Abbreviations

Acronym or term	Description
10:2 FtS	10:2 fluorotelomer sulfonate
4:2 FtS	4:2 fluorotelomer sulfonate
6:2 FtS	6:2 fluorotelomer sulfonate
6:2 FtS	fluorotelomer sulfonate
8:2 FtS	8:2 fluorotelomer sulfonate
8:2 FtS	8:2 fluorotelomer sulfonic acid
ASTDR	Agency for Toxic Substances and Disease Registry
BCL	Basic Comparison Levels
CL	Cleanup Level
Danish EPA	Danish Environmental Protection Agency
DCRB	Direct Contact Risk-Based concentration
DNEL	Derived no effect level
DW	Drinking water
EFSA	European Food Safety Authority
FSANZ	Food Standards Australia and New Zealand
FW	Fresh water
GCC	Generic Cleanup Criteria
GW	Groundwater
ISL	Interim Screening Level
MRL	Minimal risk level
NEMP	PFAS National Environmental Management Plan
NOAL	No observable adverse effect level
PCL	Protective Concentration Level
PFAS	Per- and polyfluoroalkyl substance(s)
PFBA	Perfluorobutanoic acid
PFBS	Perfluorobutane sulfonic acid

PFDS	Perfluorodecane sulfonic acid
PFHpA	Perfluoroheptanoic acid
PFHxA	Perfluorohexanoic acid
PFHxS	Perfluorohexane sulfonic acid
PFNA	Perfluorononanoic acid
PFOA	Perfluorooctanoic acid
PFOS	Perfluorooctane sulfonate (alternative name Perfluorooctane sulfonic acid)
PFPeA	Perfluoropentanoic acid
POD	Point of departure
PSRG	Preliminary Soil Remediation Goal
RfD	Reference dose
RSL	Regional Screening Level
RW	Recreational water
SRV	Soil Reference Value
SSV	Soil Screening Value
SW	Surface water and/or effluent
Swedish EPA	Swedish Environmental Protection Agency
TDI	Tolerable daily intake
UF	Uncertainty factor
UKCOT	United Kingdom Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
USEPA	United States Environmental Protection Agency

Perfluorooctane Sulfonate (PFOS) Toxicity Profile

What is PFOS?

Perfluorooctane Sulfonate (PFOS) contains eight carbon atoms and a sulfonate group ($C_8F_{17}SO_3$) and is a member of the per- and poly-fluorinated alkyl substances (PFAS) group (ATSDR 2015). PFAS, man-made compounds that do not occur naturally in the environment, are characterized by their fluorinated carbon chains where the hydrogen atoms have been replaced with fluorine atoms. The resulting carbon-fluorine bond ensures that PFAS are both highly resistant to being degraded or metabolized, and bio-accumulative (ATSDR 2015).

PFOS is commercially produced from perfluorooctanesulfonyl fluoride (POSF) via electrochemical fluorination. Either PFOS or PFOA can be the ultimate degradation or metabolic perfluorinated compound for a number of longer chain PFAS. PFOS, along with PFOA and PFHxS, is the most common PFAS found in the environment due to its widespread historic use and its physical-chemical characteristics. Analytical quantification of PFOS should include both branched and linear standards since PFOS occurs as both forms within the environment (USEPA 2016). Perfluoroalkyls are described as ubiquitous in the environment, having been found from the air (dust), soil, and groundwater near the facilities that use them to animals such as polar bears in the Arctic (ATSDR 2015). As mentioned above, these compounds bioaccumulate and are resistant to breakdown via biodegradation, photo oxidation, direct photolysis, and hydrolysis.

How is PFOS used?

Beginning in the 1940s, PFOS has been used as a component of perfluoroalkyls that have been widely used for many industrial applications and consumer products due to their ability to repel oil, grease, and water. PFAS have been produced as strong surfactants for the manufacturing of non-stick cookware, carpet/clothing protection treatments, paper/cardboard packing, and fire-fighting foams. In the early 2000s, the manufacturing processes utilizing PFAS started changing to either eliminate or reduce the amount of perfluoroalkyls used in their products (FSANZ 2017). The predominant exposure of PFOS to the general human population is expected to occur through exposure to cookware, clothing, furniture and food packing with less frequent exposures occurring from contaminated drinking water and contaminated fish consumption (ATSDR 2015).

Fate and Transport

PFAS compounds are environmentally persistent chemicals (EPA 2008) because environmental degradation processes lack sufficient energy to break the carbon-fluorine bonds, the strongest chemical bond (3M 2000). PFAS are resistant to biodegradation, direct photolysis, atmospheric photooxidation, and hydrolysis (OECD 2002, 2007).

The low pKa values for PFAS (carboxylic and sulfonic acids) suggests that these compounds primarily exist in the environment as anions. Volatilization is expected to be negligible because anions are not volatile. However, PFAS associated with water and soil surfaces may be transported through water volatilization or particulate distribution. PFAS strongly sorb to soils and sediment, but disperse upon contact with water, consistent with their high water solubility (ATSDR 2015).

The chemical and physical properties of PFOS are presented in Table 1.

Table 1. Chemical/physical properties of PFOS; CAS number 1763-23-1

Parameter	Value	Comment
Appearance [c]	White powder	
Molecular Weight [b]	500.03 g/mol	
Melting Point [a, b]	≥ 400°C	Potassium salt
Boiling Point [b, c]	No data [b]; 258 - 260°C [c]	FSANZ (2017) and ATSDR (2015) have reported different values
Density [b, c]	No data [b]; approximately 0.6 [c]	FSANZ (2017) and ATSDR (2015) have reported different values
Water Solubility [b]	570 mg/L	Potassium salt in pure water
Organic solvent solubility [b, c]	No data[b]; 56 mg/L[c]	FSANZ (2017) and ATSDR (2015) have reported different values
Log K_{ow} [a, b]	Not available/applicable	
K_{oc} [b, c]	No data [b]; 2.57 [c]	FSANZ (2017) and ATSDR (2015) have reported different values
pK_a [b, c]	0.14 [b]; approximately -3.3 [c]	FSANZ (2017) and ATSDR (2015) have reported different values (both are estimated)
Henry's Law Constant [a, b]	Not available/applicable	Because dissociated in environment
Vapor Pressure [b]	2.48×10^{-6} mm Hg at 20°C	Assumed to be experimental for K^+ salt
Conversion Factors [b]	1 ppm = 20.79 mg/m^3 1 mg/m^3 = 0.05 ppm	Estimated from molecular weight
Skin permeability	0.000001	Drew (2017)

a. *US EPA (2016)*

b. *ATSDR (2015)*

c. *Food Standards Australia New Zealand (FSANZ), Perfluorinated chemicals in food (2017)*

Exposure

The main routes of exposure to PFAS are most likely to be from:

- Drinking contaminated municipal water or private well water
- Eating fish caught from contaminated surface water
- Incidental ingestion of contaminated soil or dust
- Eating food packaged in PFAS-containing materials
- Using consumer products such as non-stick cookware, stain-resistant carpeting, and water-repellant clothing.

Exposures to PFAS from consumer products is usually low, relative to exposure from contaminated drinking water. Babies born to mothers exposed to PFAS can be exposed to PFAS during pregnancy and while breast feeding, but benefits of breast feeding outweigh the risks for exposure to PFAS. PFAS can be transported across the placenta. Negligible levels of PFAS can be dermally absorbed resulting from showering or bathing with water contaminated with PFAS. Because PFAS compounds tend to be in an ionized form at environmental pH, dermal absorption is expected to be poor (ATSDR 2018).

Toxicokinetics

Absorption

Studies of oral absorption of PFOS in rat indicate that greater than 95 percent of ^{14}C-PFOS was absorbed (Chang et al. 2012 and Johnson and Ober 1999, as cited in ATSDR 2015). Dermal absorption of PFOS is expected to be relatively low given its ionizable state. FSANZ (2017) presumes dermal absorption to be negligible for this reason.

PFOS has a relatively low volatility, but could be inhaled when associated with particulates. ATSDR (2015) indicates that absorption of inhaled perfluorinated compounds in humans can be inferred by observations of fluorochemical production worker biomonitoring data (i.e., elevated serum perfluorinated compound levels when compared with general worker populations). Inhalation studies in animals support that perfluorinated compounds are absorbed in the respiratory system, including studies of the PFOS-related compound, PFOA, showing dose-responsive serum levels with inhalation exposure. An acute inhalation study of PFOS in rat yielded an LC50, indicating that absorption of PFOS occurs via the inhalation route (Rusch et al. 1979 as cited in USEPA 2016).

Distribution

PFOS has a great affinity for proteins, and is readily distributed to albumin in blood serum upon absorption. The largest proportion of absorbed PFOS is distributed to the following tissues in mammalian species, including human: liver and blood, and to a lesser extent kidney. In liver, PFOS is associated with fatty acid binding proteins, which can carry fatty acids to the cell nucleus (and hence perhaps PFOS). There are species and sex differences in distribution. PFAS in maternal blood have been shown to transfer to the foetus via the placenta, and this may occur with PFOS, as well (ATSDR 2015).

Metabolism

There is little evidence of metabolism of PFOS in experimental animals (ATSDR 2015). This is not unexpected given the strength of the carbon-fluoride bonds in this chemical.

Excretion

Urinary excretion is the primary means of elimination of PFOS. PFOS is secreted into bile and thus eliminated to some extent in faeces, but much of the biliarily-secreted PFOS is retained in the body by enterohepatic cycling. Lactation is another potential mechanism of elimination in mammals, as PFOS has been measured in breast milk of rodents and humans.

There are sex and species differences in PFOS elimination. The most significant species differences are in biological half-life of PFOS, with human half-life in the order of years (4.1-8.7 years), while biological half-lives for a number of other species in the order of months. EPA (2016) indicates that human PFOS half-life estimates range from 4.1 – 8.7 years compared with 121 days (or approximately 4 months) for monkey, 48 days (or approximately 1.5 months) for rat, and 37 days (or just over a month) for mouse.

Toxicity

Human Epidemiological Studies

There is a large database of epidemiological studies of workers and populations near perfluorinated production facilities as well as a significant body of animal toxicity studies.

There is consensus among international regulatory agencies that the human epidemiological database for PFOS does not support the development of toxicity criteria for human health risk assessment. Health effects that have been proposed as associated with PFOS exposure include lower birth weight, increased serum cholesterol, and immunological effects. However, FSANZ (2017) evaluated the studies and concluded that the associations were not convincing.

FSANZ (2017) concludes that existing epidemiological data do not provide convincing evidence of an association between PFOS exposure and cancer.

Animal Studies

ATSDR (2015), USEPA (2016), and FSANZ (2017) summarize the body of animal toxicity studies of PFOS, and hepatoxicity and reproductive effects are key adverse effects observed in repeat dose toxicity testing.

There is a 2-year chronic oral cancer study of PFOS in rat (Thomford 2002, Butenhoff *et al.* 2012). As summarized in EPA (2016), while there were increased incidences of hepatic carcinoma, adenoma and thyroid tumors, there were not clear dose-response relationships in the effects. PFOS does not appear to be genotoxic, as assay results were negative for "Ames test, mammalian-microsome reverse mutation assay, an in vitro assay for chromosomal aberrations, an unscheduled DNA synthesis assay, and mouse micronucleus assay." (USEPA 2016).

Health Based Guidance Values and Regulatory Values

Table 2 provides a summary of the health-based guideline values (HBGV) presented in FSANZ (2017) that are derived from key toxicity studies of PFOS.

Table 2: Health-based guideline values PFOS

Regulatory Agency	HBGV (TDI)	POD	Critical Effect	Species	UF	Reference
FSANZ (2017)	TDI = 20 ng/kg bw/day	0.0006 mg/kg bw/day	Reproductive Toxicity	Rat	30	Luebker *et al.* 2005
ASTDR (2015)	MRL = 30 ng/kg bw/day	0.00252 mg/kg bw/day	Hepatotoxicity	Monkey	30	Seacat *et al.* 2002
Danish EPA (2015)	TDI = 30 ng/kg bw/day	0.033mg/kg bw/day	Hepatotoxicity	Rat	90	Thomford 2002; Butenhoff *et al.* 2012
EFSA (2008)	TDI = 150 ng/kg bw/day	0.03 mg/kg bw/day	Serum lipid & Thyroid	Monkey	200	Seacat *et al.* 2002
Swedish EPA (2012)	DNEL = 162 ng/mL serum	4040 ng/mL serum	Hepatotoxicity	Rat	150	Thomford 2002; Butenhoff *et al.* 2012
	DNEL = 196 ng/mL serum	4900 ng/mL serum	Reproductive Toxicity	Mouse	150	Luebker *et al.* 2005
	DNEL = 0.12 ng/mL serum	17.8 ng/mL serum	Immunotoxicity	Mouse	150	Peden-Adams *et al.* 2008
UKCOT (2006)	TDI = 300 ng/kg bw/day	0.03 mg/kg bw/day	Thyroid	Monkey	100	Seacat *et al.* 2002
USEPA (2016)	RfD = 20 ng/kg bw/day	0.00051 mg/kg-bw/day	Reproductive Toxicity	Rat	30	Luebker *et al.* 2005

International regulatory criteria for PFOS in water and soil are provided in Tables 3 and 4, respectively

Table 3: PFOS Regulatory Criteria Summary (Water)

Location	Year	Standard/ Guidance	Type	Foot-note	PFOS Screening Levels (µg/L)
Australia	2017	Health-based	Drinking water	e	0.07
	2017	Health-based	Recreational water	e	0.7
Canada	2016	Screening Value	Drinking water	-	0.6
Denmark	2015	Health-based	Drinking water/Groundwater	f	0.1
Germany	2006	Health-based	Drinking water	-	0.3
	-	-	Drinking water	g	0.1
Italy	2017	Health-based	Drinking water	-	-
	2017	Screening Value	Freshwater	h	-
Netherlands	2011	Health-based	Drinking water	-	0.53
	2011	Administrative	Drinking water	-	0.0053
Sweden	2014	Health-based	Drinking water	-	0.09
	2014	Administrative	Drinking water	i	0.09
UK	2009	Health-based	Drinking water	-	0.3
	2009	Admin. Level 1	Drinking water	-	0.3
	2009	Admin. Level 2	Drinking water	-	1.0
	2009	Admin. Level 3	Drinking water	-	9
USEPA	2016	Health Advisory	Drinking water	a	0.07
	2017	Regional Screening Level[b]	Groundwater	b	0.4
Alaska (AK)	2016	Cleanup Level	Groundwater	-	0.40
Connecticut (CT)	2016	Cleanup Level	Groundwater	c	0.07
Colorado (CO)	2017	Health Advisory	Drinking water	-	0.07
Delaware (DE)	2016	Regional Level	Groundwater	a	0.07
	2016	Screening Level	Groundwater	a	0.07
Iowa (IA)	2016	Statewide Standards	Protected Groundwater	a	0.07
	-		Non-protected Groundwater	-	1
Maine (ME)	2016	Health-based Maximum Exposure Guidelines	Drinking water	a	0.07
	2016	Remedial Action Guideline	Groundwater	-	0.56
	2016	-	Recreational water	-	1.2
Michigan (MI)	2015	Human Noncancer	Surface water	-	0.011
	2016	Groundwater cleanup criteria	Groundwater	-	0.08
Minnesota (MN)	2017	Short-term Health Based Value	Groundwater	d	0.027
	2017	Subchronic Health Based Value	Groundwater	d	0.027
	2017	Chornic Health Based Value	Groundwater	d	0.027
Nevada (NV)	2015	Basic Comparison Level	Drinking water	-	0.667

Location	Year	Standard/ Guidance	Type	Foot-note	PFOS Screening Levels (µg/L)
New Hampshire (NH)	2016	Ambient Groundwater Quality Standard	Groundwater	a	0.07
New Jersey (NJ)	2015	Interim specific ground water quality criteria	Groundwater	-	-
	2017	Maximum contaminant level	Groundwater	-	-
	2017	Maximum contaminant level	Drinking water	-	-
	2017	Maximum contaminant level	Drinking water	-	-
North Carolina (NC)	2006	Interim maximum allowable concentration	Groundwater	-	-
	2017	-	Drinking water	-	-
Oregon (OR)	2011	Investigation Level	Surface water	-	300
Texas (TX)	2017	Tier 1 Protective concentration level	Groundwater	-	0.56
Vermont (VT)	2016	Primary groundwater enforcement standard	Groundwater/Drinking water	a	0.02

a. Applies to the individual results for PFOA and PFOS, as well as the sum of PFOA + PFOS.

b. ERA RSLs (June 2017). Calculated by the ERA RSL calculator using EPA OW RfDs, HI of 1, residential exposure assumptions.

c. Applies to the individual results for PFOA, PFOS, PFHpA, PFNA, and PFHxS as well as the sum of concentrations of these 5 PFAS.

d. HBVs just published May 2017 and full promulgation of HRLS anticipated in 2018.

e. The Australian Government Department of Health values for PFOS/PfHxS are combined value when both are present.

f. Applies to the individual results for PFOA, PFOS, PFNA, PFBA, PFBS, PFHxS, PFHxA, PFPeA, PFHpA, PFOSA, PFDA, and 6:2 FTS as well as the sum of concentrations of these 12 PFAS.

g. The GMH administrative guidance value of 0.1 µg/L is a composite precautionary value for both PFOA and PFOS for long term exposure in drinking water.

h. Annual Average - Environmental Quality Standards. PFOA AA-EQS based on secondary poisoning of wildlife.

i. Administrative value is for the sum of seven PFAS found in drinking water: PFOS, PFOA, PFHxS, PFBS, PFHpA, PFHxA, and PFPeA. PFOS is considered to be the most toxic. Water can still be used at up to 0.9 µg/L.

Table 4: PFOS Regulatory Criteria Summary (Soil)

Location	Year	Standard/ Guidance	Type	Soil Screening Level PFOS (mg/kg)
Australia	2018	Health Based Guidance Value[c]	Human Health Screening – Residential with garden/accessible soil	0.009
			Human Health Screening – Residential with minimal opportunity for soil access	2
			Human Health Screening – Public open space	1
			Human Health Screening – Industrial /commercial	20
Canada	2017	SSV	Human Health Screening	2.1
Denmark	2015	[d]	Human Health Screening	0.4
U.S. EPA	2017	RSL	Groundwater Protection	0.000378
	2017	RSL	Human Health Screening	1.26
Alaska (AK)	2017	CL	Groundwater Protection	0.003
	2017	CL [b]	Human Health Screening	1.3
Delaware (DE)	2016	GCC	Human Health Screening	6
Michigan (MI)	2016	GCC	Groundwater Protection (Groundwater)	0.0024
	2016	GCC	Groundwater Protection (Surface Water)	0.00024
	2016	GCC	Human Health Screening	3.20
Minnesota (MN)	2016	SRV	Human Health Screening	1.70
Nevada (NV)	2017	BCL	Human Health Screening	1.56
New Hampshire (NH)	2017	DCRB	Human Health Screening	0.5
North Carolina (NC)	2016	PSRG	Groundwater Protection	-
	2016	PSRG	Human Health Screening	-
Texas (TX)	2017	PCL	Groundwater Protection (0.5-acre source)	0.05
	2017	PCL	Groundwater Protection (30-acre source)	0.025
	2017	PCL	Human Health Screening (0.5-acre source)	1.5
	2017	PCL	Human Health Screening (30-acre source)	1.5

a. EPA RSLs (June 2017). Calculated by the EPA RSL calculator using EPA OW RfDs, HI of 1, residential exposure assumptions.

b. Alaska proposed cleanup levels for Human health - most stringent value is from the "Over 40 Inch Zone".

c. Health screening level for contaminated sites (HEPA,2018). Note the screening level is for PFOS+PFHxS..

d. Applies to the individual results for PFOA, PFOS, PFNA, PFBA, PFBS, PFHxS, PFHxA, PFPxA, PFPeA, PFHpA, PFOSA, PFDA, and 6:2 FTS as well as the sum of concentrations of these 12 PFAS..

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Perfluorooctane Sulfonate (PFOA) Toxicity Profile

What is PFOA?

Perfluorooctanoic acid (PFOA) is a completely fluorinated compound with eight carbons and a carboxyl functional group ($C_8HF_{15}O_2$), and is a member of the per- and poly-fluorinated alkyl substances (PFAS) group (ATSDR 2015). PFAS, man-made compounds that do not occur naturally in the environment, are characterized by their fluorinated carbon chains where the hydrogen atoms have been replaced with fluorine atoms. The resulting carbon-fluorine bond ensures that PFAS are both highly resistant to being degraded or metabolized, and bio-accumulative, as well (ATSDR 2015).

PFOA is formed from electrochemical fluorination and telomerisation, with fluorination resulting in a variety of structural isomers including branched chain structures. As a weak acid, PFOA can exist in both the anionic and uncharged form. PFOA can be the ultimate degradation or metabolic perfluorinated compound for a number of longer chain PFAS. Along with PFOS and PFHxS, PFOA is one of the most common PFAS occurring in the environment (USEPA, 2016). Perfluoroalkyls are described as ubiquitous in the environment, having been found from the air (dust), soil, and groundwater near the facilities that use them to animals such as polar bears in the Arctic (ATSDR, 2015). As mentioned above, these compounds bioaccumulate and are resistant to breakdown via biodegradation, photo oxidation, direct photolysis, and hydrolysis.

How is PFOA used?

Beginning in the 1940s, PFOA has been used as a component of perfluoroalkyls that have been widely used for a number of industrial applications and consumer products due to their ability to repel oil, grease, and water. PFAS have been produced as strong surfactants for the manufacturing of non-stick cookware, carpet/clothing protection treatments, paper/cardboard packing, and fire-fighting foams. In the early 2000s, the manufacturing processes utilizing PFAS started changing to either eliminate or reduce the amount of perfluoroalkyls used in their products (FSANZ, 2017). The predominant exposure of PFOA to the general human population is expected to occur through exposure to cookware, clothing, furniture and food packing with less frequent exposures occurring from contaminated drinking water and contaminated fish consumption (ATSDR, 2015).

Fate and Transport

PFAS compounds are environmentally persistent chemicals (EPA 2008) because environmental degradation processes lack sufficient energy to break the carbon-fluorine bonds, the strongest chemical bond (3M 2000). PFAS are resistant to biodegradation, direct photolysis, atmospheric photooxidation, and hydrolysis (OECD 2002, 2007).

The low pKa values for PFAS (carboxylic and sulfonic acids) suggests that these compounds primarily exist in the environment as anions. Volatilization is expected to be negligible because anions are not volatile., However, it should be noted that PFOA (presumably in its un-ionized form) has a higher vapor pressure than many other PFAS. PFAS associated with water and soil surfaces may be transported through water volatilization or particulate distribution. PFAS strongly sorb to soils and sediment, but disperse upon contact with water, consistent with their high water solubility (ATSDR 2015).

The chemical and physical properties of PFOA are presented in Table 5.

Table 5. Chemical/physical properties of PFOA; CAS number 335-67-1

Parameter	Value	Comment
Appearance [c]	White to off-white powder	
Molecular Weight [b]	414.069 g/mol	
Melting Point [a, b]	54.3°C	
Boiling Point [b, c]	188°C [b]; 192.4°C [c]	FSANZ (2017) and ATSDR (2015) reported different value ranges
Density [b, c]	1.8 g/cm^3	At 20°C
Water Solubility [a, b, c]	9.5 g/L	Fresh water at 25°C
Organic solvent solubility [b]	No data	
Log K_{ow} [b, c]	Not applicable [b]; 6.30 [c]	(Estimated) in octanol-water mixture [c]; FSANZ (2017) and ATSDR (2015) reported different value ranges
K_{oc} [b, c]	17-230 [b]; 2.06-13.8 [c]	FSANZ (2017) and ATSDR (2015) reported different value ranges
pK_a [b]	3.8	Estimated
Henry's Law Constant [a, b]	Not available/applicable	Because dissociated in environment
Vapor Pressure [b]	0.017 mm Hg at 20°C; 0.962 mm Hg at 59.25°C	20°C (extrapolated); 59.25°C (measured)
Conversion Factors [b]	1 ppm = 17.21 mg/m^3 1 mg/m^3 = 0.058 ppm	Estimated from molecular weight
Skin permeability	0.000001	Fasano et al as cited in Drew (2017)

a. *US EPA (2016)*
b. *ATSDR (2015)*
c. *Food Standards Australia New Zealand (FSANZ), Perfluorinated chemicals in food (2017)*

Exposure

The main routes of exposure to PFAS are most likely to be from:

- Drinking contaminated municipal water or private well water
- Eating fish caught from contaminated surface water
- Incidental ingestion of contaminated soil or dust
- Eating food packaged in PFAS-containing materials
- Using consumer products such as non-stick cookware, stain-resistant carpeting, and water-repellant clothing.

Exposures to PFAS from consumer products is usually low, relative to exposure from contaminated drinking water. Babies born to mothers exposed to PFAS can be exposed to PFAS during pregnancy and while breast feeding, but benefits of breast feeding outweigh the risks for exposure to PFAS. PFAS can be transported across the placenta. Negligible levels of PFAS can be dermally absorbed resulting from showering or bathing with water contaminated with PFAS. Because PFAS compounds tend to be in an ionized form at environmental pH, dermal absorption is expected to be poor (ATSDR 2018).

Toxicokinetics

Absorption

Studies of oral absorption of PFOA in animals and gastrointestinal absorbance in the rat were greater than 95% (ATSDR, 2015). Absorption of PFOA after oral administration was approximately 90% in male mouse, rat, hamster and rabbit, and ranged from 61% to 88% in females of the same species (Hundley et al., 2006). Dermal absorption of PFOA is related to whether the compound is in its ionized state. *In vitro* dermal uptake studies of PFOA showed greater permeability of the compound at lower pH (below the pKa when PFOA would be in a neutral, unionized state) than at a pH at which PFOA would be in its anionic form (ATSDR 2015).

PFOA has a vapor pressure of 0.017 mmHg @ 20°C, and therefore could be inhaled as a volatile or inhaled with particles. ATSDR (2015) indicates that absorption of inhaled perfluorinated compounds in humans can be inferred by observations of fluorochemical production worker biomonitoring data (i.e., elevated serum perfluorinated compound levels when compared with general worker populations). PFOA was measured in dose-responsively increasing levels in plasma of rats following nose-only inhalation exposure of ammonium PFOA in an aerosol (Hinderliter *et al.* 2006).

Distribution

PFOA, as other perfluorinated compounds, has a great affinity for proteins and is readily distributed to albumen in blood serum upon absorption. Distribution of PFOA in a rat study showed highest concentrations in liver, blood, and the kidney. There were species differences shown in tissue distribution of PFOA in single dose study of very small numbers of rats, mice, hamsters, and rabbits (Hundley et al., 2006). In liver, PFOA has affinity for fatty acid binding proteins (FABP), but to a lesser extent than does PFOS. FSANZ (2017) notes that PFOA has a particularly high binding affinity for human serum thyroid transport hormone (TTR).

Metabolism

There is little evidence of metabolism of PFOA or any other perfluorinated compounds in experimental animals (ATSDR, 2015). This is not unexpected given the strength of the carbon-fluoride bonds in this chemical.

Excretion

Urinary excretion is the primary means of elimination of PFOA in rats. PFOA is secreted into bile and thus eliminated to some extent in faeces, but ATSDR (2015) estimates that 89% of PFOA that is secreted to bile is reabsorbed and retained in the body by enterohepatic cycling.

There were sex differences in elimination of PFOA, with female rats more rapidly eliminating the PFOA to baseline levels and male rats experiencing carryover of dosages from previous exposures (Hinderliter et al., 2006). Some female-specific elimination pathways include transplacental transfer of PFOA, lactation, menstruation, and sex hormone effects on kidney function. PFOA has been shown to cross the placental barrier, and in a human study, cord blood has been shown to have approximately 50 percent of the maternal blood concentration. Lactation is another potential mechanism of elimination in mammals, as PFOA has been measured in breast milk. It is also plausible that menstruation is another mechanism of PFOA elimination (FSANZ, 2017) as the chemical partitions to the blood. There are significant species differences in PFOA elimination, with the PFOA half-life in humans being much longer than in other species. FSANZ (2017) notes that the human half-life for PFOA ranges from 2.3 to 3.8 years, while those for monkey, rats and mice are 20.8 days, 11.5 days, and 15.6 days, respectively.

Toxicity

Human Epidemiological Studies

There is a large database of epidemiological studies of workers and populations near perfluorinated production facilities as well as a significant body of animal toxicity studies.

There is consensus among international regulatory agencies that the human epidemiological database for PFOA does not support the development of toxicity criteria for human health risk assessment. Health effects that have been proposed as associated with PFOA exposure include endocrine effects such as risks for thyroid disease and diabetes mellitus, increased serum lipid levels, and gestational effects (particularly low birthweight). However, FSANZ (2017) evaluated the studies and concluded that the associations were not unequivocal.

FSANZ (2017) also concludes that existing epidemiological data do not provide convincing evidence of an association between PFOA exposure and cancer.

Animal Studies

There is a large body of animal toxicity studies of PFOA in a range of species (e.g., rat, mouse, monkey). Key adverse effects that have been associated with PFOA exposure are hepatoxicity (increased liver weight in rodents that is a result of peroxisome proliferation, a sensitive effect in rodents), various developmental effects in rodents, and potential immunological effects (e.g., decreased thymus and spleen weights, reduced response in sheep red blood cell assay).

PFOA's chronic toxicity and carcinogenicity studies in rats (Biegel et al. 2001 and Butenhoff et al. 2012, as cited in USEPA, 2016) have shown PFOA dose responsive associations with liver adenomas, testicular mass (Leydig cell adenomas), and pancreatic acinar cell tumors. As such, USEPA (2016) considers there to be a "Suggestive Evidence of Carcinogenic Potential of PFOA in humans." IARC characterized PFOA as "possibly carcinogenic to humans (Group 2B) and considered the evidence regarding mechanisms of PFOA-associated carcinogenesis to be moderate." (as cited in USEPA, 2016)

Health Based Guidance Values and Regulatory Values

Table 6 provides a summary of the health-based guideline values (HBGV) presented in FSANZ (2017) that are derived from key toxicity studies of PFOA, and a summary of international values published by various international agencies.

Table 6: PFOA Health-based guideline values

Regulatory Agency	HBGV (TDI)	POD	Critical Effect	Species	UF	Reference
FSANZ (2017)	TDI = 160 ng/kg bw/day	0.0049 mg/kg bw/day	Developmental Toxicity	Mouse	30	Lau et al. 2006
ASTDR (2015)	MRL = 20 ng/kg/day	0.00154 mg/kg bw/day	Hepatotoxicity	Monkey	90	Butenhoff *et al.* 2002
Danish EPA (2015)	TDI = 100 ng/kg bw/day	0.003 mg/kg bw/day	Hepatotoxicity	Rat	30	Palazzolo 1993
EFSA (2008)	TDI = 1.5 µg/kg bw/day	0.3 mg/kg bw/day	Hepatotoxicity	Rodent	200	Palazzolo 1993; Perkins *et al.* 2004
Swedish EPA (2012)	DNEL = 142 ng/mL serum	7100 ng/mL serum	Hepatotoxicity	Rat	50	Perkins *et al.* 2004
	DNEL = 628 ng/mL serum	15700 ng/mL serum	Reproductive Toxicity	Mouse	25	Lau *et al.* 2006
	DNEL = 2.0 ng/mL serum	150 ng/mL serum	Immunotoxicity	Mouse	75	White *et al.* 2007, 2009, 2011
UKCOT (2006)	TDI = 1.5 µg/kg bw/day	0.3 mg/kg bw/day	Hepatotoxicity	Rodent	200	UKCOT (2006)
USEPA (2016)	RfD = 20 ng/kg bw/day	0.0053 mg/kg bw/day	Developmental Toxicity	Mouse	300	Lau et al. 2006

International regulatory criteria for PFOA in water and soil are provided in Tables 7 and 8, respectively

Table 7: PFOA Regulatory Criteria Summary (Water)

Location	Year	Standard/ Guidance	Type	Promulgated Rule (Y/N/P/R)	Footnote	PFOA Screening Levels (µg/L)
Australia	2017	Health-based	Drinking water	-	-	0.56
	2017	Health-based	Recreational water	-	-	5.60
Canada	2016	Screening Value	Drinking water	-	-	0.20
Denmark	2015	Health-based	Drinking water/ Groundwater	-	f	0.10
Germany	2006	Health-based	Drinking water	-	-	0.30
	-	-	Drinking water	-	g	0.10
Italy	2017	Health-based	Drinking water	-	-	0.50
	2017	Screening Value	Freshwater	-	h	0.10
Netherlands	2011	Health-based	Drinking water	-	-	-
	2011	Administrative	Drinking water	-	-	-
Sweden	2014	Health-based	Drinking water	-	-	-
	2014	Administrative	Drinking water	-	i	0.09
UK	2009	Health-based	Drinking water	-	-	10

Location	Year	Standard/ Guidance	Type	Promulgated Rule (Y/N/P/R)	Footnote	PFOA Screening Levels (µg/L)
	2009	Admin. Level 1	Drinking water	-	-	0.30
	2009	Admin. Level 2	Drinking water	-	-	10
	2009	Admin. Level 3	Drinking water	-	-	90
USEPA	2016	HA	Drinking water	N	a	0.07
	2017	RSL[b]	Groundwater	R	b	0.40
Alaska (AK)	2016	CL	Groundwater	Y	-	0.40
Connecticut (CT)	2016	AL	Groundwater	N	c	0.07
Colorado (CO)	2017	HA	Drinking water	N		0.07
Delaware (DE)	2016	RL	Groundwater	N	a	0.07
	2016	SL	Groundwater	N	a	0.07
Iowa (IA)	2016	Statewide Standards	Protected Groundwater	Y	a	0.07
	-		Non-protected Groundwater	Y	-	0.70
Maine (ME)	2016	Health-based MEG	Drinking water	N	a	0.07
	2016	RAG	Groundwater	N	-	0.13
	2016	-	Recreational water	N	-	0.05
Michigan (MI)	2015	HNV	Surface water	Y	-	0.42
	2016	GCC	Groundwater	P	-	0.09
Minnesota (MN)	2017	Short-term HBV	Groundwater	N	d	0.035
	2017	Subchronic HBV	Groundwater	N	d	0.035
	2017	Chornic HBV	Groundwater	N	d	0.035
Nevada (NV)	2015	BCL	Drinking water	N	-	0.667
New Hampshire (NH)	2016	AGQS	Groundwater	Y	a	0.07
New Jersey (NJ)	2015	ISGWQC	Groundwater	Y	-	-
	2017	MCL	Groundwater	P	-	-
	2017	MCL	Drinking water	P	-	-
	2017	MCL	Drinking water	Y	-	0.014
North Carolina (NC)	2006	IMAC	Groundwater	Y	-	2
	2017	-	Drinking water	N	-	-
Oregon (OR)	2011	IL	Surface water	Y	-	24
Texas (TX)	2017	Tier 1 PCL	Groundwater	Y	-	0.29
Vermont (VT)	2016	PGWES	Groundwater/ Drinking water	Y	a	0.02

Notes:

Promulgated (Yes/No/Pending/Recommended)- Values are considered promulgated Rule if they have been finalized into law or if the table of values is referenced in supporting law. Values are considered pending if either proposed into law but not yet finalized or are currently under review. Values marked as Recommended are final recommendations from an advisory board or based on available EPA calculator tool.

a. Applies to the individual results for PFOA and PFOS, as well as the sum of PFOA + PFOS.

b. ERA RSLs (June 2017). Calculated by the ERA RSL calculator using EPA OW RfDs, HI of 1, residential exposure assumptions.

c. Applies to the individual results for PFOA, PFOS, PFHpA, PFNA, and PFHxS as well as the sum of concentrations of these 5 PFAS.

d. HBVs just published May 2017 and full promulgation of HRLS anticipated in 2018.

f. Applies to the individual results for PFOA, PFOS, PFNA, PFBA, PFBS, PFHxS, PFHxA, PFPeA, PFHpA, PFOSA, PFDA, and 6:2 FTS as well as the sum of concentrations of these 12 PFAS.

g. The GMH administrative guidance value of 0.1 µg/L is a composite precautionary value for both PFOA and PFOS for long term exposure in drinking water.

h. Annual Average - Environmental Quality Standards. PFOA AA-EQS based on secondary poisoning of wildlife.

i. Administrative value is for the sum of seven PFAS found in drinking water: PFOS, PFOA, PFHxS, PFBS, PFHpA, PFHxA, and PFPeA. PFOS is considered to be the most toxic. Water can still be used at up to 0.9 µg/L.

Table 8: PFOA Regulatory Criteria Summary (Soil)

Location	Year	Standard/ Guidance	Type	Soil Screening Level PFOA (mg/kg)
Australia	2018	HHSV	Human Health Screening Value. Residential with accessible soil	0.1
			Human Health Screening Value. Residential with minimal soil access	20
			Human Health Screening Value. Public open space	10
			Human Health Screening Value. Industrial/ Commercial	50
Canada	2017	SSV	Human Health Screening	0.85
Denmark	2015	d	Human Health Screening	0.4
U.S. EPA	2017	RSL	GW Protection	0.000172
	2017	RSL	Human Health Screening	1.26
Alaska (AK)	2017	CL	GW Protection	0.0017
	2017	CL [b]	Human Health Screening	1.3
Delaware (DE)	2016	GCC	Human Health Screening	16
Michigan (MI)	2016	GCC	GW Protection (Groundwater)	0.075
	2016	GCC	GW Protection (Surface Water)	10
	2016	GCC	Human Health Screening	6
Minnesota (MN)	2016	SRV	Human Health Screening	0.33
Nevada (NV)	2017	BCL	Human Health Screening	1.56
New Hampshire (NH)	2017	DCRB	Human Health Screening	0.5
North Carolina (NC)	2016	PSRG	GW Protection	0.0081
	2016	PSRG	Human Health Screening	
Texas (TX)	2017	PCL	GW Protection (0.5-acre source)	0.003
	2017	PCL	GW Protection (30-acre source)	0.0015
	2017	PCL	Human Health Screening (0.5-acre source)	0.6
	2017	PCL	Human Health Screening (30-acre source)	0.5

Notes:

a. EPA RSLs (June 2017). Calculated by the EPA RSL calculator using EPA OW RfDs, HI of 1, residential exposure assumptions.

b. Alaska proposed cleanup levels for Human health - most stringent value is from the "Over 40 Inch Zone".

c. Interim screening level for contaminated sites.

d. Applies to the individual results for PFOA, PFOS, PFNA, PFBA, PFBS, PFHxS, PFHxA, PFPxA, PFPeA, PFHpA, PFOSA, PFDA, and 6:2 FTS as well as the sume of concentrations of these 12 PFAS.

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Perfluorohexane Sulfonic Acid (PFHxS) Toxicity Profile

What is PFHxS?

Perfluorohexane sulfonate acid (PFHxS) contains six carbons and a sulfonate group ($C_6HF_{13}O_3S$) and is a member of the per- and poly-fluorinated alkyl substances (PFAS) group (ATSDR, 2015). PFAS, man-made compounds that do not occur naturally in the environment, are characterized by their fluorinated carbon chains where the hydrogen atoms have been replaced with fluorine atoms. The resulting carbon-fluorine bond ensures that PFAS are both highly resistant to being degraded or metabolized, and bio-accumulative and toxic (ATSDR 2015).

PFHxS is formed from electrochemical fluorination and telomerisation, with fluorination resulting in a variety of structural isomers including branched chain structures. After PFOA and PFOS, PFHxS is one of the most common PFAS occurring in the environment. Perfluoroalkyls are described as ubiquitous in the environment, having been found in the air (dust), soil, and groundwater near the facilities that use them, to animals such as polar bears in the Arctic (ATSDR, 2015). As mentioned above, these compounds bioaccumulate and are resistant to breakdown via biodegradation, photooxidation, direct photolysis, and hydrolysis.

How is PFHxS used?

Beginning in the 1940s, PFHxS has been used as a component of perfluoroalkyls that have been widely used for many industrial applications and consumer products due to their ability to repel oil, grease, and water. PFAS have been produced as strong surfactants for the manufacturing of non-stick cookware, carpet/clothing protection treatments, paper/cardboard packing, and fire-fighting foams. In the early 2000s, the manufacturing processes utilizing PFAS started changing to either eliminate or reduce the amount of perfluoroalkyls used in their products (FSANZ, 2017). The predominant exposure of PFHxS to the general human population is expected to occur through exposure to cookware, clothing, furniture and food packing with less frequent exposures occurring from contaminated drinking water and contaminated fish consumption (ATSDR, 2015).

Fate and Transport

PFAS compounds are environmentally persistent chemicals (EPA 2008) because environmental degradation processes lack sufficient energy to break the carbon-fluorine bonds, the strongest chemical bond (3M 2000). PFAS are resistant to biodegradation, direct photolysis, atmospheric photooxidation, and hydrolysis (OECD 2002, 2007).

The low pKa values for PFAS (carboxylic and sulfonic acids) suggest that these compounds primarily exist in the environment as anions. Volatilization is expected to be negligible because anions are not volatile. However, PFAS associated with water and soil surfaces may be transported through water volatilization or particulate distribution. PFAS strongly sorb to soils and sediment, but disperse upon contact with water, consistent with their high water solubility (ATSDR 2015).

The chemical and physical properties of PFHxS are presented in Table 9.

Table 9. Chemical/physical properties of PFHxS; CAS number 355-46-4

Parameter	Value	Comment
Appearance [c]	White crystalline powder	
Molecular Weight [b]	400.12 g/mol	
Melting Point [b, c]	No data	
Boiling Point [c]	No data [b]; 114.7°C [c]	FSANZ (2017) and ATSDR (2015) have reported different values
Density [b, c]	No data [b]; 1.84 g/mL [c]	FSANZ (2017) and ATSDR (2015) have reported different values
Water Solubility [b, c]	No data [b]; "Slightly soluble" [c]	FSANZ (2017) and ATSDR (2015) have reported different values
Organic solvent solubility [b, c]	No data	
Log K_{ow} [a, b]	Not available/applicable	
K_{oc} [b]	No data	
pK_a [b]	0.14	Estimated
Henry's Law Constant [a, b]	Not available/applicable	Because dissociated in environment
Vapor Pressure [b]	No data	
Conversion Factors [b]	1 ppm = 16.63 mg/m^3 1 mg/m^3 = 0.06 ppm	Estimated from molecular weight

a. *US EPA (2016)*
b. *ATSDR (2015)*
c. *Food Standards Australia New Zealand (FSANZ), Perfluorinated chemicals in food (2017)*

Exposure

The main routes of exposure to PFAS are most likely to be from:

- Drinking contaminated municipal water or private well water
- Eating fish caught from contaminated surface water
- Incidental ingestion of contaminated soil or dust
- Eating food packaged in PFAS-containing materials
- Using consumer products such as non-stick cookware, stain-resistant carpeting, and water-repellant clothing.

Exposures to PFAS from consumer products is usually low, relative to exposure from contaminated drinking water. Babies born to mothers exposed to PFAS can be exposed to PFAS during pregnancy and while breast feeding, but benefits of breast feeding outweigh the risks for exposure to PFAS. PFAS can be transported across the placenta. Negligible levels of PFAS can be dermally absorbed resulting from showering or bathing with water contaminated with PFAS. Because PFAS compounds tend to be in an ionized form at environmental pH, dermal absorption is expected to be poor (ATSDR 2018).

Toxicokinetics

Absorption

Limited toxicokinetic studies have been conducted in laboratory animals or humans exposed to PFHxS. The existing studies suggest that PFHxS is readily absorbed by the oral route and that 100 percent bioavailability should be assumed (Sundström *et al*. 2012, Kim *et al.* 2016). Limited dermal absorption is expected to occur because PFHxS exists in its anionic form at environmental pH. Because PFHxS is not volatile, inhalation exposure is unlikely unless the compound is attached to particulates (FSANZ 2017). However, ATSDR (2015) indicates that absorption of inhaled perfluorinated compounds in humans can be inferred by observations of fluorochemical production worker biomonitoring data (i.e., elevated serum perfluorinated compound levels when compared with general worker populations).

Distribution

Tissue distribution has not been widely studied; however, the highest concentrations of PFHxS have been found in the liver and kidney (FSANZ 2017). PFAS cross the placenta and have also been found in breast milk at concentrations less than 10 percent of that in maternal serum (Kim *et al*. 2011). PFHxS can also cross the placenta and enter fetal circulation (ATSDR 2015).

Metabolism

PFHxS is a stable compound and, like PFOS and PFOA, does not undergo metabolic degradation (ATSDR 2015).

Excretion

There are sex and species differences in PFOS elimination. The arithmetic and geometric half-lives of serum elimination of PFHxS in humans are 8.5 years and 7.3 years, respectively (Olsen *et al*. 2007). The half-lives in monkeys are 87 to 141 days and in rats are 2 to 29 days (Sundström *et al*. 2012).

Toxicity

Human Epidemiological Studies

There is consensus among international regulatory agencies that the human epidemiological database for PFHxS does not support the development of toxicity criteria for human health risk assessment. The epidemiological studies have explored the association between PFHxS and various health endpoints, but the studies are complicated by the presence of other PFAS compounds.

ATSDR (2015) deems the number of studies examining a relationship between PFHxS serum levels and cholesterol levels insufficient to be conclusive. ATSDR (2015) also deems that studies show no relationship between PFHxS serum levels and diabetes. ATSDR (2015) notes contradicting conclusions about a significant association between PFHxS serum levels and physician-diagnosed asthma. FSANZ (2017) reports a negative association between PFAS serum levels, including PFHxS, and antibody responses to vaccinations against tetanus, diphtheria, and rubella in children.

Animal Studies

FSANZ (2017) only identified one animal toxicity study for PFHxS that would be useful for developing a health-based guideline value. Butenhoff *et al.* (2009) conducted a study with male and female rats administered PFHxS by oral gavage. A significant increase in absolute and relative liver weights was observed in male rats, but not in female rats. Histopathological changes in the liver and thyroid gland were also observed. Hematologically, there was a significant increase in albumin and significant decrease in cholesterol in male rats. There was also a statistically significant decrease in body weight gain in treated rats. Despite being a reproductive study, there were no notable reproductive effects.

Health Based Guidance Values

FSANZ (2017) provided a summary of international hazard reviews of PFHxS. The study conducted by the Swedish EPA was the only study that provided a basis for quantitatively deriving a Health Based Guidance Value (HBGV). The basis for the HBGV is the reproductive/developmental toxicity study in male and female rats conducted by Butenhoff *et al* (2009). However, there was no evidence of reproductive or developmental toxicity. The point of departure was based on hematological effects (Table 2).

While other studies on PFHxS are available from Danish EPA (2015), ATSDR (2015), and US EPA (2016a, b), general toxicological information has been deemed insufficient for the derivation of HBGVs. The HBGV derived by FSANZ for PFOS was considered to be sufficiently protective of PFHxS. On this basis, the HBGV derived for PFOS is the sum of PFOS and PFHxS where both are detected in soil or water in Australia. Internationa regulatory criteria for PFHxS in water and soil are provided in Tables 10 and 11, respectively.

Table 10: PFHxS Regulatory Criteria Summary (Water)

Location	Year	Standard/ Guidance	Type	Promulgated Rule (Y/N/P/R)	Foot-note	PFHxS Screening Levels (µg/L)
Australia	2017	Health-based	Drinking water	-	e	0.07
	2017	Health-based	Recreational water	-	e	0.70
Canada	2016	Screening Value	Drinking water	-		0.60
Denmark	2015	Health-based	Drinking water/ Groundwater	-	f	0.10
Germany	2006	Health-based	Drinking water	-	-	-
	-	-	Drinking water	-	g	-
Italy	2017	Health-based	Drinking water	-	-	-
	2017	Screening Value	Freshwater	-	h	-
Netherland	2011	Health-based	Drinking water	-	-	-
	2011	Administrative	Drinking water	-	-	-
Sweden	2014	Health-based	Drinking water	-	-	-
	2014	Administrative	Drinking water	-	i	0.09
UK	2009	Health-based	Drinking water	-	-	-
	2009	Admin. Level 1	Drinking water	-	-	-
	2009	Admin. Level 2	Drinking water	-	-	-
	2009	Admin. Level 3	Drinking water	-	-	-
USEPA	2016	HA	Drinking water	N	a	-
	2017	RSL[b]	Groundwater	R	b	-
Alaska (AK)	2016	CL	Groundwater	Y	-	-
Connecticut (CT)	2016	AL	Groundwater	N	c	-
Colorado (CO)	2017	HA	Drinking water	N	-	-
Delaware (DE)	2016	RL	Groundwater	N	a	-
	2016	SL	Groundwater	N	a	-
Iowa (IA)	2016	Statewide Standards	Protected Groundwater	Y	a	-
	-		Non-protected Groundwater	Y	-	-

Location	Year	Standard/ Guidance	Type	Promulgated Rule (Y/N/P/R)	Foot-note	PFHxS Screening Levels (µg/L)
Maine (ME)	2016	Health-based MEG	Drinking water	N	a	-
	2016	RAG	Groundwater	N	-	-
	2016		Recreational water	N	-	-
Michigan (MI)	2015	HNV	Surface water	Y	-	-
	2016	GCC	Groundwater	P	-	-
Minnesota (MN)	2017	Short-term HBV	Groundwater	N	d	-
	2017	Subchronic HBV	Groundwater	N	d	-
	2017	Chornic HBV	Groundwater	N	d	-
Nevada (NV)	2015	BCL	Drinking water	N	-	-
New Hampshire (NH)	2016	AGQS	Groundwater	Y	a	-
New Jersey (NJ)	2015	ISGWQC	Groundwater	Y	-	-
	2017	MCL	Groundwater	P	-	-
	2017	MCL	Drinking water	P	-	-
	2017	MCL	Drinking water	Y	-	-
North Carolina (NC)	2006	IMAC	Groundwater	Y	-	-
	2017	-	Drinking water	N	-	-
Oregon (OR)	2011	IL	Surface water	Y	-	-
Texas (TX)	2017	Tier 1 PCL	Groundwater	Y	-	0.093
Vermont (VT)	2016	PGWES	Groundwater/Drinking water	Y	a	-

Notes:

Promulgated (Yes/No/Pending/Recommended)- Values are considered promulgated Rule if they have been finalized into law or if the table of values is referenced in supporting law. Values are considered pending if either proposed into law but not yet finalized or are currently under review. Values marked as Recommended are final recommendations from an advisory board or based on available EPA calculator tool.

a. Applies to the individual results for PFOA and PFOS, as well as the sum of PFOA + PFOS.

b. ERA RSLs (June 2017). Calculated by the ERA RSL calculator using EPA OW RfDs, HI of 1, residential exposure assumptions.

c. Applies to the individual results for PFOA, PFOS, PFHpA, PFNA, and PFHxS as well as the sum of concentrations of these 5 PFAS.

d. HBVs just published May 2017 and full promulgation of HRLS anticipated in 2018.

e. The Australian Government Department of Health values for PFOS/PfHxS are combined value when both are present.

f. Applies to the individual results for PFOA, PFOS, PFNA, PFBA, PFBS, PFHxS, PFHxA, PFPeA, PFHpA, PFOSA, PFDA, and 6:2 FTS as well as the sum of concentrations of these 12 PFAS.

g. The GMH administrative guidance value of 0.1 µg/L is a composite precautionary value for both PFOA and PFOS for long term exposure in drinking water.

h. Annual Average - Environmental Quality Standards. PFOA AA-EQS based on secondary poisoning of wildlife.

i. Administrative value is for the sum of seven PFAS found in drinking water: PFOS, PFOA, PFHxS, PFBS, PFHpA, PFHxA, and PFPeA. PFOS is considered to be the most toxic. Water can still be used at up to 0.9 µg/L.

Table 4 PFHxS Regulatory Criteria Summary (Soil)

Location	Year	Standard/ Guidance	Type	Soil Screening Level PFHxS (mg/kg)
Australia	2018	HHSL[c]	Human Health Screening Value. Residential with accessible soil	0.009
			Human Health Screening Value. Residential with minimal soil access	2
			Human Health Screening Value. Public open space	1
			Human Health Screening Value. Industrial/ Commercial	20
Canada	2017	SSV	Human Health Screening	-
Denmark	2015	[d]	Human Health Screening	0.4
U.S. EPA	2017	RSL	GW Protection	-
	2017	RSL	Human Health Screening	-
Alaska (AK)	2017	CL	GW Protection	-
	2017	CL [b]	Human Health Screening	-
Delaware (DE)	2016	GCC	Human Health Screening	-
Michigan (MI)	2016	GCC	GW Protection (Groundwater)	-
	2016	GCC	GW Protection (Surface Water)	-
	2016	GCC	Human Health Screening	-
Minnesota (MN)	2016	SRV	Human Health Screening	-
Nevada (NV)	2017	BCL	Human Health Screening	-
New Hampshire (NH)	2017	DCRB	Human Health Screening	-
North Carolina (NC)	2016	PSRG	GW Protection	-
	2016	PSRG	Human Health Screening	-
Texas (TX)	2017	PCL	GW Protection (0.5-acre source)	0.002
	2017	PCL	GW Protection (30-acre source)	0.001
	2017	PCL	Human Health Screening (0.5-acre source)	0.3
	2017	PCL	Human Health Screening (30-acre source)	0.2

Notes:

a. EPA RSLs (June 2017). Calculated by the EPA RSL calculator using EPA OW RfDs, HI of 1, residential exposure assumptions.

b. Alaska proposed cleanup levels for Human health - most stringent value is from the "Over 40 Inch Zone".

c. Health screening level for contaminated sites (HEPA,2018). Note the screening level is for PFOS+PFHxS..

d. Applies to the individual results for PFOA, PFOS, PFNA, PFBA, PFBS, PFHxS, PFHxA, PFPxA, PFPeA, PFHpA, PFOSA, PFDA, and 6:2 FTS as well as the sume of concentrations of these 12 PFAS.

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Other PFAS Compounds

A number of other PFAS compounds were detected in various media within the Investigation Area. Limited studies are available regarding the toxicity of these compounds in humans and animals. A comparison of guidelines or screening criteria developed by various international agencies, as presented in the tables for each PFAS compound, potentially provides an indication of the relative toxicities however the wide variance in some instances suggests some uncertainties although differences in criteria setting policies also influence these differences.

6:2 Fluorotelomer Sulfonate (6:2 FTS)

CAS: 27619-97-2

Table 12: International screening levels for 6:2 FTS in water and soil

Standard and Guidance Values for Water					
Location	Regulatory Agency	Year	Type of Standard	Medium	Concentration (µg/L)
Denmark	Environmental Protection Agency	2015	Health-based	Drinking Water/ Groundwater	0.1[a]
Standard and Guidance Values for Soil					
Location	Regulatory Agency	Year	Type of Standard	Medium	Concentration (mg/Kg)
Australia	Department of Defense	2016	Interim Screening Level	Soil	60
Denmark	Environmental Protection Agency	2015	Human Health Screening Level	Soil	0.4[b]

[a]Applies to this PFAS compound and the sum of 12 other PFAS compounds

[b]Applies to this PFAS compound and the sum of 12 other PFAS compounds

Perfluorobutanoic Acid (PFBA)

CAS: 375-22-4

Health Effects

Relatively few toxicity studies have been conducted in animals exposed to PFBA by a relevant route of exposure. Short-term studies in rats administered 20 mg/kg/day PFBA for 2 weeks did not significantly affect relative liver weight, but increased absolute liver weight at 78 mg/kg/day. The increase in liver weight was accompanied by changes in enzymes involved in metabolism (ATSDR 2015). A multi-dose 5-day study conducted by 3M (2007) had no significant effect on a wide range of end points including body and organ weights, hematology, clinical chemistry, and histopathology. An intermediate duration oral development study did not affect newborn weight gain or viability. The most sensitive endpoint was a delay in eye opening in the pups at maternal doses of 35 mg/kg/day. The 28- and 90-day studies showed liver hypertrophy at 30 mg/kg/day and thyroid effects in male rats (ATSDR 2015).

Elimination Half-life

Humans exposed to PFBA (unknown dose and route of exposure) had an average elimination half-life of 72 to 81 hours. An intravenous dose of 10 mg/kg in male and female Cynomolgus monkeys resulted in elimination half-lives of 40 and 41 hours, respectively. An intravenous dose of 30 mg/kg administered to male and female Sprague-Dawley rats resulted in elimination half-lives of 6.4 and 1.0 hours for males and females, respectively. Single oral doses of PFBA of 30 mg/kg administered to male and female Sprague-Dawley rats resulted in elimination half-lives of 9.2 and 1.8 hours, respectively. Oral studies in mice with single oral doses of 10, 30 and 100 mg/kg resulted in elimination half-lives in males ranging between 5.2 and 16.3 hours and in females ranging between 2.8 and 3.1 hours (Chang et al. 2008).

Table 13: International screening levels for PFBA in water

Standard and Guidance Values for Water					
Location	Regulatory Agency	Year	Type of Standard	Medium	PFBA Concentration (µg/L)
Canada	Health Canada	2016	Screening Value	Drinking Water	30
Denmark	Environmental Protection Agency	2015	Health-based	Drinking Water/ Groundwater	0.1[b]
Italy	--	2017	Health-based	Drinking Water	7
Italy	--	2017	Screening Value	Freshwater	7[c]
USA					
Minnesota	Department of Health	2017	Short-term Health-based Value	Groundwater	7
Minnesota	Department of Health	2017	Subchronic Health-based Value	Groundwater	7
Minnesota	Department of Health	2017	Chronic Health-based Value	Groundwater	7
Texas	Commission on Environmental Quality	2017	Tier 1 Protective Concentration Level	Groundwater	71[a]

a. *Promulgated*

b. *Applies to this PFAS compound and the sum of 12 other PFAS compounds*

c. *Annual Average – Environmental Quality Standards*

Table 14: International screening levels for PFBA in soil

Standard and Guidance Values for Soil				
Location	Regulatory Agency	Year	Type of Standard	PFBA Concentration (mg/kg)
Denmark	Environmental Protection Agency	2015	Human Health Screening Level	0.4[d]
USA				
Minnesota	Department of Health	2016	Soil Reference Value	63
Texas	Commission on Environmental Quality	2017	Soil Screening Level for Groundwater Protection (0.5 acre)	0.2
Texas	Commission on Environmental Quality	2017	Soil Screening Level for Groundwater Protection (30 acre)	0.098
Texas	Commission on Environmental Quality	2017	Human Health Screening Level (0.5 acre)	180
Texas	Commission on Environmental Quality	2017	Human Health Screening Level (30 acre)	160

a. Applies to this PFAS compound and the sum of 12 other PFAS compounds

Perfluorobutane Sulfonic Acid (PFBS)

CAS: 375-73-5

Health Effects

In a 90-day rat study, PFBS did not result in alterations in kidney weights, bud did result in hyperplasia of the medullary and papillary tubular and ductal epithelial cells in the inner medullary region at 600 mg/kg/day, but not at 200 mg/kg/day (Lieder et al. 2009a). Minimal to moderate papillary epithelia tubular/acinal hyperplasia was also observed in a 2-generation rat study at 1,000 mg/kg/day, but not at 300 mg/kg/day (Lieder et al. 2009b).

A 90-day study of PFBS in rats showed no significant alterations in motor activity or performance on functional observation tests at doses as high as 600 mg/kg/day. In a 28-day neurobehavioral rat study with PFBS, the only notable effect was a significant decrease in tail flick latency to a thermal stimulus in males from all treatment groups (100, 300 and 900 mg/kg/day) relative to controls. Gross and microscopic examination of the brain, spinal cord, and sciatic nerve do not show any significant alterations (Lieder et al. 2009a).

Elimination Half-life

Humans exposed to PFBS (unknown dose and route of exposure) had an average elimination half-life of 665 hours (Olsen et al. 2009). An intravenous dose of 10 mg/kg in male and female Cynomolgus monkeys resulted in elimination half-lives of 15 and 8 hours, respectively, in one study (Chengelis et al. 2009), but resulted in elimination half-lives of 95.2 and 83.2 hours, respectively in another study (Olsen et al. 2009). Intravenous doses of 10 and 30 mg/kg administered to male and female Sprague-Dawley rats resulted in elimination half-lives ranging between 2.1 and 4.54 hours for males and 0.64 and 3.96 hours for females (Chengelis et al. 2009, Olsen et al. 2009). Single oral doses of PFBS of 30 mg/kg administered to male and female Sprague-Dawley rats resulted in elimination half-lives of 4.68 and 7.42 hours, respectively.

Table 15: International screening levels for PFBS in water

Standard and Guidance Values for Water					
Location	Regulatory Agency	Year	Type of Standard	Medium	PFBS Concentration (µg/L)
Canada	Health Canada	2016	Screening Value	Drinking Water	15
Denmark	Environmental Protection Agency	2015	Health-based	Drinking Water/ Groundwater	0.1[b]
Italy	--	2017	Health-based	Drinking Water	3
Italy	--	2017	Screening Value	Freshwater	3[c]
Sweden	Environmental Protection Agency	2014	Administrative	Drinking Water	0.09[d]
USA					
USA	Environmental Protection Agency	2017	Regional Screening Level	Groundwater	401
Delaware	Department of Natural Resources and Environmental Control	2016	Reporting Level	Groundwater	38
Minnesota	Department of Health	2017	Subchronic Health-based Value	Groundwater	9[a]
Minnesota	Department of Health	2017	Chronic Health-based Value	Groundwater	7[a]
Nevada	Department of Environmental Protection	2015	Basic Comparison Level	Drinking Water	667
Texas	Commission on Environmental Quality	2017	Tier 1 Protective Concentration Level	Groundwater	34[a]

a. *Promulgated*
b. *Applies to this PFAS compound and the sum of 12 other PFAS compounds*
c. *Annual Average – Environmental Quality Standards*
d. *Administrative value is for the sum of seven PFAS: PFOS, PFOA, PFHxS, PFBS, PFHpA, PFHxA, and PFPeA.*

Table 16: International screening levels for PFBS in soil

Standard and Guidance Values for Soil				
Location	Regulatory Agency	Year	Type of Standard	PFBS Concentration (mg/Kg)
Denmark	Environmental Protection Agency	2015	Human Health Screening Level	0.4[e]
USA				
USA	Environmental Protection Agency	2017	Regional Screening Level Protective of Groundwater	0.13
USA	Environmental Protection Agency	2017	Regional Screening Level	1260
Delaware	Department of Natural Resources and Environmental Control	2016	Human Health Soil Screening Level	160
Minnesota	Department of Health	2016	Soil Reference Value	30
Nevada	Department of Environmental Protection	2017	Basic Comparison Level	125
North Carolina	Department of Environmental Quality	2016	Preliminary Soil Remedial Goal	320
Texas	Commission on Environmental Quality	2017	Soil Screening Level for Groundwater Protection (0.5 acre)	0.11
Texas	Commission on Environmental Quality	2017	Soil Screening Level for Groundwater Protection (30 acre)	0.053
Texas	Commission on Environmental Quality	2017	Human Health Screening Level (0.5 acre)	86
Texas	Commission on Environmental Quality	2017	Human Health Screening Level (30 acre)	80

[e]Applies to this PFAS compound and the sum of 12 other PFAS compounds

Perfluorodecananoic Acid (PFDS)

CAS: 335-77-3

Table 17: International screening levels for PFDS in water

Standard and Guidance Values for Water					
Location	Regulatory Agency	Year	Type of Standard	Medium	PFDS Concentration (µg/L)
USA					
Texas	Commission on Environmental Quality	2017	Tier 1 Protective Concentration Level	Groundwater	0.29[a]

[a]Promulgated

Table 18: International screening levels for PFDS in soil

Standard and Guidance Values for Soil				
Location	Regulatory Agency	Year	Type of Standard	PFDS Concentration (mg/Kg)
USA				
Texas	Commission on Environmental Quality	2017	Soil Screening Level for Groundwater Protection (0.5 acre)	0.04
Texas	Commission on Environmental Quality	2017	Soil Screening Level for Groundwater Protection (30 acre)	0.02
Texas	Commission on Environmental Quality	2017	Human Health Screening Level (0.5 acre)	0.8
Texas	Commission on Environmental Quality	2017	Human Health Screening Level (30 acre)	0.8

Perfluoroheptanoic Acid (PFHpA)

CAS: 375-85-9

Elimination Half-life

Intravenous doses of 17.7 mg/kg administered to male and female Wistar rats resulted in elimination half-lives of 2.4 and 1.2 hours, respectively (Ohmori et al. 2003).

Table 19: International screening levels for PFHpA in water

Standard and Guidance Values for Water					
Location	Regulatory Agency	Year	Type of Standard	Medium	PFHpA Concentration (µg/L)
Canada	Health Canada	2016	Screening Value	Drinking Water	0.2
Denmark	Environmental Protection Agency	2015	Health-based	Drinking Water/ Groundwater	0.1[b]
Sweden	Environmental Protection Agency	2014	Administrative	Drinking Water	0.09[c]
USA					
Connecticut	Department of Public Health	2016	Action Level	Groundwater	0.07
Colorado	Department of Public Health and Environment	2017	Health Advisory	Drinking Water	0.07
Oregon	Department of Environmental Quality	2011	Initiation Level	Surface Water	300[a]
Texas	Commission on Environmental Quality	2017	Tier 1 Protective Concentration Level	Groundwater	0.56[a]

a. *Promulgated*

b. *Applies to this PFAS compound and the sum of 12 other PFAS compounds*

c. *Administrative value is for the sum of seven PFAS: PFOS, PFOA, PFHxS, PFBS, PFHpA, PFHxA, and PFPeA.*

Table 20: International screening levels for PFHpA in soil

Standard and Guidance Values for Soil				
Location	**Regulatory Agency**	**Year**	**Type of Standard**	**PFHpA Concentration (mg/Kg)**
Denmark	Environmental Protection Agency	2015	Human Health Screening Level	0.4[d]
USA				
Texas	Commission on Environmental Quality	2017	Soil Screening Level for Groundwater Protection (0.5 acre)	0.0046
Texas	Commission on Environmental Quality	2017	Soil Screening Level for Groundwater Protection (30 acre)	0.0023
Texas	Commission on Environmental Quality	2017	Human Health Screening Level (0.5 acre)	1.5
Texas	Commission on Environmental Quality	2017	Human Health Screening Level (30 acre)	1.5

a. *Applies to this PFAS compound and the sum of 12 other PFAS compounds*

Perfluorohexanoic acid (PFHxA)

CAS: 307-24-4

Elimination Half-life

An intravenous dose of 10 mg/kg in male and female Sprague-Dawley rats resulted in elimination half-lives of 1 and 0.42 hours, respectively. Single oral doses of PFHxA of 50, 150, and 300 mg/kg administered to male Sprague-Dawley rats resulted in elimination half-lives ranging between 2.2 and 2.5 hours; the same doses administered to female Sprague-Dawley rats resulted in elimination half-lives ranging between 2.1 and 2.6 hours (Chengelis et al., 2009).

Table 21: International screening levels for PFHxA in water

Standard and Guidance Values for Water					
Location	Regulatory Agency	Year	Type of Standard	Medium	PFHxA Concentration (µg/L)
Canada	Health Canada	2016	Screening Value	Drinking Water	0.2
Denmark	Environmental Protection Agency	2015	Health-based	Drinking Water/ Groundwater	0.1
Italy	--	2017	Health-based	Drinking Water	1
Italy	--	2017	Screening Value	Freshwater	1[b]
Sweden	Environmental Protection Agency	2014	Administrative	Drinking Water	0.09
USA					
Connecticut	Department of Public Health	2016	Private Well Action Level	Groundwater	0.07
Texas	Commission on Environmental Quality	2017	Tier 1 Protective Concentration Level	Groundwater	0.093[a]

a. *[a]Promulgated*

b. *[b]Annual Average – Environmental Quality Standards*

Table 22: International screening levels for PFHxA in soil

Standard and Guidance Values for Soil				
Location	Regulatory Agency	Year	Type of Standard	PFHxA Concentration (mg/Kg)
Denmark	Environmental Protection Agency	2015	Human Health Screening Level	0.4[c]
USA				
Texas	Commission on Environmental Quality	2017	Soil Screening Level for Groundwater Protection (0.5 acre)	0.00048
Texas	Commission on Environmental Quality	2017	Soil Screening Level for Groundwater Protection (30 acre)	0.00024
Texas	Commission on Environmental Quality	2017	Human Health Screening Level (0.5 acre)	0.3
Texas	Commission on Environmental Quality	2017	Human Health Screening Level (30 acre)	0.3

1 *[C]Applies to this PFAS compound and the sum of 12 other PFAS compounds*

Perfluorononanoic Acid (PFNA)

CAS: 375-95-1

Health Effects

Administration of 1 mg/kg/day PFNA for 14 days resulted in increases in serum glucose levels and decreases in high-density lipoprotein (HDL) cholesterol levels in rats. Liver effects were observed at 5 mg/kg/day. Immunologically, decreases in thymus and spleen weights were observed in rats at 3 mg/kg/day along with alterations in splenic lymphocyte phenotypes at 1 mg/kg/day, but there was no alteration in the response to a T-cell mitogen (ATSDR 2015).

Elimination Half-life

Intravenous doses of 22.6 mg/kg PFNA administered to male and female Wistar rats resulted in elimination half-lives of 710 and 58.6 hours, respectively (Ohmori et al. 2003). Single oral doses of PFNA of 0.2 mg/kg administered to male Sprague-Dawley rats resulted in an elimination half-life of 974 hours (Benskin et al. 2009). Oral administration of PFNA over a 12-week period with a daily dose of 0.029 mg/kg/day resulted in an elimination half-life of 1,128 hours (DeSilva et al. 2009).

Table 23: International screening levels for PFNA in water

Standard and Guidance Values for Water					
Location	Regulatory Agency	Year	Type of Standard	Medium	PFNA Concentration (µg/L)
Canada	Health Canada	2016	Screening Value	Drinking Water	0.2
Denmark	Environmental Protection Agency	2015	Health-based	Drinking Water/ Groundwater	0.1[b]
USA					
Connecticut	Department of Public Health	2016	Action Level	Groundwater	0.07
New Jersey	Department of Environmental Protection	2017	Groundwater Quality Standard	Groundwater	0.01[a]
New Jersey	Drinking Water Quality Institute	2017	Maximum Contaminant Level	Drinking Water	0.013[a]
Oregon	Department of Environmental Quality	2011	Initiation Level	Surface Water	1[a]
Texas	Commission on Environmental Quality	2017	Tier 1 Protective Concentration Level	Groundwater	0.29[a]

a. [a]*Promulgated*

b. [b]*Applies to this PFAS compound and the sum of 12 other PFAS compounds*

Table 24: International screening levels for PFNA in soil

Standard and Guidance Values for Soil				
Location	Regulatory Agency	Year	Type of Standard	PFNA Concentration (mg/Kg)
Denmark	Environmental Protection Agency	2015	Human Health Screening Level	0.4[c]
USA				
Texas	Commission on Environmental Quality	2017	Soil Screening Level for Groundwater Protection (0.5 acre)	0.003
Texas	Commission on Environmental Quality	2017	Soil Screening Level for Groundwater Protection (30 acre)	0.0015
Texas	Commission on Environmental Quality	2017	Human Health Screening Level (0.5 acre)	0.8
Texas	Commission on Environmental Quality	2017	Human Health Screening Level (30 acre)	0.7

a. [c]Applies to this PFAS compound and the sum of 12 other PFAS compounds

Perfluoropentanoic Acid (PFPeA)

CAS: 2706-90-3

Table 25: International screening levels for PFPeA in water

Standard and Guidance Values for Water					
Location	Regulatory Agency	Year	Type of Standard	Medium	PFPeA Concentration (µg/L)
Canada	Health Canada	2016	Screening Value	Drinking Water	0.2
Denmark	Environmental Protection Agency	2015	Health-based	Drinking Water/ Groundwater	0.1[b]
Italy	--	2017	Health-based	Drinking Water	3
Italy	--	2017	Screening Value	Freshwater	3[c]
Sweden	Environmental Protection Agency	2014	Administrative	Drinking Water	0.09[d]
USA					
Texas	Commission on Environmental Quality	2017	Tier 1 Protective Concentration Level	Groundwater	0.093[a]

a. *[a]Promulgated*

b. *[b]Applies to this PFAS compound and the sum of 12 other PFAS compounds*

c. *[c]Annual Average – Environmental Quality Standards*

d. *[d]Administrative value is for the sum of seven PFAS: PFOS, PFOA, PFHxS, PFBS, PFHpA, PFHxA, and PFPeA.*

Table 26: International screening levels for PFPeA in soil

Standard and Guidance Values for Soil				
Location	Regulatory Agency	Year	Type of Standard	PFPeA Concentration (mg/Kg)
Denmark	Environmental Protection Agency	2015	Human Health Screening Level	0.4[e]
USA				
Texas	Commission on Environmental Quality	2017	Soil Screening Level for Groundwater Protection (0.5 acre)	0.00032
Texas	Commission on Environmental Quality	2017	Soil Screening Level for Groundwater Protection (30 acre)	0.00016
Texas	Commission on Environmental Quality	2017	Human Health Screening Level (0.5 acre)	0.3
Texas	Commission on Environmental Quality	2017	Human Health Screening Level (30 acre)	0.3

a. *[e]Applies to this PFAS compound and the sum of 12 other PFAS compounds*

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