% was included, based on local and national biomonitoring serum concentrations (at the time of the evaluation).
Drinking water screening level	Short-term, Subchronic, Chronic (Subchronic and Chronic set to the Short-term value) health-based value of 35 ng/L (ppt)

New Jersey Department of Environmental Protection PFOA[24]

The New Jersey Department of Environmental Protection previously set drinking water guidance levels for PFOA and other PFAS, but has set health-based maximum contamination levels (regulatory values in New Jersey).

Critical study	Loveless, S.E., Finlay, C., Everds, N.E., Frame, S.R., Gillies, P.J., O'Connor, J.C., Powley, C.R., Kennedy, G.L. (2006). Comparative responses of rats and mice exposed to linear/branched, linear, or branched ammonium perfluorooctanoate (APFO). Toxicology 220: 203–217.
Description of the critical study	Male CD-1 mice were dosed with 0, 0.3, 1, 3, 10 and 30 mg/kg/day branched/linear PFOA for 14 days. Increased relative liver weight was considered the critical effect.
Point of Departure	Using the average measured serum concentration, Benchmark Dose (BMD) and the 95% lower bound Benchmark Dose (BMDL) serum levels were calculated for a 10% increase from the mean relative liver weight in control mice using US EPA Benchmark Dose Modeling Software. An average BMDL of 4351 ng/L was calculated from Polynomial (3rd degree) and Exponential (model 4 and 5) models. The serum level of 4351 ng/L was divided by the total uncertainty factor of 300 resulting in the target human serum level of 14.5 ng/milliliter (ml)
Human equivalent dose	A clearance factor (0.00014 L/kg/day) was used to calculate an RfD from the target human serum level.
Uncertainty and modifying factors	A total uncertainty factor of 300 (applied to the serum level to calculate a target human serum level of 14.5 ng/ml): 10 for human variability 3 for animal to human variability 10 for incomplete database due to the mammary gland effects occurring at a lower dose level
Toxicity value	RfD of 0.000002 mg/kg/day (2 ng/kg/day) The human equivalent serum level of 14.5 ng/ml was converted to a dose using a clearance factor of 0.00014 L/kg/day.
Exposure parameters for drinking water screening level	A water ingestion rate of 2 L for adult human (70 kg) (approximately 0.03 L/kg/day) and a relative source contribution (RSC) of 20% were used to calculate the health based Maximum Contaminant Limit.
Drinking water screening level	health-based Maximum Contaminant Limit of 14 ng/L (ppt)

[24] http://www.nj.gov/dep/watersupply/pdf/pfoa-appendixa.pdf and https://www.nj.gov/dep/srp/emerging-contaminants/

Nevada Department of Environmental Protection PFOA[25]

The Nevada Department of Environmental Protection (DEP) develops "Basic Comparison Levels" (BCLs). The BCLs are a technical screening tool and are not intended to represent an action or cleanup level. The Nevada DEP user's guide has a description of their application and also considerations to prevent misapplication of the BCLs.

The BCL for PFOA uses the U.S. EPA RfD for PFOA described above.

Critical study	See US EPA PFOA
Description of the critical study	See US EPA PFOA
Point of Departure	See US EPA PFOA
Human equivalent dose	See US EPA PFOA
Uncertainty and modifying factors	See US EPA PFOA
Toxicity value	See US EPA PFOA
Exposure parameters for drinking water screening level	Adult body weight of 70 kg and drinking water ingestion of 2.5 L/day Exposure for 350 days per year for 26 years Averaging time of 26 years The BCLs include inhalation along with ingestion, when that route of exposure is applicable.
Drinking water screening level	Basic Comparisons Level of 667 ng/L (ppt)

North Carolina Department of Environmental Quality PFOA[26]

The North Carolina Department of Environmental Quality (NC DEQ) Interim Maximum Allowable Concentrations are to be protective of groundwater used as a potential source of drinking water. The IMACs are not applied to finished water served by public water supplies.

The NC DEQ considers all IMACs to be temporary values. The current IMAC for PFOA is 2000 ng/L (ppt) with an effective date of December 2006. The NC DEQ is proposing that the US EPA PFOA+PFOS Lifetime Health Advisory of 70 ng/L be used as a new North Carolina groundwater standard.[27] Because NC DEQ is proposing to change their number to the US EPA Lifetime HA, the current IMAC is not described here.

[25] https://ndep.nv.gov/uploads/documents/july-2017-ndep-bcls.pdf and https://ndep.nv.gov/uploads/documents/july-2017-bcl-guidance-doc.pdf

[26] https://files.nc.gov/ncdeq/documents/files/2011_January%2020_%20GWSOP_signed%20Diane%20Reid_0.pdf, https://files.nc.gov/ncdeq/documents/files/APPENDIX_I_IMAC%20updated_4-06-18.docx

[27] Personal communication, B. Flaherty, North Carolina Department of Environmental Quality, September 4, 2018.

Texas Commission of Environmental Quality PFOA[28]

The Texas Commission of Environmental Quality develops protective concentration levels (PCLs) for a variety of purposes, including to help establish assessment levels, determine method quantitation limits, and identification of exposure pathways that require further action or might not require action.[29]

Critical study	Macon MB, Villanueva LR, Tatum-Gibbs K, et al. 2011. Prenatal perfluorooctanoic acid exposure in CD-1 mice: low dose developmental effects and internal dosimetry. Toxicol Sci First published online: April 11, 2011 (doi: 10.1093/toxsci/kfr076).
Description of the critical study	Macon et al. (2011) dosed timed-pregnant CD-1 mice with PFOA by gavage throughout gestation or for the latter half of gestation. For the full gestation study, mice were given 0, 0.3, 1.0, and 3.0 mg/kg-day from gestation days (GD) 1-17. In the latter half of gestation study, mice were given 0, 0.01, 0.1, 1.0 mg/kg-day from GD 10-17. Relative liver weights were statistically significantly increased in offspring in all treatment groups (0.3-3.0 mg/kg-day) in the full gestation study, and in the 1.0 mg/kg-day group in the offspring exposure during GD 10-17. A LOAEL for increased liver weight in the full gestation study was 0.3 mg/kg-day. Reduced mammary gland development was also seen in offspring exposed throughout gestation, with a LOAEL of 0.3 mg/kg-day identified. Reduced mammary gland development was also seen in the offspring exposed from GD 10-17, with a LOAEL of 0.01 mg/kg-day, however, TCEQ noted that the offspring were examined at postnatal day 21 and it is unknown whether the reduced mammary gland development would have persisted into adulthood.
Point of Departure	A LOAEL of 0.3 mg/kg-day due to reduced mammary gland development in offspring exposed throughout gestation
Human equivalent dose	No human equivalent dose was calculated. A toxicokinetic uncertainty factor of 81 was included.
Uncertainty and modifying factors	A total uncertainty factor of 24,000: a toxicokinetic animal to human data-derived extrapolation factor of 81[A] a toxicodynamic uncertainty factor of 1 a LOAEL to NOAEL uncertainty factor of 30 a human to human variability uncertainty factor of 10 a database uncertainty factor of 1
Toxicity value	RfD of 0.000012 mg/kg/day (12 ng/kg/day)
Exposure parameters for drinking water screening level	Child body weight of 15 kg Child water ingestion rate of 0.64 L/day Exposure duration of and averaging time of 6 years Exposure frequency of 350 days/year No relative source contribution included
Drinking water screening level	Groundwater Protective Concentration Level of 290 ng/L (ppt)

[28] https://www.tceq.texas.gov/assets/public/implementation/tox/evaluations/pfcs.pdf and http://txrules.elaws.us/Gateway/codepdf/TITLE30/PART1/CHAPTER350/SUBCHAPTERD/350.74/2016-11-12/PDF/200700769-5.pdf

[29] https://www.tceq.texas.gov/assets/public/comm_exec/pubs/rg/rg-366-trrp-23.pdf

A = This is based on the US EPA PFOA toxicokinetics used in their 2009 provisional PFOA health advisory (https://www.epa.gov/sites/production/files/2015-09/documents/pfoa-pfos-provisional.pdf).

Perfluorooctane sulfonate (PFOS)

US EPA PFOS[30]

Because of similar developmental effects and identical RfDs, USEPA used a conservative and health protective approach and hence recommended the LTHA value of 70 ng/L be applied to both PFOA and PFOS individually (when only one is present) or in combination, and short-term and lifetime application.

Critical study	Luebker, D.J., M.T. Case, R.G. York, J.A. Moore, K.J. Hansen, and J.L. Butenhoff. 2005b. Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats. *Toxicology* 215:126–148.
Description of the critical study	Male and female rats were given 0, 0.1, 0.4, 1.6 and 3.2 mg/kg/day PFOS by oral gavage for 6 weeks prior to and during mating. Females were treated through gestation and lactation.
Point of Departure	For the F0 generation, a NOAEL of 0.1 mg/kg/day and LOAEL of 0.4 mg/kg/day were identified based on body weight gain and food consumption. For the F1 generation, a NOAEL of 0.4 mg/kg/day and LOAEL of 1.6 mg/kg/day were identified based on decreased pup viability, pup weight, and survival. For the F2 generation, a NOAEL of 0.1 mg/kg/day and LOAEL of 0.4 mg/kg/day were identified based on decreased mean pup body weight.
Human equivalent dose	The average serum concentration for NOAEL (0.1 mg/kg/day) was estimated (6.26 mg/L) using a three-compartment pharmacokinetic model (Wambaugh et al. 2013)[A]. The relationship between external dose (mg/kg/day) and steady state serum concentration (mg/L) in humans was estimated assuming a single compartment first order model in which elimination kinetics are adequately represented by observed serum elimination $t_{1/2}$ value ($K_e = \ln(2)/t_{1/2}$), an assumed apparent volume of distribution (V_d, L/kg) and gastrointestinal absorption fraction (which is considered as 100%). The average serum concentration (6.26 mg/L) was multiplied by a clearance factor of 0.000081 L/kg/day ($K_e * V_d$) to derive a human equivalent dose of 0.00051 mg/kg/day which is defined as the continuous ingestion dose (mg/kg/day) that would result in a steady-state serum concentration (6.26 mg/L).
Uncertainty and modifying factors	A total uncertainty factor of 30: 10 for human variability 3 for animal to human variability

[30] https://www.epa.gov/sites/production/files/2016-05/documents/pfos_health_advisory_final_508.pdf and https://www.epa.gov/sites/production/files/2016-05/documents/pfos_hesd_final_508.pdf

Toxicity value	an RfD of 0.00002 mg/kg/day (20 ng/kg/day)
Exposure parameters for drinking water screening level	A water ingestion rate for lactating women (0.054 L/kg/day) and a relative source contribution (RSC) of 20% were used
Drinking water screening level	Life time health advisory of 70 ng/L (ppt)
A = Wambaugh JF, Setzer RW, Pitruzzello AM, Liu J, Reif DM, Kleinstreuer NC, Wang NC, Sipes N, Martin M, Das K, DeWitt JC, Strynar M, Judson R, Houck KA, Lau C. 2013. Dosimetric anchoring of in vivo and in vitro studies for perfluorooctanoate and perfluorooctanesulfonate. Toxicol Sci. 136(2):308-327.	

Draft ATSDR PFOS[31]

ATSDR has released four Minimal Risk Levels for PFAS, including PFOS, and uses those values in public health evaluations of environmental chemical exposure.[32]

Critical study	Luebker, D.J., M.T. Case, R.G. York, J.A. Moore, K.J. Hansen, and J.L. Butenhoff. 2005b. Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats. *Toxicology* 215:126–148.
Description of the critical study	Male and female rats were given 0, 0.1, 0.4, 1.6 and 3.2 mg/kg/day PFOS by oral gavage for 6 weeks prior to and during mating. Females were treated through gestation and lactation and across two generation.
Point of Departure	For the F1 generation, a no observed adverse effect level (NOAEL) of 0.1 mg/kg/day and LOAEL of 0.4 mg/kg/day were identified for delayed eye opening. For the F2 generation, a NOAEL of 0.1 mg/kg/day and LOAEL of 0.4 mg/kg/day were identified based on decreased mean pup body weight.

[31] https://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=1117&tid=237, Agency for Toxic Substances and Disease Registry. 2014. Exposure Dose Guidance for Water Ingestion. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. November 2014., and Agency for Toxic Substances and Disease Registry. Drinking Water Comparison Values. Atlanta, GA. [updated 2018 July 26; accessed 2018 August 21]. Available from ATSDR's Sequoia Database.

[32] More details on the ATSDR Public Health Assessment process can be found in the Public Health Assessment Guidance Manual (https://www.atsdr.cdc.gov/hac/PHAManual/toc.html).

Human equivalent dose	The average serum concentration for the NOAEL (0.1 mg/kg/day) was estimated (7.43 mg/L) using a three-compartment pharmacokinetic model (Wambaugh et al. 2013)[A]. The relationship between external dose (mg/kg/day) and steady state serum concentration (mg/L) in human was estimated assuming a single compartment first order model in which elimination kinetics are adequately represented by observed serum elimination $t_{1/2}$ value ($K_e = \ln(2)/t_{1/2}$), an assumed apparent volume of distribution (V_d, L/kg) and gastrointestinal absorption fraction (which is considered as 100%). The average serum concentration (7.43 mg/L) was multiplied by a clearance factor of 0.000069 L/kg/day ($K_e * V_d$) to derive a human equivalent dose of 0.000515 mg/kg/day which is defined as the continuous ingestion dose (mg/kg/day) that would result in a steady-state serum concentration (7.43 mg/L).
Uncertainty and modifying factors	A total uncertainty factor of 30 (applied to the human equivalent dose): 3 for animal to human variability 10 for human variability A modifying factor of 10 for concern that immunotoxicity may be more sensitive than developmental toxicity
Toxicity value	Provisional Intermediate Oral MRL of 0.000002 mg/kg/day (2 ng/kg/day)
Exposure parameters for drinking water screening level	Environmental Media Evaluation Guides for drinking water: Adult body weight of 80 kg and water ingestion rate of 3.092 L/day Child body weight of 7.8 kg and water ingestion rate of 1.113 L/day
Drinking water screening level	Intermediate EMEGs: Adult – 52 ng/L (ppt) Child – 14 ng/L (ppt)
A = Wambaugh JF, Setzer RW, Pitruzzello AM, Liu J, Reif DM, Kleinstreuer NC, Wang NC, Sipes N, Martin M, Das K, DeWitt JC, Strynar M, Judson R, Houck KA, Lau C. 2013. Dosimetric anchoring of in vivo and in vitro studies for perfluorooctanoate and perfluorooctanesulfonate. Toxicol Sci. 136(2):308-327.	

ATSDR reviewed multiple health endpoints, including hepatic, neurological, immunological and developmental effects, during their identification of the critical study for the oral intermediate PFOS MRL. They noted that the lowest administered doses in laboratory animals associated with adverse effects were found in immunotoxicity studies. Due to the lack of pharmacokinetic parameters for the mouse strains used for the studies, ATSDR stated that they could not predict a time weighted average serum concentration for PFOS, therefore, they did not use the immunotoxicity data to develop an MRL.

However, they did evaluate a "candidate MRL", which was an estimated MRL used to support the oral intermediate MRL that was proposed, using the measured serum PFOS level provided by Dong et al (2011). The NOAEL of 0.0167 mg/kg/day was for impaired immune response to sheep red blood cells[33]. The measured serum PFOS levels associated with altered immune response were up to approximately

[33] Dong GH, Liu MM, Wang D, et al. 2011. Sub-chronic effect of perfluorooctanesulfonate (PFOS) on the balance of type 1 and type 2 cytokine in adult C57BL6 mice. Arch Toxicol 85(10):1235-1244.

ten times higher than the serum concentration at NOAEL. The NOAEL from this study was selected to evaluate as it was the highest NOAEL and had the longest exposure duration (60 days).

Based on the measured serum concentration, the time weighted average serum concentration was estimated (using the trapezoid rule) to be 1.2 mg/L and used to calculate a human equivalent dose of 0.000083 mg/kg/day (1.2 mg/L x 0.000069 L/kg/day). An uncertainty factor of 30 (3 for extrapolation from animals to human and 10 for human variability) was applied to the human equivalent dose to derive MRL of 0.000003 mg/kg/day. The MRL derived from the Dong et al (2011) is similar to the MRL calculated from the developmental study (Luebker et al. (2005b)[34] (0.000002 mg/kg/day). As ATSDR used a developmental toxicity study for their draft MRL, they noted that the application of a modifying factor of ten for immunotoxicity concerns based on the candidate MRL calculated from an immunotoxicity study was supported.

Alaska Department of Environmental Conservation PFOS[35]

The PFOS groundwater cleanup value uses the U.S. EPA RfD for PFOS described above.

Critical study	See US EPA PFOS
Description of the critical study	See US EPA PFOS
Point of Departure	See US EPA PFOS
Uncertainty and modifying factors	See US EPA PFOS
Toxicity value	See US EPA PFOS
Exposure parameters for drinking water screening level	For ingestion, a child's body weight of 15 kilograms and a daily drinking water intake rate of 0.78 liters were used. The groundwater cleanup levels also incorporate dermal exposure, and inhalation, when appropriate. No Relative Source Contribution is used.
Drinking water screening level	Groundwater cleanup level of 400 ng/L (ppt)

[34] Luebker, D.J., M.T. Case, R.G. York, J.A. Moore, K.J. Hansen, and J.L. Butenhoff. 2005b. Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats. *Toxicology* 215:126–148.

[35] https://dec.alaska.gov/spar/csp/pfas-contaminants, http://dec.alaska.gov/spar/csp/guidance_forms/docs/pccl%20sept%2015,%202016%20final.pdf, and https://dec.alaska.gov/spar/csp/guidance_forms/docs/Interim%20Tech%20Memo%20-%20DEC%20cleanup%20levels%20and%20EPA%20HAs%20for%20PFOS%20and%20PFOA%20August%202016%20Final.pdf, https://dec.alaska.gov/spar/csp/guidance_forms/docs/Interim%20Tech%20Memo%20-%20DEC%20cleanup%20levels%20and%20EPA%20HAs%20for%20PFOS%20and%20PFOA%20August%202016%20Final.pdf, https://dec.alaska.gov/spar/csp/guidance_forms/docs/Interim%20Tech%20Memo%20-%20DEC%20cleanup%20levels%20and%20EPA%20HAs%20for%20PFOS%20and%20PFOA%20August%202016%20Final.pdf

The Alaska Department of Health and Human Services has recommended an alternate water supply when PFOS and PFOA levels are higher than the US EPA's Lifetime HA of 70 ng/L.[36]

California Environmental Protection Agency State Water Resources Control Board Division of Drinking Water PFOS – Notification Level[37]

The California Environmental Protection Agency (CA EPA) establishes both "notification levels" and "response levels" for chemicals that lack a Maximum Contaminant Limit. There are certain requirements and recommendations that apply when chemicals are found at concentrations greater than their respective notification level. CA EPA adopted the NJ DEP PFOS value as a notification level. There are additional recommendations that apply when chemicals are present above their respective response levels. For PFOS, the response level is five times the notification level. See the discussion below for the CA EPA PFOS response level.

Critical study	See NJ DEP PFOS
Description of the critical study	See NJ DEP PFOS
Point of Departure	See NJ DEP PFOS
Human equivalent dose	See NJ DEP PFOS
Uncertainty and modifying factors	See NJ DEP PFOS
Toxicity Value	See NJ DEP PFOS
Exposure parameters for drinking water screening level	See NJ DEP PFOS
Drinking water screening level	Notification level of 13 ng/L (ppt)

California Environmental Protection Agency State Water Resources Control Board Division of Drinking Water PFOS – Response Level[38]

The California Environmental Protection Agency (CA EPA) establishes both "notification levels" and "response levels" for chemicals that lack a Maximum Contaminant Limit. There are certain requirements

[36] http://dhss.alaska.gov/dph/Epi/eph/Documents/PFCs/2017_12_14%20FAI%20PFAS%20Fact%20Sheet.pdf
[37] https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/NotificationLevels.html, https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/documents/notificationlevels/notification_levels_response_levels_overview.pdf, https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/documents/pfos_and_pfoa/OEHHA_Recommended_Int_NL_Jun_26_2018.pdf, and https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/PFOA_PFOS.html
[38] https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/NotificationLevels.html, https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/documents/notificationlevels/notification_levels_response_levels_overview.pdf, https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/documents/pfos_and_pfoa/OEHHA_Reco

and recommendations that apply when chemicals are found at concentrations greater than their respective notification level. CA EPA adopted the NJ DEP PFOS value as a notification level. See the discussion above for the CA EPA PFOS notification level. There are additional recommendations that apply when chemicals are present above their respective response levels. For PFOS, the response level is five times the notification level. CA EPA adopted the US EPA PFOS value as a response level.

Critical study	See US EPA PFOS
Description of the critical study	See US EPA PFOS
Point of Departure	See US EPA PFOS
Human equivalent dose	See US EPA PFOS
Uncertainty and modifying factors	See US EPA PFOS
Toxicity Value	See US EPA PFOS
Exposure parameters for drinking water screening level	See US EPA PFOS
Drinking water screening level	Response level of 70 ng/L (ppt) (total concentration of PFOA and PFOS)

Minnesota Department of Health PFOS[39] - Short-term, Subchronic, Chronic (Subchronic and Chronic set to the Short-term value)

The Minnesota Department of Health developed health-based values and limits for as guidance for evaluation of human health risks of chemicals in groundwater or drinking water.[40]

MDH selected a single PFOS health-based value short-term, subchronic, and chronic exposures as short-term exposures may potentially stay in the body for an extended period of time. The PFOS health based values were developed using a toxicokinetics model to predict serum concentrations in infants exposed from birth to steady-state serum levels. The model incorporates the infant's preexisting body burden from the transfer through the placenta using a maternal body burden at steady-state serum levels.[41]

Critical study	Luebker, D., MT Case, RG York, JA Moore, KJ Hansen, JL Butenhoff, (2005b). "Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats." Toxicology 215: 126-148.

mmended_Int_NL_Jun_26_2018.pdf, and
https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/PFOA_PFOS.html

[39] http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfos.pdf

[40] http://www.health.state.mn.us/divs/eh/risk/guidance/gw/index.html

[41] Minnesota Department of Health. May 2017. Background Document Toxicokinetic Model for Perfluorooctane Sulfonate (PFOS) and Perfluorooctanoic Acid (PFOA) and Its Use in the Derivation of Human Health-Based Water Guidance Values

Description of the critical study	Male and female rats were given 0, 0.1, 0.4, 1.6 and 3.2 mg/kg/day PFOS by oral gavage for 6 weeks prior to and during mating. Females were treated through gestation and lactation and across two generation. Reduced survival and body weight gain was observed in the F1 pups in the maternal dose groups of 1.6 mg/kg/day and higher. Eye opening was delayed in F1 pups in the 0.4 mg/kg/day group and additional developmental delays were observed in the 1.6 mg/kg/day group. F2 pup body weight was also reduced in the 0.4 mg/kg/day group.
Point of Departure	The average F2 serum concentration for the NOAEL for decreased pup body weight was estimated (6.26 mg/L) using a pharmacokinetic model by the US EPA.
Human equivalent dose	The point of departure (6.26 mg/L) was multiplied by a toxicokinetic adjustment based on chemicals specific clearance rate of 0.000081 L/kg/day for a human equivalent dose of 0.00051 mg/kg/day.
Uncertainty and modifying factors	A total uncertainty factor of 100: 10 for intraspecies difference (for toxicodynamics) 3 for animal to human difference 3 for database deficiency
Toxicity value	an RfD of 0.0000051 mg/kg/day (5.1 ng/kg/day) The serum concentration associated with the RfD is 0.063 mg/L, however, it was noted that this value is inappropriate to use for individual assessment.
Exposure parameters for drinking water screening level	Two exposure scenarios for water intake were considered: 1: an infant fed formula reconstituted with contaminated water starting at birth and continuing ingestion of contaminated water through life and 2: an infant exclusively breast-fed for 12 months, followed by drinking contaminated water through life). The more protective exposure scenario for a breast-fed infant was selected to use as the water intake rate. A placental transfer factor of 46% (percent of maternal serum level) and a breastmilk transfer factor of 1.3% (percent of maternal serum level) were used in the calculation of the health-based drinking water value. An RSC of 50% was included, based on local and national biomonitoring serum concentrations (at the time of the evaluation).
Drinking water screening level	Short-term, Subchronic, Chronic (Subchronic and Chronic set to the Short-term value) health-based value of 27 ng/L (ppt)

New Jersey Department of Environmental Protection Draft PFOS[42]

The New Jersey Department of Environmental Protection has a draft health-based maximum contamination levels (regulatory values in New Jersey) for PFOS.

[42] https://www.state.nj.us/dep/watersupply/pdf/pfos-recommendation-appendix-a.pdf and https://www.nj.gov/dep/srp/emerging-contaminants/

Critical study	Dong GH, Zhang YH, Zheng L, Liu W, Jin YH, He QC. (2009). Chronic effects of perfluorooctanesulfonate exposure on immunotoxicity in adult male C57BL/6 mice. Arch Toxicol. 83(9):805-815.
Description of the critical study	Adult male C57BL/6 mice were exposed to PFOS daily via oral gavage for 60 days with 0, 0.5, 5, 25, 50 or 125 mg/kg total administered dose, equivalent to 0 or approximately 0.008, 0.08, 0.4, 0.8 or 2.1 mg/kg/day.
Point of Departure	The NOAEL for suppression of plaque forming cell response and increase in liver mass was 0.5 mg/kg total administered dose which corresponded to a serum concentration of 674 ng/L.
Human equivalent dose	A clearance factor (0.000081 L/kg/day) was used to calculate an RfD from the target human serum level (674 ng/L).
Uncertainty and modifying factors	A total uncertainty factor of 30 (applied to derive a target human serum level of 22.5 ng/ml): 10 for human variability 3 for animal to human variability
Toxicity value	A RfD of 0.0000018 mg/kg day (1.8 ng/kg/day) calculated by multiplying the target human serum by clearance factor of 0.000081 L/kg/day
Exposure parameters for drinking water screening level	A water ingestion rate of 2 L for adult human (70 kg) (approximately 0.03 L/kg/day) and a relative source contribution (RSC) of 20% were used.
Drinking water screening level	Draft health-based Maximum Contaminant Limit of 13 ng/L (ppt)

Nevada Department of Environmental Protection PFOS[43]

The Nevada Department of Environmental Protection (DEP) develops "Basic Comparison Levels" (BCLs). The BCLs are a technical screening tool and are not intended to represent an action or cleanup level. The Nevada DEP user's guide has a description of their application and also considerations to prevent misapplication of the BCLs.

Critical study	See US EPA PFOS
Description of the critical study	See US EPA PFOS
Point of Departure	See US EPA PFOS
Human equivalent dose	See US EPA PFOS
Uncertainty and modifying factors	See US EPA PFOS
Toxicity value	See US EPA PFOS
Exposure parameters for	Adult body weight of 70 kg and drinking water ingestion of 2.5 L/day Exposure for 350 days per year for 26 years Averaging time of 26 years

[43] https://ndep.nv.gov/uploads/documents/july-2017-ndep-bcls.pdf and https://ndep.nv.gov/uploads/documents/july-2017-bcl-guidance-doc.pdf

drinking water screening level	The BCLs include inhalation along with ingestion, when that route of exposure is applicable. No RSC is included.
Drinking water screening level	Basic comparisons level (BCL) for PFOS in drinking water of 667 ng/L (ppt)

Texas Commission of Environmental Quality PFOS[44]

The Texas Commission of Environmental Quality develops protective concentration levels (PCLs) for a variety of purposes, including to help establish assessment levels, determine method quantitation limits, and identification of exposure pathways that require further action or might not require action.[45]

Critical study	Zeng HC, Li YY, Zhang L, et al. 2011. Prenatal exposure to perfluorooctanesulfonate in rat resulted in long-lasting changes of expression of synapsins and synaptophysin. Synapse 65(3): 225-33.
Description of the critical study	Zeng et al. (2011) gave pregnant Sprague Dawley (SD) rats 0, 0.1, 0.6, and 2.0 mg/kg-day by gavage from GD 0 to GD20. PFOS concentration in the hippocampus of offspring was measured on postnatal day (PND) 0 and PND21. Hippocampus from offspring treated with PFOS showed significant adverse changes in the synaptic structure beginning at 0.1 mg/kg/day (active zone length decreased 10%), with all three measures (active zone length, number of vesicles per area, synaptic interface curvature) statistically significantly affected at 0.6 mg/kg/day and above Synaptic structure affects the connection between neurons, which is critical to normal functioning of the central nervous system. The synaptic vesicle associated proteins and levels of synapsin1 (Syn1), synapsin2 (Syn2), and synaptophysin (Syp) mRNA in offspring from PFOS-treated groups were decreased significantly from levels in control offspring on PND0 and on PND21. These results showed significant adverse synaptic structural changes in the hippocampus (and lower mRNA levels of synaptic vesicle associated proteins) after PFOS treatment.
Point of Departure	A LOAEL of 0.6 mg/kg-day based on all three measures of hippocampus synaptic structure
Human equivalent dose	No Human equivalent dose was calculated. A toxicokinetic uncertainty factor of 263 was included.
Uncertainty and modifying factors	A total uncertainty factor of 26,300: a toxicokinetic animal to human data-derived extrapolation factor of 263[A] a toxicodynamic uncertainty factor of 1 a LOAEL to NOAEL uncertainty factor of 10 a human to human variability uncertainty factor of 10 a database uncertainty factor of 1
Toxicity value	RfD of 0.000023 mg/kg/day (23 ng/kg/day)

[44] https://www.tceq.texas.gov/assets/public/implementation/tox/evaluations/pfcs.pdf
[45] https://www.tceq.texas.gov/assets/public/comm_exec/pubs/rg/rg-366-trrp-23.pdf

Exposure parameters for drinking water screening level	Child body weight of 15 kg Child water ingestion rate of 0.64 L/day Exposure duration of and averaging time of 6 years Exposure frequency of 350 days/year No relative source contribution included
Drinking water screening level	Groundwater Protective Concentration Level of 560 ng/L (ppt)
A = This is based on the US EPA PFOA toxicokinetics used in their 2009 provisional PFOA health advisory (https://www.epa.gov/sites/production/files/2015-09/documents/pfoa-pfos-provisional.pdf).	

Perfluorononanoic acid (PFNA)

Draft ATSDR PFNA[46]

ATSDR has released four Minimal Risk Levels for PFAS, including PFNA, and uses those values in public health evaluations of environmental chemical exposure.[47]

Critical Study	Das KP, Grey BE, Rosen MB, et al. 2015. Developmental toxicity of perfluorononanoic acid in mice. *Reproductive Toxicology* 51:133-144.
Description of the Critical Study	Timed-pregnant mice were given 0, 1, 3, 5 or 10 mg/kg PFNA by oral gavage daily from gestational day (GD) 1 to 17 and control received an equivalent amount of water i.e. 10 ml/kg body weight. *Body weight endpoints* – Decreased body weight *Developmental endpoints* – Developmental delays in mice
Point of Departure	A NOAEL of 1 mg/kg/day was identified for developmental effects.
Human Equivalent Dose	The average serum concentration for NOAEL (1 mg/kg/day) was estimated (8.91 µg/mL) in dams using an empirical clearance model. The estimated time-weighted average serum concentration corresponding to the NOAEL was 6.8 µg/mL. ATSDR was provided the serum concentrations. ATSDR used a serum elimination rate constant (k_e) of 7.59 x 10^{-4} /day and an estimated volume of distribution for PFNA in humans of 0.2 L/kg. ATSDR assumed that PFNA is well absorbed after oral exposure, and used an absorbance factor (AF) of 1, based on animal studies of PFNA and other perfluorocarboxylic acid analogs. $NOAEL_{HED}$ = (TWA serum x k_e x V_d)/AF = 0.001 mg/kg/day
Uncertainty and Modifying Factors	A total uncertainty factor of 30: 3 for extrapolation from animals to humans with dosimetric adjustments 10 for human variability A modifying factor of 10 for database deficiencies was used.
Toxicity Value	Provisional Intermediate oral MRL of 0.000003 mg/kg/day (3 ng/kg/day)
Exposure Parameters for Drinking Water Screening Level	Environmental Media Evaluation Guides for drinking water: Adult body weight of 80 kg and water ingestion rate of 3.092 L/day Child body weight of 7.8 kg and water ingestion rate of 1.113 L/day

[46] https://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=1117&tid=237, Agency for Toxic Substances and Disease Registry. 2014. Exposure Dose Guidance for Water Ingestion. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. November 2014., and Agency for Toxic Substances and Disease Registry. Drinking Water Comparison Values. Atlanta, GA. [updated 2018 July 26; accessed 2018 August 21]. Available from ATSDR's Sequoia Database.

[47] More details on the ATSDR Public Health Assessment process can be found in the Public Health Assessment Guidance Manual (https://www.atsdr.cdc.gov/hac/PHAManual/toc.html).

Drinking Water Screening Level	Intermediate EMEGs: Adult – 78 ng/L (ppt) Child – 21 ng/L (ppt)

New Jersey Department of Environmental Protection PFNA[48]

The New Jersey Department of Environmental Protection (DEP) has a draft health-based maximum contamination level (regulatory values in New Jersey) for PFNA.

Critical study	Das, K.P., Grey, B.E., Rosen, M.B., Wood, C.R., Tatum-Gibbs, K.R., Zehr, R.D., Strynar, M.J., Lindstrom, A.B., Lau, C. (2015). Developmental toxicity of perfluorononanoic acid in mice. Reproductive Toxicology 51:133-144.
Description of the critical study	Timed-pregnant CD-1 mice were dosed with 0, 1, 3 and 5 mg/kg/day PFNA throughout gestation and increased in maternal liver weight was used to derive the health based value. Using the average serum concentration measured on GD 17, BMD and BMDL serum levels were calculated for a 10% increase from the mean liver weight in pregnant control mice.
Point of Departure	Average BMDL of 4900 ng/mL was calculated using the Hill model and Exponential model 5.
Human equivalent dose	NJ DEP did not convert the serum levels to a dose.
Uncertainty and modifying factors	A total uncertainty factor of 1000 (applied to derive a target human serum level of 4.9 ng/ml): 10 for human variability, 3 for animal to human variability and 10 for sub-chronic to chronic exposure extrapolation 3 for incomplete database
Toxicity value	A target human serum level of 4.9 ng/ml
Exposure parameters for drinking water screening level	A Relative Source Contribution of 50%[A] was applied to the target serum level. NJ DEP concluded that, based on limited human data, the half-life of PFNA is at least twice as long as for PFOA, and used a 200:1 ratio between PFNA serum levels and drinking water concentrations, which is meant to represent a central tendency estimate.
Drinking water screening level	health-based MCL of 13 ng/L (ppt)
A = Calculated using the US EPA "subtraction" approach (US EPA 2000) and calculated using 2011-2012 National Health and Nutrition Examination Survey 95th percentile PFNA serum levels, ages 12 and older. US EPA (2000). Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health. Office of Science and Technology. Office of Water. Washington, DC. EPA 822- B-00-004. October 2000. https://www.nj.gov/drbc/library/documents/EPA_human-health-criteria2000.pdf	

[48] http://www.nj.gov/dep/watersupply/pdf/pfna-health-effects.pdf

Texas Commission of Environmental Quality PFNA[49]

The Texas Commission of Environmental Quality develops protective concentration levels (PCLs) for a variety of purposes, including to help establish assessment levels, determine method quantitation limits, and identification of exposure pathways that require further action or might not require action.[50]

Critical study	Fang X, Fenga Y, Wang J, et al. 2010. Perfluorononanoic acid-induced apoptosis in rat spleen involves oxidative stress and the activation of caspase-independent death pathway. Toxicology 267: 54-59.
Description of the critical study	Fang et al. (2010), gave rats 0, 1, 3, or 5 mg/kg/day for 2 weeks. Dose-dependent decreases in the absolute spleen weight (decreased by 22.2%, 28.7% and 57.9%, respectively; $p < 0.01$) were observed compared to the control group. However, the ratio of spleen weight to body weight only significantly decreased (91.5% of the control, $p < 0.01$) in the group given the highest dose (5 mg/kg/day). Significantly increased levels of pro-inflammatory cytokines, IL-1, IL-6, and TNF-α also occurred at 5 mg/kg/day. These cytokines are involved in apoptosis, programmed cell death. The number of apoptotic spleen cells significantly increased in animals receiving 3 and 5 mg/kg/day.
Point of Departure	A NOAEL of 1 mg/kg/day for spleen cell apoptosis, which is also protective against spleen weight decreases and other effects
Human equivalent dose	No Human equivalent dose was calculated. A toxicokinetic uncertainty factor of 81 was included.
Uncertainty and modifying factors	A total uncertainty factor of 81,000: a toxicokinetics interspecies extrapolation factor of 81[A] a toxicodynamic interspecies uncertainty factor of 1 an intrahuman uncertainty factor of 10 an uncertainty factor of 10 for extrapolation from subacute to chronic exposure a database uncertainty factor of 10
Toxicity value	RfD of 0.000012 mg/kg/day (12 ng/kg/day)
Exposure parameters for drinking water screening level	Child body weight of 15 kg Child water ingestion rate of 0.64 L/day Exposure duration of and averaging time of 6 years Exposure frequency of 350 days/year No relative source contribution included
Drinking water screening level	Groundwater Protective Concentration Level of 290 ng/L (ppt)
A = This is based on the US EPA PFOA toxicokinetics used in their 2009 provisional PFOA health advisory (https://www.epa.gov/sites/production/files/2015-09/documents/pfoa-pfos-provisional.pdf).	

[49] https://www.tceq.texas.gov/assets/public/implementation/tox/evaluations/pfcs.pdf
[50] https://www.tceq.texas.gov/assets/public/comm_exec/pubs/rg/rg-366-trrp-23.pdf

Perfluorohexane sulfonate (PFHxS)

Draft ATSDR PFHxS[51]

ATSDR has released four Minimal Risk Levels for PFAS, including PFHxS, and uses those values in public health evaluations of environmental chemical exposure.[52]

Critical Study	Butenhoff JL, Chang S, Ehresman DJ, et al. 2009a. Evaluation of potential reproductive and developmental toxicity of potassium perfluorohexanesulfonate in Sprague Dawley rats. *Reproductive Toxicology* 27:331-341. Hoberman AM, York RG. 2003. Oral (gavage) combined repeated dose toxicity study of T-7706 with the reproduction/developmental toxicity screening test. *Argus Research*.
Description of the Critical Study	Sprague-Dawley rats were given 0.3, 1, 3 or 10 mg/kg PFHxS by oral gavage one time daily for 42-56 days (intermediate exposure). Control group animals (0 mg/kg) received an equivalent volume of water (10 ml/kg). Two major health endpoint categories were identified: *Hepatic endpoints* – Increased liver weight; centrilobular hepatocellular hypertrophy *Thyroid endpoints* – Hypertrophy and hyperplasia of thyroid follicular cells
Point of Departure	a NOAEL of 1 mg/kg/day due to thyroid effects (noted as the most sensitive endpoint)
Human Equivalent Dose (HED)	The average serum concentration for the NOAEL (1 mg/kg/day) was estimated (89.12 µg/mL) using an empirical clearance model. As a pharmacokinetic model for predicting the time-weighted average (TWA) serum concentrations was not identified for PFHxS, a TWA serum concentration of 73.22 µg/mL was estimated from measured serum concentrations of adult males exposed to 1 mg/kg/day. ATSDR also used a serum elimination rate constant (k_e) of 0.000223/day, a volume of distribution (V_d) of 0.287 L/kg and an absorption fraction (AF) of 1 based on published studies. $NOAEL_{HED}$ = (TWA serum x k_e x V_d)/AF = 0.0047 mg/kg/day

[51] https://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=1117&tid=237, Agency for Toxic Substances and Disease Registry. 2014. Exposure Dose Guidance for Water Ingestion. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. November 2014., and Agency for Toxic Substances and Disease Registry. Drinking Water Comparison Values. Atlanta, GA. [updated 2018 July 26; accessed 2018 August 21]. Available from ATSDR's Sequoia Database.

[52] More details on the ATSDR Public Health Assessment process can be found in the Public Health Assessment Guidance Manual (https://www.atsdr.cdc.gov/hac/PHAManual/toc.html).

Uncertainty and Modifying Factors	A total uncertainty factor of 30: 3 for extrapolation from animals to humans with dosimetric adjustments 10 for human variability A modifying factor of 10 for database limitations was used.
Toxicity Value	Provisional Intermediate oral MRL of 0.00002 mg/kg/day (20 ng/kg/day)
Exposure Parameters for Drinking Water Screening Level	Environmental Media Evaluation Guides for drinking water: Adult body weight of 80 kg and water ingestion rate of 3.092 L/day Child body weight of 7.8 kg and water ingestion rate of 1.113 L/day
Drinking Water Screening Level	Intermediate EMEGs: Adult – 520 ng/L (ppt) Child – 140 ng/L (ppt)

Minnesota Department of Health PFHxS[53]

The Minnesota Department of Health developed health-based values and limits for as guidance for evaluation of human health risks of chemicals in groundwater or drinking water.[54]

The complete listing of the Minnesota Department of Health Toxicological Summaries can be found at http://www.health.state.mn.us/divs/eh/risk/guidance/gw/table.html.

The Minnesota Department of Health concluded there was insufficient data to recommend risk assessment advice for PFHxS. However, the Minnesota Department of Health is currently recommending that the heath-based value for PFOS (health-based value of 27 ng/L) be currently used as a surrogate for PFHxS as PFHxS has a longer half-life in humans and has similar health outcomes as those seen with PFOS.

Critical study	Minnesota Department of Health concluded there was insufficient data
Description of the critical study	Minnesota Department of Health concluded there was insufficient data
Point of Departure	Minnesota Department of Health concluded there was insufficient data
Human equivalent dose	Minnesota Department of Health concluded there was insufficient data
Uncertainty and modifying factors	Minnesota Department of Health concluded there was insufficient data
Toxicity value	Minnesota Department of Health concluded there was insufficient data
Exposure parameters for drinking water screening level	Minnesota Department of Health concluded there was insufficient data
Drinking water screening level	Recommending use of the PFOS health-based value of 27 ng/L

[53] http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfhxs.pdf and http://www.health.state.mn.us/divs/eh/risk/review/index.html

[54] http://www.health.state.mn.us/divs/eh/risk/guidance/gw/index.html

Texas Commission of Environmental Quality PFHxS[55]

The Texas Commission of Environmental Quality develops protective concentration levels (PCLs) for a variety of purposes, including to help establish assessment levels, determine method quantitation limits, and identification of exposure pathways that require further action or might not require action.[56]

Critical study	Hoberman AM, York RG. 2003. Oral (gavage) combined repeated dose toxicity study of T-7706 with the reproduction/developmental toxicity screening test. Argus Research.
Description of the critical study	Hoberman and York (2003) evaluated the reproductive and developmental effects of 0, 0.3, 1, 3, or 10 mg/kg/day PFHxS in male and female rats exposed from premating until PND 21 in females (42-56 days). Rats were treated by oral gavage. No significant reproductive or developmental parameter was altered by PFHxS treatment. Maternal toxicity, as evaluated by clinical chemistry and hematology tests and organ histopathology, was not seen in any treatment group. Male rats treated with 0.3 mg/kg/day PFHxS or more did have hematological alterations (increased prothrombin time after 42 days of 0.3 mg/kg/day or more; decreased hemoglobin concentration in those treated with 1 mg/kg/day or more; decreased erythrocyte count and hematocrit in the 3 mg/kg/day or higher treatment groups). Liver and thyroid effects were also observed in male rats treated with 3 and 10 mg/kg/day PFHxS. These effects were not observed in female rats.
Point of Departure	A LOAEL 0.3 mg/kg/day for hematological alterations in male rats
Human equivalent dose	No Human equivalent dose was calculated. A toxicokinetic uncertainty factor of 263 was included.
Uncertainty and modifying factors	A total uncertainty factor of 78,900: a TK interspecies extrapolation factor of 263 (based on the similarity of PFHxS to PFOS) a toxicodynamic interspecies uncertainty factor of 1 a LOAEL-to-NOAEL uncertainty factor of 3 an intrahuman uncertainty factor of 10 a database UF of 10 for significant insufficiencies (e.g., only one study)
Toxicity value	RfD of 0.0000038 mg/kg-day (3.8 ng/kg/day)
Exposure parameters for drinking water screening level	Child body weight of 15 kg Child water ingestion rate of 0.64 L/day Exposure duration of and averaging time of 6 years Exposure frequency of 350 days/year No relative source contribution included
Drinking water screening level	Groundwater Protective Concentration Level of 93 ng/L (ppt)

[55] https://www.tceq.texas.gov/assets/public/implementation/tox/evaluations/pfcs.pdf
[56] https://www.tceq.texas.gov/assets/public/comm_exec/pubs/rg/rg-366-trrp-23.pdf

Perfluorobutane sulfonate (PFBS)

US EPA PFBS[57]

The US EPA developed the subchronic and chronic PFBS RfDs as provisional peer-reviewed toxicity values (PPRTVs). PPRTVs are a toxicity value developed for use in the Superfund Program and are internally reviewed by a standing National Center for Environmental Assessment scientist panel and also by three external scientific experts. These PPRTV values were finalized in 2014.

Critical Study	Lieder PH, SC Chang, RG York, JL Butenhoff. 2009a. Toxicological evaluation of potassium perfluorobutanesulfonate in a 90-day oral gavage study with Sprague-Dawley rats. Toxicology 255:45-52.
Description	A 90-day rat oral gavage study was conducted with potassium PFBS (K+PFBS). Rats were dosed with K+PFBS at doses of 0, 60, 200, and 600 milligrams per kilogram per day (mg/kg/day). No treatment-related mortality, body weight, or neurological effects were noted. Chromorhinorrhea (perioral) and urine-stained abdominal fur were observed in males at 600 mg/kg/day. Red blood cell counts, hemoglobin, and hematocrit values were reduced in males receiving 200 and 600 mg/kg/day; however, there were no adverse histopathological findings in bone marrow. Total serum protein and albumin were lower in females at 600 mg/kg/day. There were no significant changes in clinical chemistry in either sex. All rats appeared normal at sacrifice. Microscopic changes were observed only at the highest dose in the stomach. These changes consisted of hyperplasia with some necrosis of the mucosa with some squamous metaplasia. These effects likely were due to a cumulative direct irritation effect resulting from oral dosing with K+PFBS. Histopathological changes were also observed in the kidneys. The changes observed were minimal-to-mild hyperplasia of the epithelial cells of the medullary and papillary tubules and the ducts in the inner medullary region. There were no corresponding changes in kidney weights. Clinical chemistry parameters related to kidney function were unchanged. These kidney findings are likely due to a response to high concentration of K+PFBS in tubules and ducts and represent a minimal-to-mild effect. Microscopic changes of an equivocal and uncertain nature were observed in the nasal mucosa and were likely attributable to the route of dosing (oral gavage). Lieder et al. (2009a) identified a NOAEL for the female rat in this study of 600 mg/kg/day (highest dose of study) and a NOAEL for the male rat of 60 mg/kg/day based on hematological effects. The US EPA identified a NOAEL of 200 mg/kg/day for both female and male rats. US EPA noted that the hematological changes in male rats were not dose-dependent and not observed in female rats.

[57] Additional information on these values can be found in the "Provisional Peer-Reviewed Toxicity Values for Perfluorobutane Sulfonate (CASRN 375-73-5) and Related Compound Potassium Perfluorobutane Sulfonate (CASRN 29420-49-3)" document located at https://cfpub.epa.gov/ncea/pprtv/documents/PotassiumPerfluorobutaneSulfonate.pdf.

Point of Departure	Subchronic and chronic: $BMDL_{10}$ of 78.7 mg/kg-day based on increased incidence of kidney hyperplasia in females is selected as the point of departure
Human Equivalent Dose	Subchronic and chronic: 18.9 mg/kg/day calculated using dosimetric adjustment factor (based on body weight scaling)
Uncertainty and Modifying Factors	Subchronic- a total uncertainty factor of 100: 3 for animal to human toxicodynamic differences 10 for human to human variability 3 for a database gap Chronic – a total uncertainty factor of 1000: 3 for animal to human toxicodynamic differences 10 for human to human variability 3 for a database gap 10 for use of a subchronic study for the chronic duration
Toxicity Value	Subchronic provisional RfD: 0.2 mg/kg/day (200,000 ng/kg/day) Chronic provisional RfD: 0.02 mg/kg/day (20,000 ng/kg/day)
Exposure parameters for drinking water screening level	The chronic provisional RfD is used for calculation of a residential tapwater Regional Screening Level (RSL) for a child using a 15 kg body weight and a 0.78 L/day water intake. The RSLs assume a residential 350 day exposure for 6 years for a child. The RSC is 100%.
Drinking water screening level	Tapwater RSL of 400,000 ng/L (ppt; 400 micrograms [µg]/L or parts per billion)

Minnesota Department of Health PFBS[58] - Short-term and Subchronic (set to the Short-term value) health-based value

Short-term, subchronic, and chronic non-cancer health-based values (nHBVs) were developed by the MDH and published in 2017.[59] These values are drinking water levels and use non-cancer toxicity values along with drinking water exposure scenario inputs and relative source contributions. The 2017 values were an update of previous values promulgated in 2011 as Health Risk Limits.[60] MDH noted that they updated their derivation of human equivalent doses using new or updated half-life values, incorporated recently published studies for short-term value calculation, used their most recent risk assessment methodology, and rounded to one significant digit. MDH set the subchronic nHBV equal to the short-term nHBV as the subchronic nHBV "must be protective of short-term exposures that occur within the subchronic period". Because of this the short-term RfD is described here.

[58] http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfbssummary.pdf
[59] http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfbssummary.pdf
[60] http://www.health.state.mn.us/divs/eh/risk/guidance/gw/table.html

Critical study	Feng, X., X Cao, S Zhao, X Wang, X Hua, L Chen, L Chen. (2017). "Exposure of Pregnant Mice to Perfluorobutanesulfonate Causes Hypothyroxinemia and Developmental Abnormalities in Female Offspring." Toxicological Sciences 155(2): 409-419.
Description of the critical study	Feng et al. (2017) treated pregnant ICR mice with 0, 50, 200, or 500 mg/kg/day K+PFBS from gestational day 1 to gestational day 20. Male offspring were not used in this experiment. Fifty female offspring (from 10 dams) had perinatal survival and growth, pubertal onset and ovarian and uterine development examined. Hormone levels (hypothalamic-pituitary-gonadal and hypothalamic- pituitary- and thyroid hormones were examined in 30 female offspring on postnatal day 1, 10 offspring on postnatal day 30, and 10 offspring on postnatal day 60. Serum PFBS was measured in offspring from 10 dams. Decreased total T3 and T4 levels were observed in mice with prenatal exposure to 200 or 500 mg/kg/day in all three postnatal groups. Total T3 and free and total T4, measured on gestational day 20, were also decreased in dams exposed to 200 and 500 mg/kg/day. Offspring postnatally treated with 200 and 500 mg/kg/day also had decreases in perinatal growth, pubertal onset, and reproductive organ development.
Point of Departure	NOAEL of 50 mg/kg-day was selected
Human equivalent dose	A human equivalent dose (0.158 mg/kg-day) was calculated based on NOAEL and dose adjustment factor (ratio of the half-life of PFBS in human versus female mouse; 665 hr /2.1 hr = 317).
Uncertainty and modifying factors	A total uncertainty factor of 100: 3 for animal to human differences 10 for intraspecies variability 3 for database uncertainty
Toxicity value	RfD of 0.0016 mg/kg/day (1600 ng/kg/day)
Exposure parameters for drinking water screening level	A water ingestion rate of 0.285 L/kg/day (time-weighted average of the 95th percentile for 1 up to 3 months of age) and RSC of 50% were taken into consideration to calculate the short-term health-based value.
Drinking water screening level	Short-term and Subchronic (set to the Short-term value) health-based value of 3,000 ng/L (ppt)

Minnesota Department of Health PFBS[61] - Chronic health-based value

Short-term, subchronic, and chronic non-cancer health-based values (nHBVs) were developed by the MDH and published in 2017. These values are drinking water levels and use non-cancer toxicity values along with a drinking water exposure scenario inputs and a relative source contributions. The 2017 values were an update of previous values promulgated in 2011. MDH noted that they updated their derivation of human equivalent doses using new or updated half-life values, incorporated recently

[61] http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfbssummary.pdf

published studies for short-term value calculation, used their most recent risk assessment methodology, and rounded to one significant digit.

Critical study	Leider PH, RG York, DC Hakes, JL Butenhoff. 2009b. A Two-Generation Oral Gavage Reproduction Study with Potassium Perfluorobutanesulfonate (K+PFBS) in Sprague Dawley Rats. Toxicology 259:33-45. and York RG 2003b. Oral (Gavage) Two-Generation (One Litter per Generation) Reproduction Study of Perfluorobutane Sulfonate (PFBS) in Rats. Argus Research Protocol Number 418-021.
Description of the critical study	Lieder et al. (2009b) conducted a two-generation reproductive study in Sprague-Dawley rats orally dosed with 0, 30, 100, 300, or 1,000 mg/kg/day K+PFBS, with 30 rats per sex per group. Parental (F0) generation rats were treated 10 weeks prior to mating and through mating for male and female rats and through gestation and lactation for female rats. F1 generation rats were weaned and treated as described for the parental generation. F2 generation rats were only exposed to K+PFBS through placental transfer and during nursing. Parental and F1 generation rats were evaluated for fertility, including sperm parameters, measures of gestation and outcomes, and body and organ weights. Liver and kidneys from all parental (F0), F1, and F2 generation rats were examined microscopically. Reproductive tissues were examined from 10 rats per sex in the parental and F1 generations in the control and 1000 mg/kg/day groups. Enlargement of the liver cells (mild hypertrophy) and hyperplasia of kidney medullary/papillary tubular and ductular epithelial cells were observed in male parental generation rats in the 300 and 1000 mg/kg/day groups. F1 male rats treated with 300 or 1000 mg/kg/day also had liver hypertrophy, which the authors described as minimal. Kidney hyperplasia (minimal-to-moderate) was also observed in female generation rats in the 300 and 1000 mg/kg/day groups, but females did not have observable liver hypertrophy. F1 female rats treated with 300 or 1000 mg/kg/day also had kidney hyperplasia, which the authors described as minimal-to-mild. The study authors noted that the NOAEL was 100 mg/kg/day due to the effects observed in the parental and F1 generation rats. Body weight effects were noted in the F1 generation, with a NOAEL of 300 mg/kg/day. No effects on reproductive function were noted in the parental or F1 generations.
Point of Departure	Based on epithelial hyperplasia in the kidneys of F0 females Sprague Dawley rats, a Benchmark Dose lower limit, 10 % ($BMDL_{10}$) of 45 mg/kg-day was estimated.
Human equivalent dose	A human equivalent dose (0.129 mg/kg-day) was calculated based on the point of departure (45 mg/kg/day) and dose adjustment factor (ratio of the half-life of PFBS in human versus female rat; 665 hr /1.9 hr = 350).
Uncertainty and modifying factors	A total uncertainty factor of 300: 3 for animal to human differences

	10 for intraspecies variability 3 for database uncertainty 3 for use of a subchronic study for the chronic duration
Toxicity value	RfD of 0.00043 mg/kg/day (430 ng/kg/day)
Exposure parameters for drinking water screening level	A water ingestion rate of 0.044 L/kg/day (time-weighted average over a lifetime of approximately 70 years of age) and RSC of 20% were taken into consideration to calculate the chronic health-based value.
Drinking water screening level	Chronic health-based value of 2,000 ng/L (ppt)

Nevada Department of Environmental Protection PFBS[62]

They have basic comparisons levels (BCL) for PFAS in drinking water.

Critical study	See US EPA PFBS (chronic RfD)
Description of the critical study	See US EPA PFBS (chronic RfD)
Point of Departure	See US EPA PFBS (chronic RfD)
Human equivalent dose	See US EPA PFBS (chronic RfD)
Uncertainty and modifying factors	See US EPA PFBS (chronic RfD)
Toxicity value	See US EPA PFBS (chronic RfD)
Exposure parameters for drinking water screening level	Adult body weight of 70 kg and drinking water ingestion of 2.5 L/day Exposure for 350 days per year for 26 years Averaging time of 26 years The BCLs include inhalation along with ingestion, when that route of exposure is applicable.
Drinking water screening level	BCL of 667,000 ng/L (ppt or 667 µg/L [ppb])

Texas Commission of Environmental Quality PFBS[63]

The Texas Commission of Environmental Quality develops protective concentration levels (PCLs) for a variety of purposes, including to help establish assessment levels, determine method quantitation limits, and identification of exposure pathways that require further action or might not require action.[64]

Critical study	Leider PH, SC Chang, RG York, JL Butenhoff. 2009. Toxicological evaluation of potassium perfluorobutanesulfonate in a 90-day oral gavage study with Sprague-Dawley rats. Toxicology 255:45-52.

[62] https://ndep.nv.gov/uploads/documents/july-2017-ndep-bcls.pdf and https://ndep.nv.gov/uploads/documents/july-2017-bcl-guidance-doc.pdf
[63] https://www.tceq.texas.gov/assets/public/implementation/tox/evaluations/pfcs.pdf
[64] https://www.tceq.texas.gov/assets/public/comm_exec/pubs/rg/rg-366-trrp-23.pdf

	York RG 2003. Oral (Gavage) Repeated Dose 90-Day Toxicity Study of Potassium Perfluorobutane Sulfonate (PFBS) in Rats. Argus Research Protocol Number 418-026.
Description of the critical study	A 90-day rat oral gavage study was conducted with potassium PFBS (K+PFBS). Rats were dosed with K+PFBS at doses of 0, 60, 200, and 600 mg/kg/day. No treatment-related mortality, body weight, or neurological effects were noted. Chromorhinorrhea (perioral) and urine-stained abdominal fur were observed in males at 600 mg/kg/day. Red blood cell counts, hemoglobin, and hematocrit values were reduced in males receiving 200 and 600 mg/kg/day; however, there were no adverse histopathological findings in bone marrow. Total serum protein and albumin were lower in females at 600 mg/kg/day. There were no significant changes in clinical chemistry in either sex. All rats appeared normal at sacrifice. Microscopic changes were observed only at the highest dose in the stomach. These changes consisted of hyperplasia with some necrosis of the mucosa with some squamous metaplasia. These effects likely were due to a cumulative direct irritation effect resulting from oral dosing with K+PFBS. Histopathological changes were also observed in the kidneys. The changes observed were minimal-to-mild hyperplasia of the epithelial cells of the medullary and papillary tubules and the ducts in the inner medullary region. There were no corresponding changes in kidney weights. Clinical chemistry parameters related to kidney function were unchanged. These kidney findings are likely due to a response to high concentration of K+PFBS in tubules and ducts and represent a minimal-to-mild effect. Microscopic changes of an equivocal and uncertain nature were observed in the nasal mucosa and were likely attributable to the route of dosing (oral gavage). Lieder et al. (2009) identified a NOAEL of 600 mg/kg/day (highest dose of study) for the female rat in this study and a NOAEL of 60 mg/kg/day for the male rat based on hematological effects.
Point of Departure	The Texas Commission of Environmental Quality used the NOAEL as 60 mg/kg/day, as identified in the Minnesota Department of Health 2011 subchronic PFBS Health Risk Limit
Human equivalent dose	No Human equivalent dose was calculated. A toxicokinetic uncertainty factor of 142 was included.
Uncertainty and modifying factors	A total uncertainty factor of 42,600: a toxicokinetic interspecies factor of 142 a toxicodynamic uncertainty factor of 1 a 10 for intrahuman variability a 3 for subchronic to chronic extrapolation 10 for significant database insufficiencies (i.e., only one study available)
Toxicity value	RfD of 0.0014 mg/kg/day (1,400 ng/kg/day)
Exposure parameters for drinking water screening level	Child body weight of 15 kg Child water ingestion rate of 0.64 L/day

	Exposure duration of and averaging time of 6 years Exposure frequency of 350 days/year No relative source contribution included
Drinking water screening level	Groundwater Protective Concentration Level of 34,000 ng/L (ppt; 34 µg/L [ppb])

Perfluorobutanoic acid (PFBA)

Minnesota Department of Health PFBA[65] - Short term, Subchronic (set to the Short-term value), and Chronic (set to the Short-term value) health-based value

Critical study	NOTOX 2007a. Project 470677 Final Report. Repeated dose 28-day oral toxicity study with MTDID-8391 by daily gavage in the rat, followed by a 21-day recovery period. June 21, 2007. And Butenhoff, JL. 2007a. E-mail correspondence conveying benchmark dose calculations conducted by 3M for liver weight and cholesterol – 28 day PFBA study. February 6, 2007. And Butenhoff, JL. 2007b. Memorandum to Helen Goeden. October 9, 2007. Subject: Data Summary for mechanistic investigation results from samples for NOTOX study no. 470677. And Butenhoff, JL. 2007c. E-mail correspondence conveying BMD estimates from Dr. Gaylor. Attachments: Benchmark Dose Calculations for Ammonium Perfluorobutyrate (PFBA) and Benchmark Dose Calculations for Ammonium Perfluorobutyrate (PFBA) based on Thyroid Hypertrophy/Hyperplasia by Dr. David W. Gaylor, Gaylor and Associates, LLC. December 13, 2007.
Description of the critical study	The study was not available to summarize. MDH listed the critical effect as decreased cholesterol, and co-critical effects of increased relative thyroid weight, decreased serum total thyroxine, and decreased dialysis free thyroxine.
Point of Departure	Based on reduction of cholesterol levels in rat, the Benchmark Dose, lower limit -1SD ($BMDL_{1SD}$) of 3.01 mg/kg-day
Human equivalent dose	A human equivalent dose (0.38 mg/kg/day) was calculated based on the point of departure (3.01 mg/kg/day) and dose adjustment factor (ratio of the half-life of PFBA in human versus male rat; 72 hr /9.22 hr = 8).
Uncertainty and modifying factors	A total uncertainty factor of 100: 3 for animal to human differences 10 for intraspecies variability 3 for database uncertainty
Toxicity value	RfD of 0.0038 mg/kg/day (3,800 ng/kg/day)
Exposure parameters for drinking water screening level	A water ingestion rate of 0.285 L/kg/day (time-weighted average of the 95th percentile for 1 up to 3 months of age) and RSC of 50% were

[65] http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfba2summ.pdf

	taken into consideration to calculate the short-term health-based value.
Drinking water screening level	Short term, Subchronic (set to the Short-term value), and Chronic (set to the Short-term value) health-based value of 7,000 ng/L (ppt; 7 µg/L or ppb)

Texas Commission of Environmental Quality PFBA[66]

The Texas Commission of Environmental Quality develops protective concentration levels (PCLs) for a variety of purposes, including to help establish assessment levels, determine method quantitation limits, and identification of exposure pathways that require further action or might not require action.[67]

Critical study	van Otterdijk FM. 2007. Repeated dose 90-day oral toxicity study with MTDID 8391 by daily gavage in the rat followed by a 3-week recovery period. 3M.
Description of the critical study	The Texas Commission of Environmental Quality identified a study previously used as the basis of a Minnesota Department of Health subchronic RfD. That subchronic RfD was based on a subchronic (90-day) rat study with a NOAEL of 6.9 mg/kg-day for liver weight changes, morphological changes in the liver and thyroid gland, decreased TT4, and decreased red blood cells, hematocrit, and hemoglobin (van Otterdijk 2007). Increased relative thyroid weight, decreased serum TT4 and dFT4, decreased cholesterol and delayed eye opening were identified as co-critical effects.
Point of Departure	The Texas Commission of Environmental Quality used the NOAEL as 6.9 mg/kg/day, as identified in the Minnesota Department of Health 2011 subchronic PFBS Health Risk Limit
Human equivalent dose	No Human equivalent dose was calculated. A toxicokinetic uncertainty factor of 8 was included.
Uncertainty and modifying factors	A total uncertainty factor of 2,400: a toxicokinetics interspecies factor of 8 (adjusting for half-life duration of 3 days in humans versus 9.22 hours in male rats) to this NOAEL a 1 for interspecies toxicokinetics differences a 10 for intrahuman variability a 3 for subchronic to chronic extrapolation a 10 for significant database insufficiencies (e.g., neither a chronic nor a multi-generation reproductive study has been conducted)
Toxicity value	an RfD of 0.0029 mg/kg-day (2,900 ng/kg/day)
Exposure parameters for drinking water screening level	Child body weight of 15 kg Child water ingestion rate of 0.64 L/day Exposure duration of and averaging time of 6 years Exposure frequency of 350 days/year

[66] https://www.tceq.texas.gov/assets/public/implementation/tox/evaluations/pfcs.pdf
[67] https://www.tceq.texas.gov/assets/public/comm_exec/pubs/rg/rg-366-trrp-23.pdf

	No relative source contribution included
Drinking water screening level	Groundwater Protective Concentration Level of 71,000 ng/L (ppt; 71 µg/L or ppb)

Perfluorohexanoic acid (PFHxA)

Texas Commission of Environmental Quality PFHxA[68]

The Texas Commission of Environmental Quality develops protective concentration levels (PCLs) for a variety of purposes, including to help establish assessment levels, determine method quantitation limits, and identification of exposure pathways that require further action or might not require action.[69]

The Texas Commission of Environmental Quality assessed the available literature and found no toxicity data for PFHxA. Based on elimination rate information and with the knowledge that assignment of surrogate values includes uncertainty, they selected RfDs from the same or longer carbon chain PFAS for PFHxA.

Critical study	See Texas Commission of Environmental Quality PFHxS
Description of the critical study	See Texas Commission of Environmental Quality PFHxS
Point of Departure	See Texas Commission of Environmental Quality PFHxS
Human equivalent dose	See Texas Commission of Environmental Quality PFHxS
Uncertainty and modifying factors	See Texas Commission of Environmental Quality PFHxS
Toxicity value	RfD for PFHxS of 0.0000038 mg/kg-day (3.8 ng/kg/day)
Exposure parameters for drinking water screening level	Child body weight of 15 kg Child water ingestion rate of 0.64 L/day Exposure duration of and averaging time of 6 years Exposure frequency of 350 days/year No relative source contribution included
Drinking water screening level	Groundwater Protective Concentration Level of 93 ng/L (ppt)

[68] https://www.tceq.texas.gov/assets/public/implementation/tox/evaluations/pfcs.pdf
[69] https://www.tceq.texas.gov/assets/public/comm_exec/pubs/rg/rg-366-trrp-23.pdf

Perfluoroheptanoic acid (PFHpA)

Texas Commission of Environmental Quality PFHpA[70]

The Texas Commission of Environmental Quality develops protective concentration levels (PCLs) for a variety of purposes, including to help establish assessment levels, determine method quantitation limits, and identification of exposure pathways that require further action or might not require action.[71]

The Texas Commission of Environmental Quality assessed the available literature and found no toxicity data for PFHpA. Based on elimination rate information and with the knowledge that assignment of surrogate values includes uncertainty, they selected RfDs from the same or longer carbon chain PFAS for PFHpA.

Critical study	See Texas Commission of Environmental Quality PFOS
Description of the critical study	See Texas Commission of Environmental Quality PFOS
Point of Departure	See Texas Commission of Environmental Quality PFOS
Human equivalent dose	See Texas Commission of Environmental Quality PFOS
Uncertainty and modifying factors	See Texas Commission of Environmental Quality PFOS
Toxicity value	RfD for PFOS of 0.000023 mg/kg/day (23 ng/kg/day)
Exposure parameters for drinking water screening level	Child body weight of 15 kg Child water ingestion rate of 0.64 L/day Exposure duration of and averaging time of 6 years Exposure frequency of 350 days/year No relative source contribution included
Drinking water screening level	Groundwater Protective Concentration Level of 560 ng/L (ppt)

Perfluoropentanoic acid (PFPeA)

Texas Commission of Environmental Quality PFPeA[72]

The Texas Commission of Environmental Quality develops protective concentration levels (PCLs) for a variety of purposes, including to help establish assessment levels, determine method quantitation limits, and identification of exposure pathways that require further action or might not require action.[73]

The Texas Commission of Environmental Quality assessed the available literature and found no toxicity data for PFPeA. Based on elimination rate information and with the knowledge that assignment of surrogate values includes uncertainty, they selected RfDs from the same or longer carbon chain PFAS for PFPeA.

[70] https://www.tceq.texas.gov/assets/public/implementation/tox/evaluations/pfcs.pdf
[71] https://www.tceq.texas.gov/assets/public/comm_exec/pubs/rg/rg-366-trrp-23.pdf
[72] https://www.tceq.texas.gov/assets/public/implementation/tox/evaluations/pfcs.pdf
[73] https://www.tceq.texas.gov/assets/public/comm_exec/pubs/rg/rg-366-trrp-23.pdf

Critical study	See Texas Commission of Environmental Quality PFHxS
Description of the critical study	See Texas Commission of Environmental Quality PFHxS
Point of Departure	See Texas Commission of Environmental Quality PFHxS
Human equivalent dose	See Texas Commission of Environmental Quality PFHxS
Uncertainty and modifying factors	See Texas Commission of Environmental Quality PFHxS
Toxicity value	RfD for PFHxS of 0.0000038 mg/kg-day (3.8 ng/kg/day)
Exposure parameters for drinking water screening level	Child body weight of 15 kg Child water ingestion rate of 0.64 L/day Exposure duration of and averaging time of 6 years Exposure frequency of 350 days/year No relative source contribution included
Drinking water screening level	Groundwater Protective Concentration Level of 93 ng/L (ppt)

6:2 Fluorotelomer sulfonic acid (6:2 FTS)

No toxicity values have been identified for this PFAS.

Summary of the drinking water screening levels

Table 2 presents a summary of the drinking water screening levels described above. There are also several states that have adopted or use the US EPA PFOA+PFOS Lifetime HA. These are Alabama, Arizona, Colorado, Connecticut, Delaware, Iowa, Maine, New Hampshire, Pennsylvania, Rhode Island, and West Virginia.[74] The Michigan Department of Environmental Quality has also promulgated the US EPA Lifetime HA into their Part 201 Cleanup Criteria. See Appendix 2 for a description of various state's inclusion of other PFAS along with PFOA and PFOS.

The New Hampshire Department of Environmental Services (NHDES) has held work sessions for technical comments in October 2018 and will be holding a general public comment period beginning in January 2019 for setting public drinking water and groundwater standards for PFOA, PFOS, PFNA, and PFHxS.[75]

[74] This list is from the Interstate Technology Regulatory Council (ITRC) Section 4 Tables (updated July 2018) available at https://pfas-1.itrcweb.org/fact-sheets/.
[75] https://www.des.nh.gov/media/pr/2018/20181003-pfas-meetings.htm

Table 2: Summary of the drinking water screening levels used by US EPA, ATSDR, and various state agencies

Drinking Water Screening Level	Agency							
	USEPA	ATSDR[A]	AKDEC	MDH	NJDEP	NDEP	NCDEQ	TCEQ
PFOA (ng/L or ppt)	70[B]	78 (adult) 21 (child)	400	35	14	667	2,000[C]	290
PFOS (ng/L or ppt)	70[B]	52 (adult) 14 (child)	400	27	13	667	NA[C,D]	560
PFNA (ng/L or ppt)	NA	78 (adult) 21 (child)	NA	NA	13	NA	NA	290
PFHxS (ng/L or ppt)	NA	520 (adult) 140 (child)	NA	27	NA	NA	NA	93
PFBS (ng/L or ppt)	400,000	NA	NA	3,000[E] 2,000[F]	NA	667,000	NA	34,000
PFBA (ng/L or ppt)	NA	NA	NA	7,000	NA	NA	NA	71,000
PFHxA (ng/L or ppt)	NA	NA	NA	NA	NA	NA	NA	93
PFHpA (ng/L or ppt)	NA	NA	NA	NA	NA	NA	NA	560
PFPeA (ng/L or ppt)	NA	NA	NA	NA	NA	NA	NA	93
6:2 FTS (ng/L or ppt)	NA	NA	NA	NA	NA	NA	NA	NA

A = ATSDR has stated that consultation may be needed to evaluation mixtures.
B = PFOA and PFOS levels should be evaluated in combination if both are present in a sample.
C = NC DEQ is proposing use of the US EPA PFOA+PFOS Lifetime Health Advisory of 70 ng/L
D = None available
E = Short-term and subchronic duration
F = Chronic duration

Comparison of US EPA and ATSDR pharmacokinetic modeling and inputs for PFOA and PFOS

USEPA and ATSDR used the same pharmacokinetic model to calculate average PFOA and PFOS serum concentration from administered doses. The average serum PFOA or PFOS concentrations were extrapolated to human equivalent steady-state concentrations using a first order one compartment model. The two agencies used different model input parameters, which lead to different estimated human equivalent doses. The parameters used for PFOA were notably different (Table 3). Please see the discussion below for further details.

Table 3: Model Input Parameters used by the US Environmental Protection Agency (US EPA) and the Agency for Toxic Substances and Disease Registry (ATSDR) for PFOA and PFOS.

Model input parameter	PFOA		PFOS	
	US EPA[1]	ATSDR[2]	US EPA[3]	ATSDR[2]
Serum elimination half-life (days)	840 (2.3 years)	1400 (3.8 years)	1971 (5.4 years)	2000 (5.5 years)
Serum elimination rate constant(1/day)	0.00083	0.000495	0.000351	0.000347
Apparent volume of distribution (L/kg)	0.17	0.2	0.23	0.2

1 = https://www.epa.gov/sites/production/files/2016-05/documents/pfoa_health_advisory_final_508.pdf
2 = https://www.atsdr.cdc.gov/toxprofiles/tp200.pdf
3 = https://www.epa.gov/sites/production/files/2016-05/documents/pfos_health_advisory_final_508.pdf

US EPA and ATSDR selected a different serum elimination half-life parameter for PFOA. This was a major difference between the two agencies' approaches to modeling PFOA serum levels. Several studies have estimated PFOA and PFOS half-lives in workers and highly exposed residents. Olson et al. (2007)[76] estimated half-lives of PFOA (1,387 days: 3.8 years) and PFOS (1,971 days: 5.4 years) from 26 fluorochemical production workers followed more than 5 years. Costa et al. (2009)[77] reported a half-life for PFOA of 1,862 days (5.1 years) from 16 previous PFOA production workers. Bartell et al. (2010)[78] estimated PFOA half-life (840 days: 2.3 years) in a population of 200 residents who had been drinking publicly supplied water contaminated with PFOA. The residents were followed for 6-12 months after they were no longer drinking their PFOA-contaminated water. ATSDR selected the Olson et al. (2007) estimated PFOA half-life as that study had a longer follow-up time, and the estimate of the terminal half-life appeared to increase with the longer follow-ups. This may have been due to slower kinetics making a larger contribution to the terminal half-life (Seals et al. 2011)[79]. The variation in serum

[76] Olsen GW, Burris JM, Ehresman DJ, Froehlich JW, Seacat AM, Butenhoff JL, Zobel LR. 2007. Half-life of serum elimination of perfluorooctanesulfonate, perfluorohexanesulfonate, and perfluorooctanoate in retired fluorochemical production workers. Environ Health Perspect. 115(9):1298-1305.
[77] Costa G, Sartori S, Consonni D. 2009. Thirty years of medical surveillance in perfluooctanoic acid production workers. J Occup Environ Med. 51(3):364-372.
[78] Bartell SM, Calafat AM, Lyu C, Kato K, Ryan PB, Steenland K. 2010. Rate of decline in serum PFOA concentrations after granular activated carbon filtration at two public water systems in Ohio and West Virginia. Environ Health Perspect. 118 (2):222-228.
[79] Seals R, Bartell SM, Steenland K. 2010. Accumulation and clearance of perfluorooctanoic acid (PFOA) in current and former residents of an exposed community. Environ Health Perspect. 119(1):119-124.

elimination rate constant (K_e) for PFOA selected by the two agencies are due to the observed difference in serum elimination $t_{1/2}$ value ($K_e = \ln(2)/t_{1/2}$).

While the PFOA and PFOS volume of distribution values are similar, the two agencies cite different sources. US EPA used the apparent volume of distribution values for PFOA and PFOS from a human study (Thompson et al. 2010)[80] whereas ATSDR used values from nonhuman primate studies (Butenhoff et al. 2004[81]; Chang et al. 2012[82]). Neither the US EPA nor the ATSDR provide any justification for the selections.

Summaries of supporting toxicological and epidemiological literature

The US EPA and ATSDR have provided summaries of PFAS research in laboratory animals and human epidemiology studies. However, the PFAS health effects research is an active field. The two studies summarized below were not included in the recent ATSDR Toxicological Profile for Perfluoroalkyls, draft for public comment released in June 2018. Given the interest in expanding the knowledge base on PFAS, it is likely that additional studies will be available prior to the finalization ATSDR draft Toxicological Profile for Perfluoroalkyl. These studies, or other studies published in the future, may be used in the development of toxicity studies as a critical study or supporting information.

ATSDR noted that a single oral acute duration (less than 14 days), two intermediate (more than 14 days to one year), and no chronic duration PFHxS studies were identified. The below study would add to the intermediate study duration database.

- Chang Sue, Butenhoff John L, Parker George A, Coder Pragati S, ZitzowJeremiah D, Krisko Ryan M, Bjork James A,WallaceKendall B, Seed Jennifer G. Reproductive and Developmental Toxicity of Potassium Perfluorohexanesulfonate in CD-1 Mice. Reproductive Toxicology https://doi.org/10.1016/j.reprotox.2018.04.007

Potassium perfluorohexanesulfoante (K+PFHxS) was evaluated for reproductive/developmental toxicity in CD-1 mice. Up to 3 mg/kg/day K+PFHxS was administered (n=30/sex/group) before mating, for at least 42 days in F0 males, and for F0 females, through gestation and lactation. F1 pups were directly dosed with K+PFHxS for 14 days after weaning.

There was an equivocal decrease in live litter size at 1 and 3 mg/kg/day, but the pup-born-to-implant ratio was unaffected. Adaptive hepatocellular hypertrophy was observed, and in 3 mg/kg/day F0 males, it was accompanied by concomitant decreased serum cholesterol and increased alkaline phosphatase.

There were no other toxicologically significant findings on reproductive parameters, hematology/clinical pathology/thyroid stimulating hormone (TSH), neurobehavioral effects, or histopathology. There were

[80] Thompson J, Lorber M, Toms LL, Kato K, Calafat AM, Mueller JF. 2010. Use of simple pharmacokinetic modeling to characterize exposure of Australians to perfluorooctanoic acid and perfluorooctane sulfonic acid. Environ Int. 36(4):390-397.
[81] Butenhoff JL, Kennedy GL Jr, Hinderliter PM, Lieder PH, Jung R, Hansen KJ, Gorman GS, Noker PE, Thomford PJ. 2004. Pharmacokinetics of perfluorooctanoate in cynomolgus monkeys. Toxicol Sci. 82(2):394-406.
[82] Chang SC, Noker PE, Gorman GS, Gibson SJ, Hart JA, Ehresman DJ, Butenhoff JL. 2012. Comparative pharmacokinetics of perfluorooctanesulfonate (PFOS) in rats, mice, and monkeys. Reprod Toxicol. 33(4):428-440.

no treatment-related effects on postnatal survival, development, or onset of preputial separation or vaginal opening in F1 mice.

ATSDR noted that there were no oral acute duration (less than 14 days) studies for PFBS. ATSDR also noted that there were no intermediate (more than 14 days to one year) developmental toxicity or immunotoxicity studies, and that no chronic duration PFBS studies were identified. The below study would add to the intermediate study duration database as it was a developmental toxicity study.

- Feng, X., X Cao, S Zhao, X Wang, X Hua, L Chen, L Chen. (2017). "Exposure of Pregnant Mice to Perfluorobutanesulfonate Causes Hypothyroxinemia and Developmental Abnormalities in Female Offspring." Toxicological Sciences 155(2): 409-419.

Feng et al. (2017) treated pregnant ICR mice with 0, 50, 200, or 500 mg/kg/day K+PFBS from gestational day 1 to gestational day 20. Male offspring were not used in this experiment. Fifty female offspring (from 10 dams) had perinatal survival and growth, pubertal onset and ovarian and uterine development examined. Hormone levels (hypothalamic-pituitary-gonadal and hypothalamic- pituitary- and thyroid hormones were examined in 30 female offspring on postnatal day 1, 10 offspring on postnatal day 30, and 10 offspring on postnatal day 60. Serum PFBS was measured in offspring from 10 dams. Decreased total T3 and T4 levels were observed in mice with prenatal exposure to 200 or 500 mg/kg/day in all three postnatal groups. Total T3 and free and total T4, measured on gestational day 20, were also decreased in dams exposed to 200 and 500 mg/kg/day. Offspring postnatally treated with 200 and 500 mg/kg/day also had decreases in perinatal growth, pubertal onset, and reproductive organ development.

Description of the equations used in the calculations of federal agency and other states drinking water screening levels

This section describes the calculation of drinking water screening levels, using existing equations and exposure parameters and the toxicity values described above.

US Environmental Protection Agency (US EPA)

The US EPA developed the PFOA and PFOS Lifetime Health Advisory using the below equations[83]:

$$Drinking\ water\ equivalent\ level\ (DWEL) = \frac{Reference\ Dose}{drinking\ water\ intake\ rate}$$

$$Lifetime\ Health\ Advisory = DWEL\ x\ Relative\ Source\ Contribution$$

Where:

- The drinking water intake rate is 0.054 L/kg/day. This is the estimated 90th percentile for direct and indirect community water ingestion by lactating women.[84]
- Relative Source Contribution of 20%

The US EPA lifetime health advisory for PFOA and PFOA covers both PFOA and PFOS, either individually or in combination if both are present.

The US EPA has developed Regional Screening Levels (RSLs) for tapwater[85]. RSLs are used to screen chemicals at Superfund sites nationwide.[86] The residential RSLs include ingestion, inhalation, and dermal contact, when applicable. The equation used for noncarcinogenic effects is based on a child exposed for 6 years.

$$Tapwater\ RSL\ for\ ingestion$$

$$= \frac{Target\ Hazard\ Quotient\ x\ Averging\ Time\ x\ Body\ Weight\ x\ conversion\ factor}{Exposure\ Frequency\ x\ Exposure\ Duration\ x\ \frac{1}{RfD}\ x\ Ingestion\ Rate\ for\ Water}$$

Where:

- Target Hazard Quotient = 1
- Averaging Time = 365 days/year x Exposure Duration
- Body Weight = 15 kilograms
- Conversion Factor = 1000 µg/milligrams
- Exposure Frequency = 350 days/year
- Exposure Duration = 6 years

[83] The US EPA calculated an advisory for PFOA and PFOS separately, then made a determination that both PFOA and PFOS should be evaluated together.
[84] Table 3-81 in the 2011 US EPA Exposure Factors Handbook (http://ofmpub.epa.gov/eims/eimscomm.getfile?p_download_id=522996)
[85] https://www.epa.gov/risk/regional-screening-levels-rsls-equations
[86] https://www.epa.gov/risk/regional-screening-levels-rsls

- RfD = chemical-specific
- Ingestion Rate for Water = 0.78 L/day

There is no relative source contribution used in the RSLs.

Agency for Toxic Substances and Disease Registry (ATSDR)

ATSDR develops Environmental Media Evaluation Guides (EMEGs) for drinking water for both adults and children using the below body weights and water intake rates.

- Adult body weight of 80 kilograms (kg)
- Adult water intake rate of 3.092 Liters per day (L/day)
- Child, birth to one year old, body weight of 7.8 kg
- Child, birth to one year old, water ingestion rate of 1.113 L/day

ATSDR uses the below equation:

$$Environmental\ Media\ Evaluation\ Guide = \frac{Minimal\ Risk\ Level\ x\ body\ weight}{water\ intake\ rate}$$

ATSDR develops EMEGs using their Minimal Risk Levels, however, the equation is the same if an RfD was used in place of an MRL.

Michigan Department of Environmental Quality (MDEQ)

The MDEQ also calculates drinking water values as part of the Part 201 program. The residential drinking water value equation for noncarcinogenic effects includes an age-adjusted water intake rate and also an RSC of 20%.

Draft proposed residential drinking water value equation for noncarcinogenic effects using an age-adjusted water intake rate to account for exposure to both children and adults:

$$DWV_{nc} = \frac{THQ \times AT_{res} \times RfD \times RSC_{w} \times CF}{EF_{res} \times IF_{dw}}$$

where,

DWV_{nc}	(Drinking water value)	=	chemical-specific, µg/L or ppb
THQ	(Target hazard quotient)	=	1
AT_{res}	(Averaging time)	=	11,680 days
RfD	(Oral reference dose)	=	chemical-specific, mg/kg-day
RSC_{w}	(Relative source contribution)	=	chemical-specific or 0.2
CF	(Conversion factor)	=	1,000 µg/mg
EF_{res}	(Exposure frequency)	=	350 days/year
IF_{dw}	(Age-adjusted drinking water ingestion factor)	=	1.1 L-year/kg-day

The MDEQ also has two equations for calculating drinking water values for chemicals with developmental effects. The one listed below is for exposure to a child. The other equation is for exposure to a pregnant woman. The developmental equation for child exposure results in the lowest value and is protective for the fetus during a pregnant woman's exposure and also protective for the adult population. An RSC of 20% is also used in these equations.

Draft proposed residential drinking water equation for developmental noncarcinogenic effects for a child's exposure:

$$DWV_{dev} = \frac{THQ \times AT_{child} \times RfD_{dev} \times BW_{child} \times RSC_{w} \times CF}{ED_{child} \times EF_{res} \times IR_{dw,child}}$$

where,

DWV_{dev}	(Drinking water value)	=	chemical-specific, µg/L or ppb
THQ	(Target hazard quotient)	=	1
AT_{child}	(Averaging time)	=	2,190 days
RfD_{dev}	(Oral reference dose)	=	chemical-specific, mg/kg-day
BW_{child}	(Body weight)	=	15 kg
RSC_{w}	(Relative source contribution)	=	0.2 or chemical-specific
CF	(Conversion factor)	=	1,000 µg/mg
ED_{child}	(Exposure duration)	=	6 years
EF_{res}	(Exposure frequency)	=	350 days/year
$IR_{dw,\ child}$	(Drinking water ingestion rate)	=	0.78 L/day

Minnesota Department of Health (MDH)

The Minnesota Department of Health (MDH) used this equation for their PFBS nHBVs[87]:

$$nHBV = \frac{(Reference\ Dose)x(relative\ source\ contribution)x\ (Conversion\ Factor)}{Water\ intake\ rate}$$

Along with the RfDs described above, MDH used these water ingestion rates:

- Chronic: 0.044 L/kg/day (time-weighted average over a lifetime of approximately 70 years of age).
- Subchronic: 0.070 L/kg/day (time-weighted average up to 8 years of age).
- Short-term: 0.285 L/kg/day (time-weighted average of the 95th percentile for 1 up to 3 months of age).

[87] http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfbssummary.pdf

And these relative source contributions (RSC):

- Chronic RSC = 20%
- Subchronic RSC = 20%
- Short-term RSC = 50%

MDH uses the above default RSCs for chemicals that are not highly volatile. These RSCs were selected based on a US EPA decision tree. For the short-term RSC, 50% was selected as infants less than three months old are unlikely to have a significant known or potential source of exposure other than drinking water.[88]

The Conversion factor is 1000 µg/mg.

For PFOA and PFOS, MDH used a toxicokinetic model to evaluate two exposure scenarios. Both exposure scenarios used a

The two exposure scenarios were:

- an infant fed formula reconstituted with contaminated water starting at birth and continuing ingestion of contaminated water through life and
- an infant exclusively breast-fed for 12 months, followed by drinking contaminated water through life).

The more protective exposure scenario for a breast-fed infant was selected to use as the water intake rate. A placental transfer factor of 87% (percent of maternal serum level) and a breastmilk transfer factor of 5.2% (percent of maternal serum level) were used in the calculation of the health-based drinking water value.

An RSC of 50% was included, based on local and national biomonitoring serum concentrations (at the time of the evaluation).

Calculation of potential drinking water screening levels

The described toxicity values developed by various agencies were used in the different equations described above. This section compares the drinking water screening levels resulting from use of the various toxicity values in a standard set of equations. Other agencies may not consider this an appropriate use of their toxicity values as all have a specific exposure scenario and equations to calculate their drinking water screening levels.

[88] http://www.health.state.mn.us/divs/eh/risk/rules/water/hrlsonar08.pdf

Calculated PFOA drinking water screening levels in nanograms per Liter (ng/L) or parts per trillion (ppt)

The range of calculated PFOA drinking water screening levels was 7.4 to 517 ppt. However, the New Jersey PFOA RfD is not based on a developmental endpoint. If those two screening levels were removed, the range would be 11 to 517 ppt.

Toxicity value	EPA Lifetime Health Advisory equations	EPA Tapwater RSL (Ingestion) equation	ATSDR Comparison Value equation - adult	ATSDR comparison value equation - child	MDEQ Residential Drinking water criteria equation – age adjusted	MDEQ Residential Drinking water criteria equation – child developmental	MDH equation[A]
US EPA PFOA RfD[B]	74 ppt	401 ppt	517 ppt	140 ppt	121 ppt	80 ppt	Not calculated
Draft ATSDR PFOA MRL	11 ppt	60 ppt	78 ppt	21 ppt	18 ppt	12 ppt	Not calculated
MDH short-term PFOA RfD	67 ppt	361 ppt	466 ppt	126 ppt	109 ppt	72 ppt	35 ppt
NJ DEP PFOA RfD	7.4 ppt [C]	40 ppt	52 ppt	14 ppt	12 ppt	8 ppt [C]	Not calculated
TCEQ PFOA RfD	44 ppt	240 ppt	310 ppt	84 ppt	73 ppt	48 ppt	Not calculated

A = MDH used a toxicokinetic model to develop their PFOA noncancer health-based values. The model uses the Reference Dose (RfD) as a serum level. Other agency RfDs were not converted to a serum level and therefore could not be used in the MDH model.
B = Alaska DEC, Nevada DEP, and Michigan DEQ use the EPA PFOA RfD.
C = The NJ PFOA RfD is not based on a developmental endpoint and the exposure scenarios for these equations are meant to be protective of developmental effects. These values, while health protective, may be more conservative than the others.

Calculated PFOS drinking water screening levels in nanograms per Liter (ng/L) or parts per trillion (ppt)

The range of calculated PFOS drinking water screening levels was 6.7 to 595 ppt. However, the New Jersey PFOS RfD is not based on a developmental endpoint. If those two screening levels were removed, the range would be 7.4 to 595 ppt.

Toxicity value	EPA Lifetime Health Advisory equations	EPA Tapwater RSL (Ingestion) equation	ATSDR Comparison Value equation - adult	ATSDR comparison value equation - child	MDEQ Residential Drinking water criteria equations – age adjusted	MDEQ Residential Drinking water criteria equation – child developmental	MN equation[A]
US EPA PFOS RfD	74 ppt	401 ppt	517 ppt	140 ppt	121 ppt	80 ppt	Not calculated
Draft ATSDR PFOS MRL	7.4 ppt	40 ppt	52 ppt	14 ppt	12 ppt	8 ppt	Not calculated
MDH short-term PFOS RfD	19 ppt	102 ppt	132 ppt	36 ppt	31 ppt	20 ppt	27 ppt
NJ DEP PFOS RfD	6.7 ppt [C]	36 ppt	47 ppt	13 ppt	11 ppt	7.2 ppt [C]	Not calculated
TCEQ PFOS RfD	85 ppt	461 ppt	595 ppt	161 ppt	140 ppt	92 ppt	Not calculated

A = MDH used a toxicokinetic model to develop their PFOS noncancer health-based values. The model uses the Reference Dose (RfD) as a serum level. Other agency RfDs were not converted to a serum level and could not be used in the MDH model.
B = Alaska DEC, Nevada DEP, and Michigan DEQ use the EPA PFOS RfD.
C = The NJ PFOS RfD is not based on a developmental endpoint and the exposure scenarios for these equations are meant to be protective of developmental effects. These values, while health protective, may be more conservative than the others.

Calculated PFNA drinking water screening levels in nanograms per Liter (ng/L) or parts per trillion (ppt)

The range of calculated PFNA drinking water screening levels was 11 to 310 ppt. The TCEQ PFNA RfD was not based on a developmental endpoint, however, removal of those values does not change the range.

Toxicity value	EPA Lifetime Health Advisory equations	EPA Tapwater RSL (Ingestion) equation	ATSDR Comparison Value equation - adult	ATSDR comparison value equation - child	MDEQ Residential Drinking water criteria equations – age adjusted	MDEQ Residential Drinking water criteria equation – child developmental	MN equation
Draft ATSDR PFNA MRL	11 ppt	60 ppt	78 ppt	21 ppt	18 ppt	12 ppt	14 ppt
NJ DEP PFNA target serum level [A]	Not calculated	Not calculated	Not calculated	Not calculated	Not calculated	Not calculated	Not calculated
TCEQ PFNA RfD	44 ppt [B]	241 ppt	310 ppt	84 ppt	73 ppt	48 ppt [B]	55 ppt

A = The NJ DEP PFNA is a target serum level and not a dose. This target serum level cannot be used in the other agency equations without a conversion to a dose. As the NJ DEP did not do that conversion, the target serum level was not used to calculate other drinking water screening levels.

B = The TCEQ RfD is not based on a developmental endpoint and the exposure scenarios for these equations are meant to be protective of developmental effects. These values, while health protective, may be more conservative than the others.

Calculated PFHxS drinking water screening levels in nanograms per Liter (ng/L) or parts per trillion (ppt)

The range of calculated PFHxS drinking water screening levels was 14 to 517 ppt. However, the ATSDR draft PFHxS MRL and TCEQ PFHxS RfD are not based on a developmental endpoint. If those screening levels were removed, the range would be 17 to 517 ppt.

Toxicity value	EPA Lifetime Health Advisory equations	EPA Tapwater RSL (Ingestion) equation	ATSDR Comparison Value equation - adult	ATSDR comparison value equation - child	MDEQ Residential Drinking water criteria equation – age adjusted	MDEQ Residential Drinking water criteria equation – child developmental	MN equation
Draft ATSDR PFHxS MRL	74 ppt [A]	401 ppt	517 ppt	140 ppt	121 ppt	80 ppt [A]	91 ppt
TCEQ PFHxS RfD	14 ppt [A]	76 ppt	98 ppt	27 ppt	23 ppt	15 ppt [A]	17 ppt
A = The ATSDR draft PFHxS MRL and TCEQ PFHxS RfD are not based on a developmental endpoint and the exposure scenarios for these equations are meant to be protective of developmental effects. These values, while health protective, may be more conservative than the others.							

Calculated PFBS drinking water screening levels in micrograms per Liter (µg/L) or parts per billion (ppb)

The range of calculated PFBS drinking water screening levels was 1.6 to 5,174 ppb (1,600 to 5,174,000 ppt). However, the US EPA chronic provisional reference dose (pRfD), MDH chronic RfD, and TCEQ RfD are not based on a developmental endpoint. If those screening levels were removed, the range would be 2 to 5,174 ppb (3,000 to 5,174,000 ppt).

Toxicity value	EPA Lifetime Health Advisory equations	EPA Tapwater RSL (Ingestion) equation	ATSDR Comparison Value equation - adult	ATSDR comparison value equation - child	MDEQ Residential Drinking water criteria equation – age adjusted	MDEQ Residential Drinking water criteria equation – child developmental	MN equation
US EPA chronic PFBS pRfD[A]	740 ppb [B]	4,010 ppb	5,174 ppb	1,401 ppb	1,213 ppb	802 ppb [V]	909 ppb
MDH short-term PFBS RfD	5.9 ppb	32 ppb	41 ppb	11 ppb	10 ppb	6.4 ppb [B]	3 ppb
MDH chronic PFBS RfD	1.6 ppb [B]	8.6 ppb	11 ppb	3 ppb	2.6 ppb	1.7 ppb [B]	2 ppb
TCEQ PFBS RfD	5.2 ppb [B]	28 ppb	36 ppb	10 ppb	8.5 ppb	5.6 ppb [B]	6 ppb
A = Nevada DEP uses the US EPA chronic PFBS pRfD. B = The US EPA chronic pRfD, MDH chronic RfD, and TCEQ RfD are not based on a developmental endpoints and the exposure scenarios for these equations are meant to be protective of developmental effects. These values, while health protective, may be more conservative than the others.							

Calculated PFBA drinking water screening levels in micrograms per Liter (µg/L) or parts per billion (ppb)

The range of calculated PFBA drinking water screening levels was 7 to 98 ppb (7,000 to 98,000 ppt). However, the MDH short-term PFBA RfD and TCEQ PFBA RfD are not based on a developmental endpoint. Removal of those screening levels would not change the range.

Toxicity value	EPA Lifetime Health Advisory equation	EPA Tapwater RSL (Ingestion) equation	ATSDR Comparison Value equation - adult	ATSDR comparison value equation - child	MDEQ Residential Drinking water criteria equation – age adjusted	MDEQ Residential Drinking water criteria equation – child developmental	MN equation
MDH short-term PFBA RfD	14 ppb [A]	76 ppb	98 ppb	26 ppb	23 ppb	15 ppb [A]	7 ppb
TCEQ PFBA RfD	11 ppb [A]	58 ppb	75 ppb	20 ppb	18 ppb	12 ppb [A]	13 ppb
A = The MDH short-term PFBA RfD and TCEQ PFBA RfD are not based on a developmental endpoints and the exposure scenarios for these equations are meant to be protective of developmental effects. These values, while health protective, may be more conservative than the others.							

Calculated PFHxA drinking water screening levels in nanograms per Liter (ng/L) or parts per trillion (ppt)

The range of calculated PFHxA drinking water screening levels was 14 to 98 ppt. As the TCEQ PFHxA RfD is not based on a developmental endpoints, removal of two screening levels would change the range to 17 to 98 ppt.

Toxicity value	EPA Lifetime Health Advisory equation	EPA Tapwater RSL (Ingestion) equation	ATSDR Comparison Value equation - adult	ATSDR comparison value equation - child	MDEQ Residential Drinking water criteria equation – age adjusted	MDEQ Residential Drinking water criteria equation – child developmental	MN equation
TCEQ PFHxA RfD	14 ppt [A]	76 ppt	98 ppt	27 ppt	23 ppt	15 ppt [A]	17 ppt
A = The TCEQ PFHxA RfD is not based on a developmental endpoints and the exposure scenarios for these equations are meant to be protective of developmental effects. These values, while health protective, may be more conservative than the others.							

Calculated PFHpA drinking water screening levels in nanograms per Liter (ng/L) or parts per trillion (ppt)

The range of calculated PFHxA drinking water screening levels was 85 to 595 ppt.

Toxicity value	EPA Lifetime Health Advisory equations	EPA Tapwater RSL (Ingestion) equation	ATSDR Comparison Value equation - adult	ATSDR comparison value equation - child	MDEQ Residential Drinking water criteria equation – age adjusted	MDEQ Residential Drinking water criteria equations– child developmental	MN equation
TCEQ PFHxA RfD	85 ppt	461 ppt	595 ppt	161 ppt	140 ppt	92 ppt	105 ppt

Calculated PFPeA drinking water screening levels in nanograms per Liter (ng/L) or parts per trillion (ppt)

The range of calculated PFPeA drinking water screening levels was 14 to 98 ppt. As the TCEQ PFPeA RfD is not based on a developmental endpoints, removal of two screening levels would change the range to 17 to 98 ppt.

Toxicity value	EPA Lifetime Health Advisory equations	EPA Tapwater RSL (Ingestion) equation	ATSDR Comparison Value equation - adult	ATSDR comparison value equation - child	MDEQ Residential Drinking water criteria equations – age adjusted	MDEQ Residential Drinking water criteria equation – child developmental	MN equation
TCEQ PFPeA RfD	14 ppt [A]	76 ppt	98 ppt	27 ppt	23 ppt	15 ppt [A]	17 ppt
A = The TCEQ PFPeA RfD is not based on a developmental endpoints and the exposure scenarios for these equations are meant to be protective of developmental effects. These values, while health protective, may be more conservative than the others.							

Calculated 6:2 FTS drinking water screening levels

There are no toxicity values and so no drinking water screening levels can be calculated.

As is apparent with the calculated health-based drinking water values in the above tables, the combination of the toxicity value with the drinking water screening level equations influence the resulting value. Discrepancies between agencies are common and occur due to different methods of calculation and programmatic purposes. This is why even well-studied chemicals and long-established health-based drinking water screening levels used by various agencies often vary. With emerging contaminants, such as PFAS, updates are to be expected as the science evolves and more is known.

Appendix 1: Additional PFAS toxicity values and drinking water screening levels

North Carolina Department of Health and Human Services[89]

The North Carolina Department of Health and Human Services (NC DHHS) uses the US EPA Lifetime Health Advisory (HA) value of 70 nanograms per liter (ng/L) for PFOA and PFOS, individually (when only one is present) or in combination, as a drinking water screening level to consider use of alternate water. They have also developed a "health goal" (non-regulatory, non-enforceable level of a chemical) for Gen X (Perfluoro-2-propoxypropanoic acid).

Critical study	North Carolina Department of Health and Human Services, GenX Health Studies and Health Advisories presentation to the Secretaries' Science Advisory Board Meeting, December 4, 2017 https://files.nc.gov/ncdeq/GenX/SAB/GenX%20Health%20Studies%20and%20Advisories%20SSAB%2012_4_2017.pdf
Description of the critical study	Mice were given 0, 0.1, 3, or 30 mg/kg/day for 28 days. Single cell necrosis of hepatocytes and increases in liver enzymes were identified at 3 and 30 mg/kg/day in male mice.
Point of Departure	NOAEL of 0.1 mg/kg/day for liver effects in mice
Human equivalent dose	No human equivalent dose was calculated
Uncertainty and modifying factors	Total uncertainty factor of 1000: a 10 for interspecies variability a 10 for intraspecies variability a 10 for subchronic to chronic extrapolation
Toxicity value	An RfD of 0.0001 mg/kg/day (100 ng/kg/day)
Exposure parameters for drinking water screening level	Body Weight of 7.8 kg (bottle-fed infant) Water Intake of 1.1 L/day (bottle-fed infant) Relative Source Contribution of 20% Unit Conversion = 10^6 ng/mg
Drinking water screening level	Health goal of 140 ng/L (ppt)

[89] https://ncdenr.s3.amazonaws.com/s3fs-public/GenX/NC%20DHHS%20Risk%20Assessment%20FAQ%20Final%20Clean%20071417%20PM.pdf, https://files.nc.gov/ncdeq/GenX/GenX%20factsheet%20FINAL%2013Sep2017.pdf and, https://deq.nc.gov/news/hot-topics/genx-investigation/secretaries-science-advisory-board

Oregon Department of Environmental Quality[90]

The Oregon Department of Environmental Quality has "Initiation Levels" for PFAS in surface water. If PFAS levels in municipal wastewater are over these initiation levels, a pollution reduction plan is required.

For PFAS, Oregon DEQ's Initiation Levels are:

PFAS	Oregon DEQ Initiation Level in micrograms per Liter (µg/L or parts per billion) and nanograms per Liter (ng/L or parts per trillion [ppt])
Perfluoroheptanoic acid [PFHpA]	300 (300,000 ng/L)
Perfluorononanoic acid [PFNA]	1 (1,000 ng/L)
Perfluorooctane sulfonamide [PFOSA]	0.2 (200 ng/L)
Perfluorooctane sulfonic acid [PFOS]	300 (300,000 ng/L)
Perfluorooctanoic acid [PFOA]	24 (24,000 ng/L)

[90] https://www.deq.state.or.us/regulations/rules/summary/PersistentPollutants2010-07-06.htm, https://secure.sos.state.or.us/oard/viewReceiptPDF.action?filingRsn=36054

Texas Commission of Environmental Quality[91]

The Texas Commission of Environmental Quality has selected toxicity values for 16 PFAS. All 16 PFAS RfDs are used to calculate Protective Concentration Levels (PCLs). PCLs are used for a variety of purposes, including to help establish assessment levels, determine method quantitation limits, and identification of exposure pathways that require further action or might not require action.[92]

PFOSA

As there was limited toxicity data available for PFOSA, the Texas Commission of Environmental Quality used the RfD for PFOS as a surrogate for PFOSA based on similarity in the oral rodent lethal dose resulting in the death of 50% of the animals exposed.

Critical study	See Texas Commission of Environmental Quality PFOS
Description of the critical study	See Texas Commission of Environmental Quality PFOS
Point of Departure	See Texas Commission of Environmental Quality PFOS
Human equivalent dose	See Texas Commission of Environmental Quality PFOS
Uncertainty and modifying factors	See Texas Commission of Environmental Quality PFOS
Toxicity value	RfD of 0.000012 mg/kg/day (12 ng/kg/day)
Exposure parameters for drinking water screening level	Child body weight of 15 kg Child water ingestion rate of 0.64 L/day Exposure duration of and averaging time of 6 years Exposure frequency of 350 days/year No relative source contribution included
Drinking water screening level	Groundwater Protective Concentration Level of 290 ng/L (ppt)

PFDeA

TCEQ developed an RfD based on a subacute rat study, but noted that interspecies extrapolation for PFDeA has significant uncertainty as there is no chemical-specific half-life data for derivation of a rat-to-human toxicokinetic factor; available rat data indicates that the elimination rate trend decreases as PFAS chain length increases, and that the elimination in rats is estimated to be much slower than the PFOA elimination, by about 7-140 times.

Critical study	Kawashima Y, Kobayashi H, Miura H, et al. 1995. Characterization of hepatic responses of rat to administration of perfluorooctanoic and perfluorodecanoic acids at low levels. Toxicology 99(3):169178.
Description of the critical study	Kawashima et al. (1995) exposed male rats for seven days to PFDeA (1.2-9.5 mg/kg-day) and PFOA (2.4-38 mg/kg-day) in the diet. PFDeA reduced body weight gain and food consumption and caused hepatomegaly. PFDeA also lowered GSH-related enzyme activity, which was also seen for PFOA. A LOAEL for increased liver

[91] https://www.tceq.texas.gov/assets/public/implementation/tox/evaluations/pfcs.pdf
[92] https://www.tceq.texas.gov/assets/public/comm_exec/pubs/rg/rg-366-trrp-23.pdf

	weight (≈ 30%) of 2.4 mg/kg/day and a NOAEL of 1.2 mg/kg/day was identified.
Point of Departure	a NOAEL of 1.2 mg/kg/day
Human equivalent dose	No human equivalent dose was calculated. A toxicokinetic uncertainty factor of 81 was included.
Uncertainty and modifying factors	A total uncertainty factor of 81,000: a toxicokinetic animal to human data-derived extrapolation factor of 81[A] a toxicodynamic uncertainty factor of 1 a human to human variability uncertainty factor of 10 a database uncertainty factor of 10 a subacute to chronic uncertainty factor of 10 a database uncertainty factor of 1
Toxicity value	RfD of 0.000015 mg/kg/day (15 ng/kg/day)
Exposure parameters for drinking water screening level	Child body weight of 15 kg Child water ingestion rate of 0.64 L/day Exposure duration of and averaging time of 6 years Exposure frequency of 350 days/year No relative source contribution included
Drinking water screening level	Groundwater Protective Concentration Level of 290 ng/L (ppt)
A = This is based on the US EPA PFOA toxicokinetics used in their 2009 provisional PFOA health advisory (https://www.epa.gov/sites/production/files/2015-09/documents/pfoa-pfos-provisional.pdf).	

PFDoA

TCEQ developed an RfD based on a subacute rat study, but noted that interspecies extrapolation for PFDoA has significant uncertainty as there is no chemical-specific half-life data for derivation of a rat-to-human toxicokinetic factor and available rat data indicates that the elimination rate trend decreases as PFAS chain length increases.

Critical study	Shi Z, Zhang H, Liu Y, et al. 2007. Alterations in gene expression and testosterone synthesis in the testes of male rats exposed to perfluorododecanoic acid. Toxicol Sci 98(1):206-215.
Description of the critical study	Shi et al. (2007) gavaged Sprague-Dawley rats for 14 days with PFDoA. A dose of 5 mg/kg/day caused a 25% reduction in body weight and decreased serum testosterone and estradiol. There was a NOAEL of 1.0 mg/kg/day for reduced body weight.
Point of Departure	a NOAEL of 1.0 mg/kg/day (subacute study)
Human equivalent dose	No human equivalent dose was calculated. A toxicokinetic uncertainty factor of 81 was included.
Uncertainty and modifying factors	A total uncertainty factor of 81,000:

	a toxicokinetic animal to human data-derived extrapolation factor of 81[A] a toxicodynamic uncertainty factor of 1 a human to human variability uncertainty factor of 10 a database uncertainy factor of 10 a subacute to chronic uncertainty factor of 10 a database uncertainty factor of 1
Toxicity value	RfD of 0.000012 mg/kg/day (12 ng/kg/day)
Exposure parameters for drinking water screening level	Child body weight of 15 kg Child water ingestion rate of 0.64 L/day Exposure duration of and averaging time of 6 years Exposure frequency of 350 days/year No relative source contribution included
Drinking water screening level	Groundwater Protective Concentration Level of 290 ng/L (ppt)
A = This is based on the US EPA PFOA toxicokinetics used in their 2009 provisional PFOA health advisory (https://www.epa.gov/sites/production/files/2015-09/documents/pfoa-pfos-provisional.pdf).	

PFPeA, PFHxA, PFHpA, PFDS, PFUA, PFTrDA and PFTeDA

The Texas Commission of Environmental Quality found no toxicity data for PFPeA, PFHxA, PFHpA, PFDS, PFUA, PFTrDA and PFTeDA. They selected other PFAS RfDs as surrogates for the above PFAS. The selection was based on elimination rate information and carbon chain length (same length or longer carbon chains).

PFAS	Surrogate PFAS used for Reference Dose	Reference Dose in milligrams per kilogram per day or mg/kg/day (nanograms [ng]/kg/day)	Protective Concentration Level in nanograms per Liter (ng/L or ppt)
PFPeA	PFHxS	0.0000038 mg/kg-day (3.8 ng/kg/day)	93 ng/L (ppt)
PFHxA	PFHxS	0.0000038 mg/kg-day (3.8 ng/kg/day)	93 ng/L (ppt)
PFHpA	PFOS	0.000023 mg/kg/day (23 ng/kg/day)	560 ng/L (ppt)
PFDS	PFDoA	0.000012 mg/kg/day (12 ng/kg/day)	290 ng/L (ppt)
PFUA	PFDoA	0.000012 mg/kg/day (12 ng/kg/day)	290 ng/L (ppt)
PFTrDA[1]	PFDoA	0.000012 mg/kg/day (12 ng/kg/day)	290 ng/L (ppt)
PFTeDA[1]	PFDoA	0.000012 mg/kg/day (12 ng/kg/day)	290 ng/L (ppt)
1 = No RfD was identified for a PFAS with 13 or 14 carbons.			

Appendix 2: States that combine PFAS into one drinking water screening level

Several states used the US EPA Lifetime Health Advisory (HA) of 70 ng/L (ppt) for more than PFOA and PFOS.

Connecticut Department of Health

The Connecticut Department of Health (CT DPH) set a drinking water Action Level for private wells of 70 ng/L (ppt). Along with the US EPA recommended combination of PFOA+PFOS, CT DPH recommends that three other PFAS also be added together. These three PFAS are PFNA, PFHxS, and PFHpA.

The Connecticut Department of Public Health guidance can be found at

- https://portal.ct.gov/-/media/Departments-and-Agencies/DPH/dph/environmental_health/eoha/Groundwater_well_contamination/DrinkingWaterActionLevelPerfluorinatedAlkylSubstances-PFAS.pdf?la=en
- https://portal.ct.gov/-/media/Departments-and-Agencies/DPH/dph/environmental_health/eoha/Toxicology_Risk_Assessment/2018-uploads/Perfluoroalkyl-Substances-PFASs-in-DWHealth-Concerns.pdf?la=en

Massachusetts Department of Environmental Protection

The Massachusetts Department of Environmental Protection recommended that the US EPA Lifetime HA of 70 ng/L (ppt) be used for PFOA, PFOS, PFHxS, PFNA, and PFHpA, when present individually or in combination.

See the full description at https://www.mass.gov/files/documents/2018/06/11/orsg-pfas-20180608.pdf.

Vermont Department of Health

The Vermont Department of Health has a health advisory of 20 ng/L (ppt) for five PFAS: PFOA, PFOS, PFHxS, PFHpA, and PFNA.

The Vermont Department of Health drinking water health advisory guidance can be found at http://www.healthvermont.gov/sites/default/files/documents/pdf/ENV_DW_PFAS_HealthAdvisory.pdf.

While Minnesota has developed health-based values for drinking water for individual PFAS, they have an "Administrative Rule" that requires the risk from multiple chemicals be evaluated in groundwater.

Minnesota Department of Health

The Minnesota Department of Health recommends concurrent evaluation of multiple chemicals using an additive approach. The additive approach is the health risk index, where each chemical level in the groundwater is divided by the applicable health-based guidance value. These ratios are added together. This approach is used to evaluate similar noncancer health endpoints and carcinogens.

Additional information on the Minnesota Department of Health approach can be found at http://www.health.state.mn.us/divs/eh/risk/guidance/gw/additivity.html, http://www.health.state.mn.us/divs/eh/risk/guidance/gw/additivity.html, and https://www.revisor.mn.gov/rules/4717.7890/. .

Appendix 3. International Values for PFAS in Drinking Water

	Canada[1]	Australia[2]	Denmark[3]	Germany[4]				The Netherlands[5]	Sweden[6]	United Kingdom[7]	Italy[8]	
	Health Canada	Department of Health	Ministry of the Environment	Ministry of health				RIVM	National Food Agency	Public Health England	Working Group on Environmental Quality Standard	
	Screening Value	Health-Based Guidance Value	Health-Based Guidance	Health-Based Precautionary Value	Health-Based Value	Precautionary Action Value-Infants	Precautionary Action Value-Adults	Maximum Permissible Concentration	Maximum Tolerable Level	Public Health Guidance	Health-Based Value	Screening Value
	DW	DW	DW	DW	DW	DW	DW	SW used for drinking	DW	DW	DW	FW
	Concentrations in ng/L											
PFBS	15,000	---	---	---	---	---	---	---	90**	---	3,000	3,000
PFBA	30,000	---	---	---	---	---	---	---	---	---	7,000	7,000
PFPeA	200	---	---	---	---	---	---	---	90**	---	3,000	3,000
PFHxA	200	---	---	---	---	---	---	---	90**	---	1,000	1,000
PFHxS	600	70	---	---	---	---	---	---	90**	---	---	---
PFHpA	200	---	---	---	---	---	---	---	90**	---	---	---
PFOA	200	560	300*	100**	300**	500**	5,000**	---	90**	10,000	500	100
PFOS	600	70	100*	100**	300**	500**	5,000**	530	90**	300	---	---
PFOSA	---	---	100*	---	---	---	---	---	---	---	---	---
PFNA	200	---	---	---	---	---	---	---	---	---	---	---

[1]Health Canada. Health Canada's Drinking Water Screening Values for Perfluoroalkylated Substances (PFAS). February 2016.
[2]Australian Government Depart of Health. Health Based Guidance Values for PFAS.
[3]Danish Ministry of the Environment, Environmental Protection Agency. Perfluoroalkylated substances: PFOA, PFOS and PFOS. Evaluation of health hazards and proposal of a health based quality criterion for drinking water, soil and ground water. Environmental Project No. 1665, 2015.
[4] German Ministry of Health, Drinking Water Commission. Provisional evaluation of PFT in drinking water with the guide substances perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) as examples. July 13, 2006 revision
[5]National Institute for Public Health and the Environment (RIVM). Environmental risk limits for PFOs. Report 601714013/2010
[6]Sweden National Food Administration (NFA) 2016. Risk management of PFAA in drinking water and fish (In Swedish, sections in English at www.livsmedelsverket.se, National Food Agency Sweden website).

[7]Public Health England. PFOS and PFOA General Information. 2009.
[8]Deriving Environmental Quality Standard for PFOA and related short chain perfluorinated alkyl acids. Journal of Hazardous Materials, 323 (A), 2017, 84-89.
* = An additive approach is implemented when PFOS, PFOA and PFOSA occur in drinking water at the same time: PFOA (conc. µg/L) / 0.3 µg/L + PFOS (conc. µg/L) / 0.1 µg/L + PFOSA (conc. µg/L) /0.1 µg/L < 1
** = Summed concentration of PFAS cannot exceed value listed. PFAS to sum is determined by federal and state agencies.
--- = No value established.

Note: Table adapted from the ITRC PFAS Fact Sheet Table 4-1 and Port of Portland report by Apex (https://www.deq.state.or.us/Webdocs/Controls/Output/PdfHandler.ashx?p=5defcbb4-6644-4ad7-90ec-b90414ae30e9.pdf&s=Phase%20II%20Fire%20Training% 20Investigation%20Report.pdf)

DW= Drinking water; FW= Fresh water; SW= Surface water

Appendix 4: Summary of Reference Doses for perfluorobutane sulfonate (PFBS) and identification of drinking water screening levels

This appendix summarizes the available toxicity values, such as reference doses, for perfluorobutane sulfonate (PFBS)[93] and provides a range of drinking water screening levels calculated with those values. The purpose of this appendix is to assist with the public health evaluation of PFBS in drinking water. As such, the information contained in this appendix was critically evaluated and best professional judgment was used to select a toxicity value.

The Agency for Toxic Substances and Disease Registry (ATSDR) *Toxicological Profile for Perfluoroalkyls*, draft for public comment was released in June 2018. ATSDR included descriptions of the available studies for PFBS exposure in laboratory animals and humans. However, ATSDR did not develop any minimal risk levels for PFBS. ATSDR stated that no acute (less than 14 days of exposure) or chronic (over a year of exposure) duration laboratory animal studies for PFBS were identified. ATSDR identified four intermediate duration (more than 14-day but less than a year of exposure) laboratory animal studies, however, they noted that immunotoxicity and developmental toxicity have not been assessed for PFBS exposure. Therefore, ATSDR considered the database "inadequate for identifying a critical endpoint and evaluating dose-response relationships". For the studies evaluated by ATSDR, liver, kidney, stomach, and hematological systems were noted as targets of PFBS toxicity.[94]

Two agencies, the Minnesota Department of Health and the US Environmental Protection Agency have developed reference doses (RfDs) for PFBS.[95] The Minnesota Department of Health used their short-term[96], subchronic, and chronic RfDs in development of non-cancer health-based values (nHBVs), which are health-based screening levels for drinking water. They also discussed some of the available information on immunotoxicity and developmental toxicity from PFBS exposure in humans and laboratory animals. The US Environmental Protection Agency's provisional subchronic and chronic RfDs are currently included in the Regional Screening Levels, which are health-based screening levels for evaluation of exposure to drinking water, soil and air (note, there are no air values for PFBS).

Below is a brief description of the development of these RfDs. The RfDs are summarized in Table 1.

US Environmental Protection Agency (US EPA)

The US EPA developed the subchronic and chronic PFBS RfDs as provisional peer-reviewed toxicity values (PPRTVs). PPRTVs are toxicity values developed for use in the Superfund Program and are internally reviewed by a standing National Center for Environmental Assessment scientist panel and also by three external scientific experts. The PFBS PPRTV values were final in 2014. Additional information on

[93] PFBS is also known as Perfluorobutane sulfonic acid (PFBuS).
[94] https://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=1117&tid=237
[95] The Texas Commission of Environmental Quality also has an RfD for PFBS but it is an older RfD developed by and referenced to the Minnesota Department of Health, that has since been updated.
[96] Note, the study used by the MDH for their short-term RfD was not included in the 2018 ATSDR draft *Toxicological Profile for Perfluoroalkyls*.

these values can be found in the "Provisional Peer-Reviewed Toxicity Values for Perfluorobutane Sulfonate (CASRN 375-73-5) and Related Compound Potassium Perfluorobutane Sulfonate (CASRN 29420-49-3)".[97]

The study used by US EPA for development of their subchronic and chronic RfDs was:

- Lieder PH, SC Chang, RG York, JL Butenhoff. 2009a. Toxicological evaluation of potassium perfluorobutanesulfonate in a 90-day oral gavage study with Sprague-Dawley rats. Toxicology 255:45-52.

A 90-day rat oral gavage study was conducted with potassium PFBS (K+PFBS). Rats were dosed with K+PFBS at doses of 0, 60, 200, and 600 milligrams per kilogram per day (mg/kg/day). No treatment-related mortality, body weight, or neurological effects were noted. Chromorhinorrhea (perioral) and urine-stained abdominal fur were observed in males at 600 mg/kg/day. Red blood cell counts, hemoglobin, and hematocrit values were reduced in males receiving 200 and 600 mg/kg/day; however, there were no adverse histopathological findings in bone marrow. Total serum protein and albumin were lower in females at 600 mg/kg/day. There were no significant changes in clinical chemistry in either sex. All rats appeared normal at sacrifice. Microscopic changes were observed only at the highest dose in the stomach. These changes consisted of hyperplasia with some necrosis of the mucosa with some squamous metaplasia. These effects likely were due to a cumulative direct irritation effect resulting from oral dosing with K+PFBS. Histopathological changes were also observed in the kidneys. The changes observed were minimal-to-mild hyperplasia of the epithelial cells of the medullary and papillary tubules and the ducts in the inner medullary region. There were no corresponding changes in kidney weights. Clinical chemistry parameters related to kidney function were unchanged. These kidney findings are likely due to a response to high concentration of K+PFBS in tubules and ducts and represent a minimal-to-mild effect. Microscopic changes of an equivocal and uncertain nature were observed in the nasal mucosa and were likely attributable to the route of dosing (oral gavage). Lieder et al. (2009a) identified a NOAEL for the female rat in this study of 600 mg/kg/day (highest dose of study) and a NOAEL for the male rat of 60 mg/kg/day based on hematological effects. The US EPA identified a NOAEL of 200 mg/kg/day for both female and male rats. US EPA noted that the hematological changes in male rats were not dose-dependent and not observed in female rats.

US EPA used their Benchmark Dose Software (BMDS version 2.3) and a modeled the lower limit on a Benchmark Dose associated with a benchmark response of 10% ($BMDL_{10}$). The health endpoint selected for the modeling was the kidney hyperplasia data.[98] The $BMDL_{10}$ of 78.7 mg/kg/day was selected as a point of departure for development of subchronic and chronic provisional RfDs.

The point of departure was converted to a human equivalent dose by applying a dosimetric adjustment factor based on body weight scaling, resulting in a human equivalent dose of 18.9 mg/kg/day. See Table 1 for further discussion of the dosimetric adjustment factor.

[97] The document can be found at https://cfpub.epa.gov/ncea/pprtv/documents/PotassiumPerfluorobutaneSulfonate.pdf.

[98] The US EPA also modeled kidney hyperplasia data from the two-generational Lieder et al (2009b) study used by MDH. The $BMDL_{10}$ for that study was 26.6 mg/kg/day for F0 generation female rats and 52.4 mg/kg/day for F1 generation female rats. However, the US EPA noted that these are less reliable estimates as there is no data point near the benchmark response, which is recommended for Benchmark Dose modeling.

For the subchronic provisional RfD, the human equivalent dose was divided by a total uncertainty factor of 100. The breakdown of the uncertainty factors is listed below.

- Total uncertainty factor of 100:
    - A 3 for toxicodynamic differences in mice and humans
    - A 3 for database gap as no developmental toxicity study has been conducted
    - A 10 for human to human variability

This results in a subchronic provisional RfD of 0.2 mg/kg/day.[99]

For the chronic provisional RfD, the human equivalent dose was divided by a total uncertainty factor of 1,000. The breakdown of the uncertainty factors is listed below.

- Total uncertainty factor of 1,000:
    - A 3 for toxicodynamic differences in rats and humans
    - A 3 for database gap as no developmental toxicity study has been conducted
    - A 10 for human to human variability
    - A 10 for less than chronic duration

This results in a chronic provisional RfD of 0.02 mg/kg/day.

The US EPA included an assessment of the confidence in the study (high), the database (medium), and overall confidence in the subchronic and chronic provisional RfDs (medium). The overall confidence determined by the US EPA cannot be higher than the lowest designation of confidence in the assessment.

US EPA used the chronic provisional RfD (0.02 mg/kg/day) in the calculation for their noncancer Regional Screening Levels (RSLs) for tapwater. The noncancer tapwater RSLs are calculated for a child ingestion exposure, resulting in a PFBS RSL of 400 micrograms per Liter (µg/L or parts per billion [ppb]).[100] This is equal to 400,000 nanograms per Liter (ng/L or parts per trillion [ppt]). Note, the RSLs do not include a relative source contribution (RSC) for potential sources other than drinking water.[101]

<u>The Minnesota Department of Health (MDH)</u>

Short-term, subchronic, and chronic non-cancer health-based values (nHBVs) were developed by the MDH and published in 2017.[102] These values are drinking water levels and use non-cancer toxicity values along with drinking water exposure scenario inputs and relative source contributions. The 2017 values were an update of previous values promulgated in 2011 as Health Risk Limits.[103] MDH noted that they updated their derivation of human equivalent doses using new or updated half-life values, incorporated

[99] The US EPA also adjusted the subchronic and chronic provisional reference doses from the salt form of PFBS to the free acid. Due to the significant figures used, this adjustment caused no change to the either provisional RfD.
[100] US EPA Regional Screening Levels Resident Tapwater Table (TR=1E-06, HQ=1_ May 2018 https://semspub.epa.gov/work/HQ/197253.pdf
[101] If a relative source contribution of 20% was included in the RSLs, the screening level lower from 400 µg/L to 80 µg/L (80,000 ng/L).
[102] http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfbssummary.pdf
[103] http://www.health.state.mn.us/divs/eh/risk/guidance/gw/table.html

recently published studies for short-term value calculation, used their most recent risk assessment methodology, and rounded to one significant digit.

The study used by MDH for development of their chronic RfD was:

- Lieder PH, RG York, DC Hakes, JL Butenhoff. 2009b. A Two-Generation Oral Gavage Reproduction Study with Potassium Perfluorobutanesulfonate (K+PFBS) in Sprague Dawley Rats. Toxicology 259:33-45.
    - MDH cited the two-generation study as both Lieder et al (2009b) and York RG (2003) Oral (Gavage) Two-Generation (One Litter per Generation) Reproduction Study of Perfluorobutane Sulfonate (PFBS) in Rats. Argus Research Protocol Number 418-021.

Lieder et al. (2009b) conducted a two-generation reproductive study in Sprague-Dawley rats orally dosed with 0, 30, 100, 300, or 1000 mg/kg/day K+PFBS, with 30 rats per sex per group. Parental (F0) generation rats were treated 10 weeks prior to mating and through mating for male and female rats and through gestation and lactation for female rats. F1 generation rats were weaned and treated as described for the parental generation. F2 generation rats were only exposed to K+PFBS through placental transfer and during nursing. Parental and F1 generation rats were evaluated for fertility, including sperm parameters, measures of gestation and outcomes, and body and organ weights. Liver and kidneys from all parental (F0), F1, and F2 generation rats were examined microscopically. Reproductive tissues were examined from 10 rats per sex in the parental and F1 generations in the control and 1000 mg/kg/day groups. Enlargement of the liver cells (mild hypertrophy) and hyperplasia of kidney medullary/papillary tubular and ductular epithelial cells were observed in male parental generation rats in the 300 and 1000 mg/kg/day groups. F1 male rats treated with 300 or 1000 mg/kg/day also had liver hypertrophy, which the authors described as minimal. Kidney hyperplasia (minimal-to-moderate) was also observed in female generation rats in the 300 and 1000 mg/kg/day groups, but females did not have observable liver hypertrophy. F1 female rats treated with 300 or 1000 mg/kg/day also had kidney hyperplasia, which the authors described as minimal-to-mild. The study authors noted that the NOAEL was 100 mg/kg/day due to the effects observed in the parental and F1 generation rats. Body weight effects were noted in the F1 generation, with a NOAEL of 300 mg/kg/day. No effects on reproductive function were noted in the parental or F1 generations.

MDH estimated a $BMDL_{10}$ of 45 mg/kg/day for the epithelial hyperplasia in kidneys of F0 females from the study listed above. They then converted the $BMDL_{10}$ of 45 mg/kg/day to a human equivalent dose using toxicokinetic adjustment based on half-life of PFBS in humans (665 hours) and female Sprague-Dawley rats (1.9 hours). The half-life for female Sprague-Dawley rats used by MDH is similar to the half-lives presented in the draft ATSDR *Toxicological Profile for Perfluoroalkyls*, Table 1-1 and Table 3-5.[94] The human equivalent dose used by MDH for the chronic RfD is 0.129 mg/kg/day (45 mg/kg/day/350).

For the chronic RfD, the human equivalent dose was divided by a total uncertainty factor of 300. The breakdown of the uncertainty factors is listed below.

- Total uncertainty factor of 300:
    - A 3 for toxicodynamic differences in rats and humans
    - A 3 for database uncertainty for concerns regarding neurological effects and persistent effects observed following *in utero* only exposure
    - A 10 for human to human variability

- A 3 for less than chronic duration (the critical effect was the epithelial hyperplasia in the parental [F0] generation female rats exposed 10 weeks prior to mating and through gestation and lactation)

This results in a chronic RfD of 0.00043 mg/kg/day.[59]

MDH set the subchronic nHBV equal to the short-term nHBV as the subchronic nHBV "must be protective of short-term exposures that occur within the subchronic period".[59] Because of this the short-term RfD is described here.

The study used by MDH for development of their short-term RfD was:

- Feng, X., X Cao, S Zhao, X Wang, X Hua, L Chen, L Chen. (2017). "Exposure of Pregnant Mice to Perfluorobutanesulfonate Causes Hypothyroxinemia and Developmental Abnormalities in Female Offspring." Toxicological Sciences 155(2): 409-419.

Feng et al. (2017) treated pregnant ICR mice with 0, 50, 200, or 500 mg/kg/day K+PFBS from gestational day 1 to gestational day 20. Male offspring were not used in this experiment. Fifty female offspring (from 10 dams) had perinatal survival and growth, pubertal onset and ovarian and uterine development examined. Hormone levels (hypothalamic-pituitary-gonadal and hypothalamic- pituitary- and thyroid hormones were examined in 30 female offspring on postnatal day 1, 10 offspring on postnatal day 30, and 10 offspring on postnatal day 60. Serum PFBS was measured in offspring from 10 dams. Decreased total T3 and T4 levels were observed in mice with prenatal exposure to 200 or 500 mg/kg/day in all three postnatal groups. Total T3 and free and total T4, measured on gestational day 20, were also decreased in dams exposed to 200 and 500 mg/kg/day. Offspring postnatally treated with 200 and 500 mg/kg/day also had decreases in perinatal growth, pubertal onset, and reproductive organ development.

MDH used a NOAEL of 50 mg/kg/day from the study listed above. They then converted the NOAEL to a human equivalent dose using toxicokinetic adjustment based on half-life of PFBS in humans (665 hours) and female ICR mice (2.1 hours). The human equivalent dose used by MDH for the short-term RfD is 0.158 mg/kg/day (50 mg/kg/day/317).

For the short-term RfD, the human equivalent dose was divided by a total uncertainty factor of 100. The breakdown of the uncertainty factors is listed below.

- Total uncertainty factor of 100:
    - A 3 for toxicodynamic differences in rats and humans
    - A 3 for database uncertainty for concerns regarding neurological effects and persistent effects observed following *in utero* only exposure
    - A 10 for human to human variability

This results in a short-term RfD of 0.0016 mg/kg/day.[59]

As part of the MDH summaries on nHBVs, they reviewed the available published studies to examine the completeness of the database. MDH describes the available information from the mouse oral developmental study, including other effects which occurred at higher doses than those used as the basis of the short-term RfD (Feng et al [2017], the oral mouse developmental study). MDH also

discussed the available data on immunotoxicity after exposure to PFBS, and noted that, in a human epidemiology study on the association of 11 PFAS with immunological markers, associations with PFBS were fewer and weaker with asthma and asthma-related biomarkers than other PFAS. MDH also noted that there was uncertainty around neurotoxicity studies with PFBS. Due to this, a database uncertainty factor was included in all of MDH's PFBS RfDs[59].

MDH developed nHBVs of 2000 ng/L (2 µg/L) for chronic duration and 3000 ng/L (3 µg/L) for short-term duration. The short-term nHBV is also applied to the subchronic duration of exposure.[59]

MDH uses this equation for their nHBVs:

$$nHBV = \frac{(Reference\ Dose)x(relative\ source\ contribution)x\ (Conversion\ Factor)}{Water\ intake\ rate}$$

Along with the RfDs described above, MDH used these water ingestion rates[59]:

- Chronic: 0.044 L/kg/day (time-weighted average over a lifetime of approximately 70 years of age).
- Subchronic: 0.070 L/kg/day (time-weighted average up to 8 years of age).
- Short-term: 0.285 L/kg/day (time-weighted average of the 95th percentile for 1 up to 3 months of age).

And these relative source contributions (RSC)[59]:

- Chronic RSC = 20%
- Subchronic RSC = 20%
- Short-term RSC = 50%

MDH uses the above default RSCs for chemicals that are not highly volatile. These RSCs were selected based on a US EPA decision tree. For the short-term RSC, the 50% was selected as infants less than three months old are unlikely to have a significant known or potential source of exposure other than drinking water.[104]

The Conversion factor is 1000 µg/mg.

ATSDR develops Environmental Media Evaluation Guides (EMEGs) for drinking water for both adults and children using the below body weights and water intake rates.

- Adult body weight of 80 kilograms (kg)
- Adult water intake rate of 3.092 Liters per day (L/day)
- Child, birth to one year old, body weight of 7.8 kg
- Child, birth to one year old, water ingestion rate of 1.113 L/day

ATSDR uses the below equation. Note: an RSC is not included:

$$Environmental\ Media\ Evaluation\ Guide = \frac{Minimal\ Risk\ Level\ x\ body\ weight}{water\ intake\ rate}$$

[104] http://www.health.state.mn.us/divs/eh/risk/rules/water/hrlsonar08.pdf

ATSDR develops EMEGs using their Minimal Risk Levels, however, the equation is the same if an RfD was used in place of a MRL.

The Michigan Department of Environmental Quality (MDEQ) also calculates drinking water values as part of the Part 201 program. The residential drinking water value equation for noncarcinogenic effects includes an age-adjusted water intake rate and also an RSC of 20%.

Draft proposed residential drinking water value equation for noncarcinogenic effects using an age-adjusted water intake rate to account for exposure to both children and adults:

$$DWV_{nc} = \frac{THQ \times AT_{res} \times RfD \times RSC_{w} \times CF}{EF_{res} \times IF_{dw}}$$

where,

DWV_{nc}	(Drinking water value)	=	chemical-specific, µg/L or ppb
THQ	(Target hazard quotient)	=	1
AT_{res}	(Averaging time)	=	11,680 days
RfD	(Oral reference dose)	=	chemical-specific, mg/kg-day
RSC_{w}	(Relative source contribution)	=	chemical-specific or 0.2
CF	(Conversion factor)	=	1,000 µg/mg
EF_{res}	(Exposure frequency)	=	350 days/year
IF_{dw}	(Age-adjusted drinking water ingestion factor)	=	1.1 L-year/kg-day

The MDEQ also has two equations for calculating drinking water values for chemicals with developmental effects. The one listed below is for exposure to a child. The other equation is for exposure to a pregnant woman. An RSC of 20% is also used in these equations.

The lowest drinking water value from the two developmental equations and the equation using an age-adjusted water intake rate is presented in Table 2. The equation for exposure to a pregnant woman is not presented here as it does not result in the lowest drinking water value. The developmental equation for child exposure results in a lower value and is protective for a pregnant woman's exposure.

Draft proposed residential drinking water equation for developmental noncarcinogenic effects for a child's exposure:

$$DWV_{dev} = \frac{THQ \times AT_{child} \times RfD_{dev} \times BW_{child} \times RSC_{w} \times CF}{ED_{child} \times EF_{res} \times IR_{dw,child}}$$

where,

DWV_{dev}	(Drinking water value)	=	chemical-specific, µg/L or ppb
THQ	(Target hazard quotient)	=	1
AT_{child}	(Averaging time)	=	2,190 days
RfD_{dev}	(Oral reference dose)	=	chemical-specific, mg/kg-day
BW_{child}	(Body weight)	=	15 kg
RSC_w	(Relative source contribution)	=	0.2 or chemical-specific
CF	(Conversion factor)	=	1,000 µg/mg
ED_{child}	(Exposure duration)	=	6 years
EF_{res}	(Exposure frequency)	=	350 days/year
$IR_{dw, child}$	(Drinking water ingestion rate)	=	0.78 L/day

Table 2 presents the range of drinking water screening levels calculated from the equations provided by MDH, ATSDR, and MDEQ. The drinking water screening levels calculated using chronic RfDs range from 1 ppb (1,000 ppt) to 60 ppb (60,000 ppt).

Table 2: Drinking water screening levels calculated using Minnesota Department of Health (MDH), Agency for Toxic Substances and Disease Registry (ATSDR), and Michigan Department of Environmental Quality (MDEQ) equations and exposure parameters.

Reference Dose	MDH equation	ATSDR equation for an Adult	ATSDR equation for a Child	MDEQ equations[1]
MDH chronic RfD of 0.00043 mg/kg/day	2.0 ppb (2,000 ppt)	11 ppb (11,000 ppt)	3 ppb (3,000 ppt)	2.6 ppb (2,600 ppt)[2]
MDH short-term RfD of 0.0016 mg/kg/day	3.0 ppb (3,000 ppt)	41 ppb (41,000 ppt)	11 ppb (11,000 ppt)	6.4 ppb (6,400 ppb) [3]
US EPA chronic pRfD (with MDH toxicokinetic adjustment) of 0.00023 mg/kg/day	1 ppb (1,000 ppt)	6 ppb (6,000 ppt)	1.6 ppb (1,600 ppt)	1.4 ppb (1,400 ppt) [2]
US EPA's subchronic pRfD (with MDH toxicokinetic adjustment) of 0.0023 mg/kg/day	7 ppb (7,000 ppt)	60 ppb (60,000 ppt)	16 ppb (16,000 ppt)	14 ppb (14,000 ppb)[2]

1 = Note, PFBS has not been evaluated by MDEQ.
2 = Draft proposed residential drinking water value equation for noncarcinogenic effects using an age-adjusted water intake rate to account for exposure to both children and adults
3 = Draft proposed residential drinking water equation for developmental noncarcinogenic effects for a child's exposure

Table 4-1: Comparison of the US EPA and MDH reference doses.

	US EPA[1] Subchronic and chronic	Minnesota Department of Health Chronic RfD for nHBV development[2]	Minnesota Department of Health Short-term RfD for nHBV development[2]
Critical study	Lieder PH, SC Chang, RG York, JL Butenhoff. 2009a. Toxicological evaluation of potassium perfluorobutanesulfonate in a 90-day oral gavage study with Sprague-Dawley rats. Toxicology 255:45-52.	Lieder PH, RG York, DC Hakes, JL Butenhoff. 2009b. A Two-Generation Oral Gavage Reproduction Study with Potassium Perfluorobutanesulfonate (K+PFBS) in Sprague Dawley Rats. Toxicology 259:33-45. York RG 2003b. Oral (Gavage) Two-Generation (One Litter per Generation) Reproduction Study of Perfluorobutane Sulfonate (PFBS) in Rats. Argus Research Protocol Number 418-021.	Feng, X., X Cao, S Zhao, X Wang, X Hua, L Chen, L Chen. 2017. Exposure of Pregnant Mice to Perfluorobutanesulfonate Causes Hypothyroxinemia and Developmental Abnormalities in Female Offspring. Toxicological Sciences 155(2): 409-419.
Point of Departure	$BMDL_{10}$ of 78.7 mg/kg/day based on increased incidence of kidney hyperplasia in females	Based on epithelial hyperplasia in the kidneys of F0 females Sprague Dawley rats, a Benchmark Dose lower limit, 10 % ($BMDL_{10}$) of 45 mg/kg/day was estimated.	
Human Equivalent Dose	18.9 mg/kg/day calculated using dosimetric adjustment factor (based on body weight scaling)[3]	0.129 mg/kg/day calculated using a dose adjustment factor (ratio of the half-life of PFBS in human versus female rat; 665 hr /1.9 hr = 350).	0.158 mg/kg-day calculated using a dose adjustment factor (ratio of the half-life of PFBS in human versus female mouse; 665 hr /2.1 hr = 317).
Uncertainty and Modifying Factors	Subchronic: 100 (3 for animal to human toxicodynamic differences, 10 for human to human variability, and 3 for a database gap) Chronic: 1000 (3 for animal to human toxicodynamic differences, 10 for human to human variability, 3 for a database gap, and 10 for use of a subchronic study for the chronic duration)	300 (3 for animal to human differences, 10 for human to human variability, and 3 for database uncertainty and 3 for use of a subchronic study for the chronic duration)	100 (3 for animal to human differences, 10 for human to human variability, and 3 for database uncertainty)
Toxicity Value	Calculated using MDH toxicokinetic adjustment: Subchronic provisional RfD: 2.3 µg/kg/day (0.0023 mg/kg/day)[3] Chronic provisional RfD: 0.23 µg/kg/day (0.00023 mg/kg/day)[3]	Chronic RfD: 0.43 µg/kg/day (0.00043 mg/kg/day).	Short-term RfD: 1.6 µg/kg/day (0.0016 mg/kg/day)
1 = Additional detail on these RfDs can be found at https://cfpub.epa.gov/ncea/pprtv/documents/PotassiumPerfluorobutaneSulfonate.pdf. 2 = Additional detail on these RfDs can be found at http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfbssummary.pdf. 3 = If the $BMDL_{10}$ of 78.7 mg/kg/day was divided by the toxicokinetic dose adjustment factor that MDH used (350), the resulting human equivalent dose would be 0.225 mg/kg/day. This would result in a subchronic RfD of 2.3 µg/kg/day (0.0023 mg/kg/day = 0.225/100) and a chronic RfD of 0.23 µg/kg/day (0.00023 mg/kg/day = 0.225/1000) using the uncertainty factors selected by the US EPA. These possible RfDs are very similar to the ones used by MDH.		

Appendix 5: Health-based values for certain PFAS chemicals by USEPA and different state agencies

Federal/State Agencies	PFAS chemicals	Drinking water health-based values	RfD	Points of Departure and Uncertainty factors (UFs)	Water Ingestion rates (IR) and Relative Source Contribution (RSC)
Agency for Toxic Substance and Disease Registry	PFOA	Intermediate EMEGs: Adult – 78 ng/L (ppt) Child – 21 ng/L (ppt)	Draft oral intermediate Minimal Risk Level of 3 ng/kg/day	LOAEL estimated average serum concentration of 8.29 mg/L (human equivalent dose of 0.000821 mg/kg/day) Total UF = 300 (human variability = 10; animal to human = 3; LOAEL to NOAEL = 10)	Environmental Media Evaluation Guides (EMEGs) for drinking water: Adult body weight of 80 kg and water ingestion rate of 3.092 L/day Child body weight of 7.8 kg and water ingestion rate of 1.113 L/day No RSC included
Agency for Toxic Substance and Disease Registry	PFOS	Intermediate EMEGs: Adult – 52 ng/L (ppt) Child – 14 ng/L (ppt)	Draft oral intermediate Minimal Risk Level of 2 ng/kg/day	NOAEL estimated average serum concentration of 7.43 mg/L (human equivalent dose of 0.000515 mg/kg/day) Total UF = 30 (human variability = 10; animal to human = 3) A modifying factor of 10 for concern that immunotoxicity may be more sensitive than developmental toxicity	Environmental Media Evaluation Guides (EMEGs) for drinking water: Adult body weight of 80 kg and water ingestion rate of 3.092 L/day Child body weight of 7.8 kg and water ingestion rate of 1.113 L/day No RSC included
Agency for Toxic Substance and Disease Registry	PFNA	Intermediate EMEGs: Adult – 78 ng/L (ppt) Child – 21 ng/L (ppt)	Draft oral intermediate Minimal Risk Level of 3 ng/kg/day	NOAEL estimated average serum concentration of 8.91 µg/mL (human equivalent dose of 0.001 mg/kg/day) Total UF = 30 (human variability = 10; animal to human = 3 A modifying factor of 10 for database deficiencies was used.	Environmental Media Evaluation Guides (EMEGs) for drinking water: Adult body weight of 80 kg and water ingestion rate of 3.092 L/day Child body weight of 7.8 kg and water ingestion rate of 1.113 L/day No RSC included
Agency for Toxic Substance and Disease Registry	PFHxS	Intermediate EMEGs: Adult – 520 ng/L (ppt) Child – 140 ng/L (ppt)	Draft oral intermediate Minimal Risk Level of 20 ng/kg/day	NOAEL of 1 mg/kg/day Total UF = 30 (human variability = 10; animal to human = 3) A modifying factor of 10 for database limitations was used.	Environmental Media Evaluation Guides (EMEGs) for drinking water: Adult body weight of 80 kg and water ingestion rate of 3.092 L/day Child body weight of 7.8 kg and water ingestion rate of 1.113 L/day No RSC included
Alaska Department of Environmental Conservation	PFOS and/or PFOA	400 ng/L	US EPA	US EPA	USEPA ingestion rate A RSC of 100%
Alaska Department of Health and Human Services	PFOS and/or PFOA	70 ng/L (recommendation)	US EPA	US EPA	USEPA

Federal/State Agencies	PFAS chemicals	Drinking water health-based values	RfD	Points of Departure and Uncertainty factors (UFs)	Water Ingestion rates (IR) and Relative Source Contribution (RSC)
Connecticut Department of Public Health	PFOA, PFOS, PFHxS, PFNA and PFHpA (individual or sum)	70 ng/L	US EPA	US EPA	USEPA ingestion rate and RSC. Also applies default bathing/showering advice (greater than 3x the LTHA recommend no bathing/showering).
Massachusetts Office of Research and Standards	PFOS PFOA PFHxS PFNA PFHpA (combined)	70 ng/L (combined) Similarities in molecular structure and available toxicological data for PFHxS, PFNA and PFHpA led to their inclusion (additive) in the Lifetime HA	USEPA PFOA and PFOS	USEPA PFOA and PFOS	USEPA PFOA and PFOS
Minnesota Department of Health	PFOA	Short-term, Sub chronic, and Chronic: 35 ng/L	18 ng/kg/day	LOAEL PFOA serum level in mice = 38 mg/L (corresponds to a Human Equivalent Dose of 5300 ng/kg/day). Total UF = 300 (human variability = 10; animal to human = 3; LOAEL to NOAEL = 3; database uncertainty = 3).	95th percentile from breastfed infant exposure scenario (breastfed for 12 months, followed by drinking contaminated water throughout life [consumers only]) for the health-based value (formula-fed infants' exposure was also considered [consumers only]). RSC of 50%
Minnesota Department of Health	PFOS	Short-term, Sub chronic, and Chronic: 27 ng/L	5.1 ng/kg/day	NOAEL PFOS rat serum level = 6.26 mg/L (corresponds to human equivalent dose of 510 ng/kg/day). Total UF = 100 (human variability = 10; animal to human = 3; database uncertainty = 3).	95th percentile from breastfed infant exposure scenario (breastfed for 12 months, followed by drinking contaminated water throughout life [consumers only]) for the health-based value (formula-fed infants' exposure was also considered [consumers only]). RSC of 50%
Minnesota Department of Health	PFHxS	Not derived, recommend using the health-based values for PFOS	Not derived	Not derived	

Federal/State Agencies	PFAS chemicals	Drinking water health-based values	RfD	Points of Departure and Uncertainty factors (UFs)	Water Ingestion rates (IR) and Relative Source Contribution (RSC)
Minnesota Department of Health	PFBS	Chronic: 2000 ng/L Subchronic:3000 ng/L (set to short-term value) Short-term: 3000 ng/L	Chronic: 430 ng/kg/day Subchronic:1300 ng/kg/day Short-term: 1600 ng/kg/day	Chronic: 0.129 mg/kg/day Human Equivalent Dose (Benchmark Dose lower limit, 10%). Total UF: 300 (human variability = 10; animal to human = 3; database uncertainty = 3; subchronic to chronic = 3). Subchronic: 0.129 mg/kg/day Human Equivalent Dose (Benchmark Dose lower limit, 10%). Total UF: 100 (human variability = 10; animal to human = 3; database uncertainty = 3). Short-term: 0.158 mg/kg/day Human Equivalent Dose (NOAEL). Total UF: 100 (human variability = 10; animal to human = 3; database uncertainty = 3).	Chronic water ingestion rate: 0.044 L/kg/day (time-weighted average over a lifetime of approximately 70 years of age). Subchronic water ingestion rate: 0.070 L/kg/day (time-weighted average up to 8 years of age). Short-term Water ingestion rate: 0.285 L/kg/day (time-weighted average of the 95th percentile for 1 up to 3 months of age). Chronic RSC of 20% Subchronic RSC of 20% Short-term RSC of 50%
Minnesota Department of Health	PFBA	Chronic: 7000 ng/L (set to short-term value) Subchronic: 7000 ng/L (set to short-term value) Short-term: 7000 ng/L	Chronic: 2900 ng/kg/day Subchronic: 2900 ng/kg/day Short-term: 3800 ng/kg/day	Chronic: 0.86 mg/kg-day Human Equivalent Dose (NOAEL). Total UF: 300 (human variability = 10; animal to human = 3; database uncertainty = 10). Subchronic: 0.086 mg/kg/day Human Equivalent Dose (NOAEL). Total UF: 300 (human variability = 10; animal to human = 3; database uncertainty = 10). Short-term: 0.38 mg/kg/day Human Equivalent Dose (Benchmark Dose, lower limit -1SD). Total UF: 100 (human variability = 10; animal to human = 3; database uncertainty = 3).	Chronic water ingestion rate: 0.044 L/kg/day (time-weighted average over a lifetime of approximately 70 years of age). Subchronic water ingestion rate: 0.070 L/kg/day (time-weighted average up to 8 years of age). Short-term Water ingestion rate: 0.285 L/kg/day (time-weighted average of the 95th percentile for 1 up to 3 months of age). Chronic RSC of 20% Subchronic RSC of 20% Short-term RSC of 50%
Nevada Department of Environmental Protection	PFOA	667 ng/L	US EPA	US EPA	Drinking water Ingestion rate 2.5 L/day for a 80 kg adult No RSC is included.
Nevada Department of Environmental Protection	PFOS	667 ng/L	US EPA	US EPA	Drinking water Ingestion rate 2.5 L/day for a 80 kg adult No RSC is included.No RSC is included.
Nevada Department of Environmental Protection	PFBS	667,000 ng/L	US EPA (PPRTV)	US EPA (PPRTV)	Drinking water Ingestion rate 2.5 L/day for a 80 kg adult No RSC is included.No RSC is included.

Federal/State Agencies	PFAS chemicals	Drinking water health-based values	RfD	Points of Departure and Uncertainty factors (UFs)	Water Ingestion rates (IR) and Relative Source Contribution (RSC)
New Jersey Department of Environmental Protection	PFOA	14 ng/L	2 ng/kg/day	Benchmark Dose, lower limit = 4351 ng/ml (PFOA serum level; mice). Total UF: 300 (human variability = 10; animal to human = 3; incomplete database = 10). Target human serum level = 14,500 ng/L; use 1.4 x 10-4 L/kg/day as the clearance factor to calculate an RfD.	Water ingestion rate of 2 L for adult human (70 kg) (approximately 0.03 L/kg/day). RSC = 20% Matches health-based value for a target cancer risk of 1 in a million.
New Jersey Department of Environmental Protection	PFNA	13 ng/L	4.9 ng/ml (target human serum) (drinking water level calculated using 50% RSC and ration of 200:1 between PFNA serum levels to water levels) (based on increased maternal liver weight in pregnant mice).	Benchmark Dose, lower limit = 4900 ng/ml (PFNA serum level; mice). Total UF: 1000 (human variability = 10; animal to human = 3; incomplete database = 3; duration of exposure = 10).	Serum to water ratio of 200:1, intended as a central tendency estimate RSC of 50% Adjusted based on NHANES (2011-12, 95th percentile PFNA level for participants 12 years and older).
New Jersey Department of Environmental Protection	Draft PFOS value (public comment)	13 ng/L	1.8 ng/kg/day	NOAEL = 674 ng/ml PFOS serum level in mice. Target human serum level = 22.5 ng/ml; used 8.1 x 10-5 L/kg/day as the clearance factor to calculate an RfD. Total UF: 30 (human variability = 10; animal to human = 3).	Water ingestion rate of 2 L for adult human (70 kg) (approximately 0.03 L/kg/day). RSC of 20% Lower than health-based value for a target cancer risk of 1 in a million.
North Carolina Department of Environmental Quality (formerly DENR)	PFOA	2000 ng/L in GW Interim Maximum Allowable Concentrations	NC DEP is proposing to update to the US EPA PFOA+PFOS Lifetime Health Advisory. The basis of the IMAC will not be described here.	NC DEP is proposing to update to the US EPA PFOA+PFOS Lifetime Health Advisory. The basis of the IMAC will not be described here.	NC DEP is proposing to update to the US EPA PFOA+PFOS Lifetime Health Advisory. The basis of the IMAC will not be described here.
North Carolina Department of Health and Human Services	PFOA and/or PFOS	70 ng/L	USEPA	USEPA	USEPA
North Carolina Department of Health and Human Services	GenX	140 ng/L (health goal)	0.0001 mg/kg/day	NOAEL of 0.1 mg/kg/day Total UF = 1000 (interspecies variability = 10; intraspecies variability = 10; and subchronic to chronic extrapolation = 10)	Intake rate = 1.1 L/day for a bottle-fed infant; Body Weight = 7.8 kg (bottle-fed infant) Relative Source Contribution of 20%

Federal/State Agencies	PFAS chemicals	Drinking water health-based values	RfD	Points of Departure and Uncertainty factors (UFs)	Water Ingestion rates (IR) and Relative Source Contribution (RSC)
Texas Commission of Environmental Quality (TCEQ)	PFBA	71,000 ng/L	2900 ng/kg/day	NOAEL: 6.9 mg/kg/day Total UF = 2,400 (toxicokinetic animal-to-human factor = 8; toxicodynamic animal-to-human = 1; human to human = 10; subchronic to chronic = 3; database = 10)	Water IR for child: 0.64 L/day RSC: none included
Texas Commission of Environmental Quality (TCEQ)	PFBS	34,000 ng/L	1400 ng/kg/day	NOAEL: 6.9 mg/kg/day Total UF =42,600 (toxicokinetic animal-to-human factor = 142; toxicodynamic animal-to-human = 1; human to human = 10; subchronic to chronic = 3; database = 10)	Water IR for child: 0.64 L/day RSC: none included
Texas Commission of Environmental Quality (TCEQ)	PFHxS PFPeA PFHxA	93 ng/L	3.8 ng/kg/day No toxicity data were found for PFPeA and PFHxA. The PFHxS value was assigned as surrogate RfD.	LOAEL: 0.3 mg/kg/day Total UF =78,900 (toxicokinetic animal-to-human factor = 263; toxicodynamic animal-to-human = 1; human to human = 10; LOAEL to NOAEL = 3; database = 10)	Water IR for child: 0.64 L/day RSC: none included
Texas Commission of Environmental Quality (TCEQ)	PFOS PFHpA	560 ng/L	23 ng/kg/day No toxicity data were found for PFHpA. So, PFOS value was assigned as surrogate RfD.	LOAEL: 0.6 mg/kg/day Total UF =26,300 (toxicokinetic animal-to-human factor = 263; toxicodynamic animal-to-human = 1; human to human = 10; LOAEL to NOAEL = 10; database = 1)	Water IR for child: 0.64 L/day RSC: none included
Texas Commission of Environmental Quality (TCEQ)	PFOA	290 ng/L	12 ng/kg/day	LOAEL: 0.3 mg/kg/day Total UF =24,000 (toxicokinetic animal-to-human factor = 81; toxicodynamic animal-to-human = 1; human to human = 10; LOAEL to NOAEL = 30; database = 1)	Water IR for child: 0.64 L/day RSC: none included
Texas Commission of Environmental Quality (TCEQ)	PFOSA	290 ng/L	12 ng/kg/day RfD for PFOA was used as surrogate for PFOSA	See TCEQ PFOA description	Water IR for child: 0.64 L/day RSC: none included
Texas Commission of Environmental Quality (TCEQ)	PFNA	290 ng/L	12 ng/kg/day	NOAEL: 1 mg/kg/day Total UF =81,000 (toxicokinetic animal-to-human factor = 81; toxicodynamic animal-to-human = 1; human to human = 10; subacute to chronic = 10; database = 10)	Water IR for child: 0.64 L/day RSC: none included

Federal/State Agencies	PFAS chemicals	Drinking water health-based values	RfD	Points of Departure and Uncertainty factors (UFs)	Water Ingestion rates (IR) and Relative Source Contribution (RSC)
Texas Commission of Environmental Quality (TCEQ)	PFDeA	370 ng/L	15 ng/kg/day	NOAEL: 1.2 mg/kg/day Total UF =81,000 (toxicokinetic animal-to-human factor = 81; toxicodynamic animal-to-human = 1; human to human = 10; subacute to chronic = 10; database = 10)	Water IR for child: 0.64 L/day RSC: none included
Texas Commission of Environmental Quality (TCEQ)	PFDoA PFDS PFUA PFTrDA PFTeDA	290 ng/L	12 ng/kg/day (based on reduced body weight and decreased serum testosterone and estradiol in a subacute study on Sprague Dawley rats; Shi et al. 2007) No toxicity data were found for PFDS, PFUA, PFTrDA, PFTeDA. PFDoA RfD was assigned as surrogate RfD	NOAEL: 1 mg/kg/day Total UF =81,000 (toxicokinetic animal-to-human factor = 81; toxicodynamic animal-to-human = 1; human to human = 10; subacute to chronic = 10; database = 10)	Water IR for child: 0.64 L/day RSC: none included
US EPA	PFOA and/or PFOS	Short-term and chronic: 70 ng/L	PFOA: 20 ng/kg/day (based on reduced ossification of proximal phalanges in male and female mice and accelerated puberty in male mice). PFOS: 20 ng/kg/day (based on decreased birth weight in rats).	PFOA: 0.0053 mg/kg/day Human Equivalent Dose (PK) LOAEL Total UF: 300 (human variability = 10; animal to human = 3; LOAEL to NOAEL = 10) PFOS: 0.00051 mg/kg/day Human Equivalent Dose (PK) NOAEL Total UF: 30 (human variability = 10; animal to human = 3)	Water ingestion rate for lactating woman: 0.054 L/kg/day. RSC = 20%
Vermont Department of Health	PFOA, PFOS, PFHxS, PFHpA, and/or PFNA	20 ng/L	US EPA PFOA and PFOS	US EPA PFOA and PFOS	Water ingestion changed to an adjusted rate for the first year of life (combined direct and indirect water intake for consumers only) 95% percentile Body Weight Adjusted Water Intake Rate: 0.175 L/kg/day. RSC = 20%

Appendix 6: Additional PFAS values developed by other agencies after November 2018

Perfluorooctanoic acid (PFOA)

New Hampshire PFOA[105]

New Hampshire used hepatic changes as a health effect endpoint to determine proposed MCLs and Ambient Groundwater Quality Standards (AGQS). New Hampshire-specific blood data from highly-exposed areas were used to determine RfDs and RSCs. Treatment technology was not considered when setting the MCLs and AQQS.

Critical study	Loveless SE, Finlay C, Everds NE, et al. 2006. Comparative response of rats and mice exposed to linear/branched, linear, or branched ammonium perfluorooctanoate (APFO). Toxicology 220:203-217.
Description of critical study	Rats and mice were exposed to 0.3 to 30 mg/kg of linear/branched, linear, or branched APFO for 14 days. Lipids were reduced and relative liver weights increased in mice.
Point of departure	A NOAEL of 0.3 mg/kg/day was identified for increased liver weights in mice.
Human equivalent dose	The average serum concentration for the NOAEL (0.3 mg/kg/day) was estimated as 4.351 mg/L. This was multiplied by the clearance factor of 0.00012 L/kg/day to calculate a human equivalent dose of 0.00052 mg/kg/day (NJ DWQI 2017)[A].
Uncertainty and modifying factors	A total uncertainty factor of 100: a 10 for human variability a 3 for animal to human toxicodynamic difference a 3 for evidence of immune effects
Toxicity value	RfD of 0.0000052 mg/kg/day (5.2 ng/kg/day)
Exposure parameters for drinking water screening level	Water intake rate of 0.055 L/kg/day Relative Source Contribution of 40%
Drinking water screening level	Proposed Maximum Contaminant Level and Ambient Groundwater Quality Standard of 38 ng/L (ppt)
A= New Jersey Drinking Water Quality Institute. 2017. Health-based maximum contaminant level support document: Perfluorooctanoic acid (PFOA).	

Canada PFOA[106]

Canada used hepatic changes as a health effect endpoint to determine a maximum acceptable concentration (MAC). Canada did not use serum concentrations because they determined that human epidemiological studies were not consistent. Treatment technology considerations were used to establish the MAC.

Critical study	Perkins R, Butenhoff J, Kennedy G, Palazzolo M. 2004. 13-Week dietary toxicity study of ammonium perfluorooctanoate (APFO) in male rats. Drug Chem. Toxicology., 27:361-378.
Description of critical study	Rats were fed dietary levels of 0, 1, 10, 30, and 100 ppm (equivalent to 0, 0.06, 0.64, 1.94, and 6.5 mg/kg/day) for 13 weeks. Liver changes were observed in the 10 ppm and higher dose groups.
Point of departure	A NOAEL of 0.06 mg/kg/day was identified for liver changes.
Human equivalent dose	Chemical specific adjustment factors (clearance rate in animals divided by the clearance rate in humans) were used to calculate a human equivalent dose. A half-life of 1387 days (3.8 years) was used as part of the human clearance rate. The monkeys, mice, and average, male, and female rats calculated by Health Canada were 65, 74, 231, and 7774, respectively.
Uncertainty and modifying Factors	A total uncertainty factor of 25: a 10 for human variability a 2.5 for animal to human toxicodynamic difference
Toxicity value	Tolerable Daily Intake (TDI) of 0.00025 mg/kg/day (250 ng/kg/day)
Exposure parameters for drinking water screening level	Water ingestion rate of 0.02 L/kg/day and

[105] https://www.des.nh.gov/organization/commissioner/pip/publications/documents/r-wd-19-01.pdf
[106] https://www.canada.ca/en/health-canada/programs/consultation-perfluorooctanoic-acid-pfoa-in-drinking-water/document.html

	Relative Source Contribution of 20%
Drinking water screening level	Maximum Acceptable Concentration of 200 ng/L (ppt)

Perfluorooctane sulfonate (PFOS)

New Hampshire PFOS[107]

New Hampshire used developmental as a health effect endpoint to determine MCLs and Ambient Groundwater Quality Standards (AGQS). New Hampshire-specific blood data from highly-exposed areas were used to determine RfDs and RSCs. Treatment technology was not considered when setting the MCLs and AQQS.

Critical study	Luebker DJ, Case MT, York RG, Moore JA, Hansen KJ, Butenhoff JL. 2005. Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats. Toxicology 215:126-148.
Description of critical study	Male and female rats were given 0, 0.1, 0.4, 1.6, and 3.2 mg/kg/day PFOS by oral gavage for 6 weeks prior to and during mating. Females were treated through gestation and lactation across two generations.
Point of departure	For the F1 generation, a NOAEL of 0.1 mg/kg/day and LOAEL of 0.4 mg/kg/day were identified for delayed eye opening. For the F2 generation, a NOAEL of 0.1 mg/kg/day and LOAEL of 0.4 mg/kg/day were identified based on decreased mean pup body weight.
Human equivalent dose	The average serum concentration for the NOAEL (0.1 mg/kg/day) was estimated as 6.26 mg/L. This was multiplied by a clearance factor of 0.000128 L/kg/day to calculate a human equivalent dose of 0.0008 mg/kg/day.
Uncertainty and modifying factors	A total uncertainty factor of 100: a 10 for human variability a 3 for animal to human toxicodynamic difference a 3 for concern for immune effects
Toxicity value	RfD of 0.000008 mg/kg/day (8 ng/kg/day)
Exposure parameters for drinking water screening level	Water intake rate of 0.055 L/kg/day Relative Source Contribution of 50%
Drinking water screening level	Proposed Maximum Contaminant Level and Ambient Groundwater Quality Standard of 70 ppt

Canada PFOS[108]

Canada used hepatic changes as a health effect endpoint to determine a maximum acceptable concentration (MAC). Canada did not use serum concentrations because they determined that human epidemiological studies were not consistent. Treatment technology considerations were used to establish the MAC.

Critical study	Butenhoff JL, Change SC, Olsen GW, Thomford PJ. 2012. Chronic dietary toxicity and carcinogenicity study with potassium perfluorooctanesulfonate in Sprague Dawley rats. Toxicology, 293(1-3):1-15. Health Canada. 2013. Seacat reanalysis- Statistical analysis of cynomolgus monkey data. Internal report. Health Canada, Ottawa, Ontario.
Description of critical study	Butenhoff et al. (2012) • Rats were exposed to PFOS via diet at concentrations of 0, 0.5, 2, 5, and 20 ppm for up to 104 weeks. • Increases in hepatocellular adenoma were observed in the 20 ppm treatment group. • The estimated dietary dose to cause a 10% increase in hepatic tumors is 8 ppm. Health Canada (2013) • Decreases in T3 were observed in both sexes of monkeys and decreases in T4 were observed in females.
Point of departure	A NOAEL of 0.021 mg/kg/day was identified for hepatocellular hypertrophy and increased liver weights in rats and monkeys and a NOAEL of 0.03 mg/kg/day was identified for thyroid hormone changes in monkeys (Seacat et al. 2002)[A].

[107] https://www.des.nh.gov/organization/commissioner/pip/publications/documents/r-wd-19-01.pdf
[108] https://www.canada.ca/en/health-canada/services/publications/healthy-living/guidelines-canadian-drinking-water-quality-guideline-technical-document-perfluorooctane-sulfonate/document.html

Human equivalent dose	Chemical specific adjustment factors (clearance rate in animals divided by the clearance rate in humans) were used to calculate a human equivalent dose. A half-life of 1971 days (5.4 years) was used as part of the human clearance rate. The monkeys, mice, male rats and female rats calculated by Health Canada were 19, 67, 318, and 77, respectively.
Uncertainty and modifying factors	A total uncertainty factor of 25 for hepatocellular hypertrophy: a 10 for human variability a 2.5 for animal-human toxicodynamic difference A total uncertainty factor of 75 for thyroid hormone changes: a 10 for human variability a 2.5 for animal-human toxicodynamic difference a 3 for concern for chronic thyroid effects
Toxicity value	Tolerable Daily Intake (TDI) of 0.00006 mg/kg/day for hepatocellular hypertrophy and 0.0001 mg/kg/day for thyroid hormone changes
Exposure parameters for drinking water screening level	Water ingestion rate of 0.02 L/kg/day Relative Source Contribution of 20%
Drinking water screening level	Maximum Acceptable Concentration of 600 ng/L (ppt)
A = Seacat AM, Thomford PJ, Hansen KJ, Olsen GW, Case MT, Butenhoff JL. 2002. Subchronic toxicity studies on perfluorooctanesulfonate potassium salt in cynomolgus monkeys. Toxicol. Sci. 68(1): 249-64.	

Perfluorononanoic acid (PFNA)

New Hampshire PFNA[109]

New Hampshire used hepatocellular changes as a health effect endpoint to determine MCLs and Ambient Groundwater Quality Standards (AGQS). New Hampshire-specific blood data from highly-exposed areas were used to determine RfDs and RSCs. Treatment technology was not considered when setting the MCLs and AQQS.

Critical study	Das KP, Grey BE, Rosen MB, Wood CR, Tatum-Gibbs KR, Zehr RD, Strynar MJ, Lindstrom AB, Lau C. 2015. Developmental toxicity of perfluorononanoic acid in mice. Reprod. Toxicology. 51:133-44.
Description of critical study	A group of 8-10 timed-pregnant female CD-1 mice were administered 1, 3, 5, or 10 mg/kg/day PFNA via oral gavage from gestation day (GD) 1 to 17. On GD 17, selected mice from each group were sacrificed for maternal and fetal examination, while the remaining mice were allowed to give birth. Pups were observed for postnatal survival up to PND 24 as well as growth and development up to PND 287. Decreased body weight gain, delayed eye opening, and preputial separation and vaginal opening were observed at 3 mg/kg/day.
Point of departure	A NOAEL of 1 mg/kg/day was identified for developmental effects
Human equivalent dose	The average serum concentration for the NOAEL (1 mg/kg/day) was estimated to be 4.9 mg/L. This was multiplied by a clearance factor of 0.000152 L/kg/day, resulting in a human equivalent dose of 0.00074 mg/kg/day (NJ DWQI 2018)[A].
Uncertainty and modifying Factors	A total uncertainty factor of 300: a 10 for human variability a 3 for animal to human toxicodynamic difference a 10 for limited number of studies
Toxicity value	RfD of $2.5E^{-6}$ mg/kg/day
Exposure parameters for drinking water screening level	Water intake rate of 0.055 L/kg/day Relative Source Contribution of 50%
Drinking water screening level	Proposed Maximum Contaminant Level and Ambient Groundwater Quality Standard of 23 ng/L (ppt)
A=New Jersey Drinking Water Quality Institute. 2018. Health-based Maximum Contaminant Level support. Document: Perfluorononanoic acid (PFNA).	

[109] https://www.des.nh.gov/organization/commissioner/pip/publications/documents/r-wd-19-01.pdf

Perfluorohexane sulfonic acid (PFHxS)

New Hampshire PFHxS[110]

New Hampshire used impaired reproduction as a health effect endpoint to determine MCLs and Ambient Groundwater Quality Standards (AGQS). New Hampshire-specific blood data from highly-exposed areas were used to determine RfDs and RSCs. Treatment technology was not considered when setting the MCLs and AQQS.

Critical study	Chang S, et al. 2018. Reproductive and developmental toxicity of potassium perfluorohexanesulfonate in CD-1 mice. Reproductive Toxicology. 78:150-168.
Description of critical study	3 mg/kg/day PFHxS was administered to 30/sex/group of CD-1 mice before mating for at least 42 days through gestation and lactation. F1 pups were directly dosed with PFHxS for 14 days after weaning. Live litter size decreased at 1 and 3 mg/kg/day doses. Increased liver sizes were also observed.
Point of departure	A NOAEL of 0.3 mg/kg/day was established for a reduction in litter size.
Human equivalent dose	The average serum concentration for the NOAEL (0.3 mg/kg/day) was estimated to be 27.2 mg/L. This was multiplied by a clearance factor of 0.000103 L/kg/day, resulting in a human equivalent dose of 0.0028 mg/kg/day
Uncertainty and modifying factors	A total uncertainty factor of 300: a 10 for human variability a 3 for animal to human toxicodynamic difference a 10 for limited number of studies
Toxicity value	RfD of 0.0000093 mg/kg/day (9.3 ng/kg/day)
Exposure parameters for drinking water screening level	Water intake rate of 0.055 L/kg/day Relative Source Contribution of 50%
Drinking water screening level	Proposed Maximum Contaminant Level and Ambient Groundwater Quality Standard of 85 ng/L (ppt)

[110] https://www.des.nh.gov/organization/commissioner/pip/publications/documents/r-wd-19-01.pdf

Section 9: Addendum - Matrix of Agency Screening Levels Worksheet

PFOA

	MDHHS proposed	Minnesota Department of Health (MDH)	New Jersey Department of Environmental Protection	ATSDR	US EPA
Method	MDH toxicokinetic model to evaluate an infant fed formula reconstituted with contaminated water starting at birth and continuing ingestion of contaminated water through life and an infant exclusively breast-fed for 12 months, followed by drinking contaminated water through life. The more protective exposure scenario for a breast-fed infant was selected to use as the water intake rate.	MDH toxicokinetic model to evaluate an infant fed formula reconstituted with contaminated water starting at birth and continuing ingestion of contaminated water through life and an infant exclusively breast-fed for 12 months, followed by drinking contaminated water through life. The more protective exposure scenario for a breast-fed infant was selected to use as the water intake rate.	Equation with drinking water intake rate, reference dose, body weight and relative source contribution	Equation with drinking water intake rate, MRL (toxicity value), and body weight (no relative source contribution is included).	Equation with drinking water intake rate, reference dose, body weight and relative source contribution
Drinking water amount and Relative Source Contribution	MDH Upper percentile water intake rates and body weights varying by age from less than 1 month old to over 21 years (95th percentile, consumers only) (approx. 0.045 L/kg/day); to calculate a maternal serum 0.047 L/kg/day water intake was used (Source US EPA EFH) MDHHS calculated - An RSC of 50% was included, based on national biomonitoring serum concentrations (at the time of the evaluation – 2013-2014 NHANES: ages 3-11 year and 12 years and older).	Upper percentile water intake rates and body weights varying by age from less than 1 month old to 54 years (95th percentile, consumers only) (approx. 0.045 L/kg/day); to calculate a maternal serum 0.047 L/kg/day water intake was used (Source US EPA EFH) An RSC of 50% was included, based on local and national biomonitoring serum concentrations (at the time of the evaluation – 2013-2014 NHANES ages 12 and older; MN-specific: East Metro new residents).	A water ingestion rate of 2 L (~90th percentile, EPA EFH 1990) for adult human (70 kg) (approx. 0.03 L/kg/day) and a relative source contribution (RSC) of 20% (default) were used to calculate the health based Maximum Contaminant Limit. NOTE: NJ DEP noted that there was insufficient data to develop a chemical-specific RSC for PFOA, but that the default 20% RSC may partially cover the higher PFOA exposure in infants from breastmilk or formula.	Adult body weight of 80 kg and water ingestion rate of 3.092 L/day (95th percentile water ingestion rate) (approx. 0.04 L/kg/day) Child body weight of 7.8 kg and water ingestion rate of 1.113 L/day (95th percentile water ingestion rate) (approx. 0.14 L/kg/day) (Source US EPA EFH) NOTE: No Relative Source Contribution	A water ingestion rate for lactating women (0.054 L/kg/day) and a relative source contribution (RSC) of 20% were used to calculate the lifetime HA.
Toxicity Study and health endpoint	Onishchenko N, Fischer C, Wan Ibrahim WN, Negri S, Spulber S, Cottica D, Ceccatelli S. 2011. Prenatal exposure to PFOS or PFOA alters motor function in mice in a sex-related manner. Neurotox Res. 19(3):452-61. Neurobehavioral effects (decreased number of inactive periods, altered novelty induced activity) were considered the critical effects. Koskela A, Finnilä MA, Korkalainen M, Spulber S, Koponen J, Håkansson H, Tuukkanen J, Viluksela M. 2016. Effects of developmental exposure to perfluorooctanoic acid (PFOA) on long bone morphology and bone cell differentiation. Toxicol Appl Pharmacol. 301:14-21. The critical effects considered were skeletal alteration such as bone morphology and bone cell differentiation in the femurs and tibias. For both studies: Pregnant mice were exposed throughout pregnancy, assessed offspring	Lau, C., JR Thibodeaux, RG Hanson, MG Narotsky, JM Rogers, AB Lindstrom, MJ Strynar. (2006). "Effects of Perfluorooctanoic Acid Exposure during Pregnancy in the Mouse." Toxicological Sciences 90(2): 510-518. Exposed from gestational day 1-17, assessed offspring The critical effects identified were delayed ossification, accelerated preputial separation in male offspring, a trend for decreased pup body weight, and increased maternal liver weight.	Loveless, S.E., Finlay, C., Everds, N.E., Frame, S.R., Gillies, P.J., O'Connor, J.C., Powley, C.R., Kennedy, G.L. (2006). Comparative responses of rats and mice exposed to linear/branched, linear, or branched ammonium perfluorooctanoate (APFO). Toxicology 220: 203–217. 14 day exposure in adult mice Increased relative liver weight was considered the critical effect.	Onishchenko N, Fischer C, Wan Ibrahim WN, Negri S, Spulber S, Cottica D, Ceccatelli S. 2011. Prenatal exposure to PFOS or PFOA alters motor function in mice in a sex-related manner. Neurotox Res. 19(3):452-61. Neurobehavioral effects (decreased number of inactive periods, altered novelty induced activity) were considered the critical effects. Koskela A, Finnilä MA, Korkalainen M, Spulber S, Koponen J, Håkansson H, Tuukkanen J, Viluksela M. 2016. Effects of developmental exposure to perfluorooctanoic acid (PFOA) on long bone morphology and bone cell differentiation. Toxicol Appl Pharmacol. 301:14-21. The critical effects considered were skeletal alteration such as bone morphology and bone cell differentiation in the femurs and tibias.	Lau, C., J.R. Thibodeaux, R.G. Hanson, M.G. Narotsky, J.M. Rogers, A.B. Lindstrom, and M.J. Strynar. 2006. Effects of perfluorooctanoic acid exposure during pregnancy in the mouse. *Toxicological Science* 90:510–518. Exposed from gestational day 1-17, assessed offspring The critical effects were reduced ossification of proximal phalanges (forelimb and hindlimb) in male and female pups and accelerated puberty in male pups. Maternal liver weight also significantly increased in the 1 mg/kg treatment group.
Point of departure	average serum concentration was estimated in the mice (8.29 mg/L) associated with the LOAEL	average mouse maternal serum concentration (38 mg/L) corresponding to the LOAEL	serum level of 4351 ng/L, which was the $BMDL_{10}$	average serum concentration was estimated in the mice (8.29 mg/L) associated with the LOAEL	average serum concentration for LOAEL (1 mg/kg/day) was estimated as 38 mg/L
Uncertainty and Modifying factors	A total uncertainty factor of 300: 10 for use of a LOAEL 3 for animal to human variability 10 for human variability	A total uncertainty factor of 300: 3 for LOAEL to NOAEL extrapolation 10 for human to human variability 3 for animal to human difference 3 for database deficiency	A total uncertainty factor of 300 (applied to the serum level to calculate a target human serum level of 14.5 ng/ml): 10 for human variability 3 for animal to human variability	A total uncertainty factor of 300: 10 for use of a LOAEL 3 for animal to human variability 10 for human variability	A total uncertainty factor of 300: 10 for human variability 3 for animal to human toxicodynamic difference

			10 for incomplete database due to the mammary gland effects occurring at a lower dose level		10 for LOAEL to NOAEL extrapolation
Toxicity value	a different PFOA half-life was selected in the model, so the toxicity value would not would not exactly match ATSDR's MRL: 0.000005 mg/kg/day (5 ng/kg/day) would be the value corresponding to the serum level with total uncertainty factors and pharmacokinetic parameters applied	An RfD of 0.000018 mg/kg/day (18 ng/kg/day)	An RfD of 0.000002 mg/kg/day (2 ng/kg/day)	Provisional Intermediate oral MRL of 0.000003 mg/kg/day (3 ng/kg/day)	RfD of 0.00002 mg/kg/day (20 ng/kg/day)
Drinking Water Screening Level	9 ng/L (ppt)	35 ng/L (ppt)	14 ng/L (ppt)	78 ng/L (ppt) for adults 21 ng/L (ppt) for children	70 ng/L (ppt) (individually or in combination with PFOS)

PFOS

	MDHHS proposed	Minnesota Department of Health	New Jersey Department of Environmental Protection	ATSDR	US EPA
Method	MDH toxicokinetic model to evaluate an infant fed formula reconstituted with contaminated water starting at birth and continuing ingestion of contaminated water through life and an infant exclusively breast-fed for 12 months, followed by drinking contaminated water through life. The more protective exposure scenario for a breast-fed infant was selected to use as the water intake rate.	MDH toxicokinetic model to evaluate an infant fed formula reconstituted with contaminated water starting at birth and continuing ingestion of contaminated water through life and an infant exclusively breast-fed for 12 months, followed by drinking contaminated water through life. The more protective exposure scenario for a breast-fed infant was selected to use as the water intake rate.	Equation with drinking water intake rate, reference dose, body weight and relative source contribution	Equation with drinking water intake rate, MRL (toxicity value), and body weight (no relative source contribution is included).	Equation with drinking water intake rate, reference dose, body weight and relative source contribution
Drinking water amount and Relative Source Contribution	MDH Upper percentile water intake rates and body weights varying by age from less than 1 month old to 54 years (95th percentile, consumers only) (approx. 0.045 L/kg/day); to calculate a maternal serum 0.047 L/kg/day water intake was used (Source US EPA EFH) MDHHS calculated - An RSC of 50% was included, based on national biomonitoring serum concentrations (at the time of the evaluation – 2013-2014 NHANES: ages 3-11 year and 12 years and older).	Upper percentile water intake rates and body weights varying by age from less than 1 month old to 54 years (95th percentile, consumers only) (approx. 0.045 L/kg/day); to calculate a maternal serum 0.047 L/kg/day water intake was used (Source US EPA EFH) An RSC of 50% was included, based on local and national biomonitoring serum concentrations (at the time of the evaluation – 2013-2014 NHANES ages 12 and older; MN-specific: East Metro new residents).	A water ingestion rate of 2 L (~90th percentile, EPA EFH 1990) for adult human (70 kg) (approx. 0.03 L/kg/day) and a relative source contribution (RSC) of 20% were used. NOTE: NJ DEP noted that there was insufficient data to develop a chemical-specific RSC for PFOS, but that the default 20% RSC may partially cover the higher PFOA exposure in infants from breastmilk or formula.	Adult body weight of 80 kg and water ingestion rate of 3.092 L/day (95th percentile water ingestion rate) (approx. 0.04 L/kg/day) Child body weight of 7.8 kg and water ingestion rate of 1.113 L/day (95th percentile water ingestion rate) (approx. 0.14 L/kg/day) (Source US EPA EFH) No Relative Source Contribution	A water ingestion rate for lactating women (0.054 L/kg/day) and a relative source contribution (RSC) of 20% were used to calculate the lifetime HA.
Toxicity Study and health endpoint	Luebker, D.J., M.T. Case, R.G. York, J.A. Moore, K.J. Hansen, and J.L. Butenhoff. 2005b. Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats. *Toxicology* 215:126–148. Rats were exposed 6 weeks prior to and during mating, females exposed through gestation and lactation. Delayed eye opening and decreased mean pup body weight were identified as the critical effects.	Luebker, D., MT Case, RG York, JA Moore, KJ Hansen, JL Butenhoff, (2005b). "Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats." Toxicology 215: 126-148. Rats were exposed 6 weeks prior to and during mating, females exposed through gestation and lactation. The critical effect was decreased pup body weight.	Dong GH, Zhang YH, Zheng L, Liu W, Jin YH, He QC. (2009). Chronic effects of perfluorooctanesulfonate exposure on immunotoxicity in adult male C57BL/6 mice. Arch Toxicol. 83(9):805-815. Mice were exposed for 60 days. The critical effects were suppression of plaque forming cell response and increase in liver mass.	Luebker, D.J., M.T. Case, R.G. York, J.A. Moore, K.J. Hansen, and J.L. Butenhoff. 2005b. Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats. *Toxicology* 215:126–148. Rats were exposed 6 weeks prior to and during mating, females exposed through gestation and lactation. Delayed eye opening and decreased mean pup body weight were identified as the critical effects.	Luebker, D.J., M.T. Case, R.G. York, J.A. Moore, K.J. Hansen, and J.L. Butenhoff. 2005b. Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats. *Toxicology* 215:126–148. Rats were exposed 6 weeks prior to and during mating, females exposed through gestation and lactation. The critical effect was decreased pup body weight.
Point of departure	average serum concentration (7.43 mg/L) associated with the NOAEL	serum concentration for the NOAEL for decreased pup body weight was estimated (6.26 mg/L)	serum concentration of 674 ng/L associated with the NOAEL	average serum concentration (7.43 mg/L) associated with the NOAEL	average serum concentration for NOAEL (0.1 mg/kg/day) was estimated (6.26 mg/L)
Uncertainty and Modifying factors	A total uncertainty factor and modifying factors of 300 (applied to the human equivalent dose): 3 for animal to human variability 10 for human variability A modifying factor of 10 for concern that immunotoxicity may be more sensitive than developmental toxicity	A total uncertainty factor of 100: 10 for intraspecies difference (for toxicodynamics) 3 for animal to human difference 3 for database deficiency	A total uncertainty factor of 30 (applied to derive a target human serum level of 22.5 ng/ml): 10 for human variability 3 for animal to human variability	A total uncertainty factor and modifying factors of 300 (applied to the human equivalent dose): 3 for animal to human variability 10 for human variability A modifying factor of 10 for concern that immunotoxicity may be more sensitive than developmental toxicity	A total uncertainty factor of 30: 10 for human variability 3 for animal to human variability
Toxicity value	0.000002 mg/kg/day (2 ng/kg/day)	An RfD of 0.0000051 mg/kg/day (5.1 ng/kg/day)	An RfD of 0.0000018 mg/kg day (1.8 ng/kg/day)	Provisional Intermediate Oral MRL of 0.000002 mg/kg/day (2 ng/kg/day)	an RfD of 0.00002 mg/kg/day (20 ng/kg/day)
Drinking Water Screening Level	8 ng/L (ppt)	27 ng/L (ppt)	13 ng/L (ppt)	52 ng/L (ppt) for adults 14 ng/L (ppt) for children	70 ng/L (ppt) (individually or in combination with PFOA)

PFNA

	MDHHS proposed	Minnesota Department of Health	New Jersey Department of Environmental Protection	ATSDR	US EPA
Method	MDH toxicokinetic model to evaluate an infant fed formula reconstituted with contaminated water starting at birth and continuing ingestion of contaminated water through life and an infant exclusively breast-fed for 12 months, followed by drinking contaminated water through life. The more protective exposure scenario for a breast-fed infant was selected to use as the water intake rate.	No screening level for PFNA	Converted the serum level to a water level using a 200:1 water to serum ratio	Equation with drinking water intake rate, MRL (toxicity value), and body weight (no relative source contribution is included).	No screening level for PFNA
Drinking water amount and Relative Source Contribution	MDH Upper percentile water intake rates and body weights varying by age from less than 1 month old to 54 years (95th percentile, consumers only) (approx. 0.045 L/kg/day); to calculate a maternal serum 0.047 L/kg/day water intake was used (Source US EPA EFH) MDHHS calculated - An RSC of 50% was included, based on national biomonitoring serum concentrations (at the time of the evaluation – 2013-2014 NHANES: ages 3-11 year and 12 years and older).	No screening level for PFNA	The 200:1 water to serum ration is meant to represent a central tendency estimate. A RSC of 50% was applied to the target serum level.	Adult body weight of 80 kg and water ingestion rate of 3.092 L/day (95th percentile water ingestion rate) (approx. 0.04 L/kg/day) Child body weight of 7.8 kg and water ingestion rate of 1.113 L/day (95th percentile water ingestion rate) (approx. 0.14 L/kg/day) (Source US EPA EFH) No Relative Source Contribution	No screening level for PFNA
Toxicity Study and health endpoint	Das KP, Grey BE, Rosen MB, et al. 2015. Developmental toxicity of perfluorononanoic acid in mice. *Reproductive Toxicology* 51:133-144. Exposed from gestational day 1-17 *Body weight endpoints* – Decreased body weight *Developmental endpoints* – Developmental delays in mice	No screening level for PFNA	Das, K.P., Grey, B.E., Rosen, M.B., Wood, C.R., Tatum-Gibbs, K.R., Zehr, R.D., Strynar, M.J., Lindstrom, A.B., Lau, C. (2015). Developmental toxicity of perfluorononanoic acid in mice. Reproductive Toxicology 51:133-144. Exposed from gestational day 1-17 increased in maternal liver weight	Das KP, Grey BE, Rosen MB, et al. 2015. Developmental toxicity of perfluorononanoic acid in mice. *Reproductive Toxicology* 51:133-144. Exposed from gestational day 1-17 *Body weight endpoints* – Decreased body weight *Developmental endpoints* – Developmental delays in mice	No screening level for PFNA
Point of departure	average serum concentration for NOAEL (1 mg/kg/day) was estimated (8.91 µg/mL)	No screening level for PFNA	average serum concentration of 4900 ng/L 10% increase from the mean liver weight in pregnant control mice (BMDL).	average serum concentration for NOAEL (1 mg/kg/day) was estimated (8.91 µg/mL)	No screening level for PFNA
Uncertainty and Modifying factors	A total uncertainty factor of 300: 3 for extrapolation from animals to humans with dosimetric adjustments 10 for human variability A modifying factor of 10 for database deficiencies was used.	No screening level for PFNA	A total uncertainty factor of 1000 (applied to derive a target human serum level of 4.9 ng/ml): 10 for human variability, 3 for animal to human variability and 10 for sub-chronic to chronic exposure extrapolation 3 for incomplete database	A total uncertainty factor of 300: 3 for extrapolation from animals to humans with dosimetric adjustments 10 for human variability A modifying factor of 10 for database deficiencies was used.	No screening level for PFNA
Toxicity value	0.000003 mg/kg/day (3 ng/kg/day)	No screening level for PFNA	A target human serum level of 4.9 ng/ml	Provisional Intermediate oral MRL of 0.000003 mg/kg/day (3 ng/kg/day)	No screening level for PFNA
Drinking Water Screening Level	9 ng/L (ppt)	No screening level for PFNA	13 ng/L (ppt)	78 ng/L (ppt) for adults 21 ng/L (ppt) for children	No screening level for PFNA

PFHxS

	MDHHS proposed	Minnesota Department of Health	New Jersey Department of Environmental Protection	ATSDR	US EPA
Method	MDH toxicokinetic model to evaluate an infant fed formula reconstituted with contaminated water starting at birth and continuing ingestion of contaminated water through life and an infant exclusively breast-fed for 12 months, followed by drinking contaminated water through life. The more protective exposure scenario for a breast-fed infant was selected to use as the water intake rate.	Minnesota Department of Health is currently recommending that the heath-based value for PFOS (health-based value of 27 ng/L)	No screening level for PFHxS	Equation with drinking water intake rate, MRL (toxicity value), and body weight (no relative source contribution is included).	No screening level for PFHxS
Drinking water amount and Relative Source Contribution	MDH Upper percentile water intake rates and body weights varying by age from less than 1 month old to 54 years (95th percentile, consumers only) (approx. 0.045 L/kg/day); to calculate a maternal serum 0.047 L/kg/day water intake was used (Source US EPA EFH) MDHHS calculated - An RSC of 50% was included, based on national biomonitoring serum concentrations (at the time of the evaluation – 2013-2014 NHANES: ages 3-11 year and 12 years and older).	Minnesota Department of Health is currently recommending that the heath-based value for PFOS (health-based value of 27 ng/L)	No screening level for PFHxS	Adult body weight of 80 kg and water ingestion rate of 3.092 L/day (95th percentile water ingestion rate) (approx. 0.04 L/kg/day) Child body weight of 7.8 kg and water ingestion rate of 1.113 L/day (95th percentile water ingestion rate) (approx. 0.14 L/kg/day) No Relative Source Contribution	No screening level for PFHxS
Toxicity Study and health endpoint	Butenhoff JL, Chang S, Ehresman DJ, et al. 2009a. Evaluation of potential reproductive and developmental toxicity of potassium perfluorohexanesulfonate in Sprague Dawley rats. *Reproductive Toxicology* 27:331-341. Hoberman AM, York RG. 2003. Oral (gavage) combined repeated dose toxicity study of T-7706 with the reproduction/developmental toxicity screening test. *Argus Research*. Exposure through oral gavage one time daily for 42-56 days *Hepatic endpoints* – Increased liver weight; centrilobular hepatocellular hypertrophy *Thyroid endpoints* – Hypertrophy and hyperplasia of thyroid follicular cells	Minnesota Department of Health is currently recommending that the heath-based value for PFOS (health-based value of 27 ng/L)	No screening level for PFHxS	Butenhoff JL, Chang S, Ehresman DJ, et al. 2009a. Evaluation of potential reproductive and developmental toxicity of potassium perfluorohexanesulfonate in Sprague Dawley rats. *Reproductive Toxicology* 27:331-341. Hoberman AM, York RG. 2003. Oral (gavage) combined repeated dose toxicity study of T-7706 with the reproduction/developmental toxicity screening test. *Argus Research*. Exposure through oral gavage one time daily for 42-56 days *Hepatic endpoints* – Increased liver weight; centrilobular hepatocellular hypertrophy *Thyroid endpoints* – Hypertrophy and hyperplasia of thyroid follicular cells	No screening level for PFHxS
Point of departure	average serum concentration for the NOAEL (1 mg/kg/day) was estimated (89.12 µg/mL)	Minnesota Department of Health is currently recommending that the heath-based value for PFOS (health-based value of 27 ng/L)	No screening level for PFHxS	average serum concentration for the NOAEL (1 mg/kg/day) was estimated (89.12 µg/mL)	No screening level for PFHxS
Uncertainty and Modifying factors	A total uncertainty factor of 300: 3 for extrapolation from animals to humans with dosimetric adjustments 10 for human variability A modifying factor of 10 for database limitations was used.	Minnesota Department of Health is currently recommending that the heath-based value for PFOS (health-based value of 27 ng/L)	No screening level for PFHxS	A total uncertainty factor of 300: 3 for extrapolation from animals to humans with dosimetric adjustments 10 for human variability A modifying factor of 10 for database limitations was used.	No screening level for PFHxS
Toxicity value	0.00002 mg/kg/day (20 ng/kg/day)	Minnesota Department of Health is currently recommending that the heath-based value for PFOS (health-based value of 27 ng/L)	No screening level for PFHxS	Provisional Intermediate oral MRL of 0.00002 mg/kg/day (20 ng/kg/day)	No screening level for PFHxS
Drinking Water Screening Level	84 ng/L (ppt)	27 ng/L (ppt) (recommendation using PFOS value)	No screening level for PFHxS	520 ng/L (ppt) for adults 140 ng/L (ppt) for children	No screening level for PFHxS

PFBS

	MDHHS proposed	Minnesota Department of Health	New Jersey Department of Environmental Protection	ATSDR	US EPA
Method	MDH equation with reference dose, relative source contributions, conversion factor, and water intake rate	MDH equation with reference dose, relative source contributions, conversion factor, and water intake rate	No screening level for PFBS	No screening level for PFBS	Equations using body weight, water intake rate, days of exposure for 6 years of childhood.
Drinking water amount and Relative Source Contribution	MDH values: A water ingestion rate of 0.044 L/kg/day (time-weighted average of 95th percentile over a lifetime of approximately 70 years of age) and RSC of 20% were taken into consideration to calculate the chronic health-based value. (Source US EPA EFH)	A water ingestion rate of 0.044 L/kg/day (time-weighted average 95th percentile over a lifetime of approximately 70 years of age) and RSC of 20% were taken into consideration to calculate the chronic health-based value. (Source US EPA EFH)	No screening level for PFBS	No screening level for PFBS	Regional Screening Level (RSL) for a child using a 15 kg body weight and a 0.78 L/day water intake (approx. 0.05 L/kg/day). The RSLs assume a residential 350 day exposure for 6 years for a child. No RSC is included.
Toxicity Study and health endpoint	Lieder PH, SC Chang, RG York, JL Butenhoff. 2009a. Toxicological evaluation of potassium perfluorobutanesulfonate in a 90-day oral gavage study with Sprague-Dawley rats. Toxicology 255:45-52. 90 day exposure Increased incidence of kidney hyperplasia in females was the critical effect.	Leider PH, RG York, DC Hakes, JL Butenhoff. 2009b. A Two-Generation Oral Gavage Reproduction Study with Potassium Perfluorobutanesulfonate (K+PFBS) in Sprague Dawley Rats. Toxicology 259:33-45. and York RG 2003b. Oral (Gavage) Two-Generation (One Litter per Generation) Reproduction Study of Perfluorobutane Sulfonate (PFBS) in Rats. Argus Research Protocol Number 418-021. Exposure 10 weeks prior to mating and through gestation and lactation for parental and first general rats Epithelial hyperplasia in the kidneys of F0 females Sprague Dawley rats were the critical effect.	No screening level for PFBS	No screening level for PFBS	Lieder PH, SC Chang, RG York, JL Butenhoff. 2009a. Toxicological evaluation of potassium perfluorobutanesulfonate in a 90-day oral gavage study with Sprague-Dawley rats. Toxicology 255:45-52. 90 day exposure Increased incidence of kidney hyperplasia in females was the critical effect.
Point of departure	$BMDL_{10}$ of 78.7 mg/kg-day with a dose adjustment factor (ratio of the half-life of PFBS in human versus female rat; 665 hr /1.9 hr = 350)	a Benchmark Dose lower limit, 10 % ($BMDL_{10}$) of 45 mg/kg-day was estimated	No screening level for PFBS	No screening level for PFBS	$BMDL_{10}$ of 78.7 mg/kg-day based on increased incidence of kidney hyperplasia in females
Uncertainty and Modifying factors	A total uncertainty factor of 1000: 3 for animal to human toxicodynamic differences 10 for human to human variability 3 for a database gap 10 for use of a subchronic study for the chronic duration	A total uncertainty factor of 300: 3 for animal to human differences 10 for intraspecies variability 3 for database uncertainty 3 for use of a subchronic study for the chronic duration	No screening level for PFBS	No screening level for PFBS	A total uncertainty factor of 1000: 3 for animal to human toxicodynamic differences 10 for human to human variability 3 for a database gap 10 for use of a subchronic study for the chronic duration
Toxicity value	RfD of 0.00023 mg/kg/day (230 ng/kg/day)	RfD of 0.00043 mg/kg/day (430 ng/kg/day)	No screening level for PFBS	No screening level for PFBS	Chronic provisional RfD: 0.02 mg/kg/day (20,000 ng/kg/day)
Drinking Water Screening Level	1000 ng/L (ppt)	2000 ng/L (ppt)	No screening level for PFBS	No screening level for PFBS	400,000 ng/L (ppt; 400 µg/L [ppb])

US EPA EFH = US EPA Exposure Factors Handbook

L/kg/day = liters of water per kilogram body weight per day

NJ DEP = New Jersey Department of Environmental Protection

RSC = Relative Source Contribution

lifetime HA = lifetime health advisory

MDH = Minnesota Department of Health

LOAEL = Lowest Observable Adverse Effect Level

NOAEL – No Observed Adverse Effect Level