Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment.

Summary of health-based guidance values for per- and polyfluoroalkyl substances

Introduction

1. The COT has previously considered per- or poly-fluoroalkyl substances (PFAS) on a number of occasions and has recently published a statement on the European Food Safety Authority (EFSA) opinion “Risk to human health related to the presence of perfluoroalkyl substances in food”. The Committee is now asked to consider what further guidance can be provided to support human health risk assessments undertaken by UK Government Departments and Agencies.

2. An initial paper on further work on PFAS was discussed at the October 2022 COT meeting (TOX/2022/53). This paper noted that a number of health-based guidance values (HBGVs) from other countries and international bodies are available for PFAS. In outlining a plan for a series of papers for COT consideration on PFAS, it was noted that a detailed review of available HBGVs would be useful.

3. This present paper contains a compilation of HBGVs published worldwide by authoritative bodies and their derivations.

Data searches

4. A search for HBGVs published by authoritative bodies was carried out, including websites of authoritative bodies and chemical/toxicological information summary databases. Search terms included ‘PFAS’, ‘perfluoro’, ‘polyfluoro’, and related terms. Websites were accessed in September 2022. Searches were not

conducted using the individual PFAS chemical names unless the presence of specifically relevant information was indicated within an identified data source.

Exclusion criteria

5. Data listed pertain to standards set by national or international bodies; data from sub-national regions (for example, individual US states) are not included. This required dataset should exclude non-authoritative body data, for example REACH derived no-effect levels (DNELs).

Results

6. HBGVs were identified for perfluorooctanoic acid (PFOA) (Table 1), perfluorooctane sulphonate (PFOS) (Table 2), perfluorobutanoic acid (PFBA) (Table 3), perfluorobutanesulfonic acid (PFBS) (Table 4), perfluorohexanoic acid (PFHxA) (Table 5), perfluorohexanesulfonic acid (PFHxS) (Table 6), perfluorononanoic acid (PFNA) (Table 7), perfluorooctanesulfonamide (PFOSA) (Table 8), group of per- and polyfluoroalkyl substances (GenX chemicals) (Table 9) and mixtures of PFOS, PFOA, PFNA and PFHxS (Table 10) and PFOS and PFHxS (Table 11).

7. Subchronic and chronic HBGVs were identified and included tolerable daily or weekly intakes (TDIs or TWIs), reference doses (RfDs), minimal risk levels (MRLs), chronic indicative toxicity value (iTVs), derived no-effect level (DNELs) and chronic toxicity reference value (TRVs).

8. A no observed adverse effect level (NOAEL), lowest observed adverse effect level (LOAEL) or 95th lower confidence interval of the benchmark dose benchmark dose (BMDL) were determined as the point of departure (POD) prior to application of uncertainty factors (UFs) in order to derive the HBGV. Some organisations also used physiologically-based pharmacokinetic (PBPK) modelling and derived human equivalent doses (HEDs (also called HEQs)) as their POD.

Table 1. HBGVs for PFOA.

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day)	POD / Sensitive endpoint	UF
RIVM 2021[1]	TWI: 0.0044 µg/kg bw/week	0.00063 (0.63)	Implementation of the EFSA 2020 TWI (Table 11) for summed exposure to PFOA, PFOS, PFNA, and PFHxS. $BMDL_{10}$ of 0.00175 µg/mL for the sum of PFOA, PFNA, PFHxS and PFOS in serum in 1-year-old children based on reduced antibody response to vaccination. Converted to 0.00063 µg/kg bw/day by PBPK modelling.	Use of the EFSA TWI with PFOA as the index chemical, together with RPFs[2] for other PFAS chemicals (although EFSA had assumed equipotency) (Bil et al 2021).
U.S. EPA 2021a[3] U.S. EPA 2022a	Chronic RfD (draft): 0.0000015 µg/kg bw/day	0.0000015 (0.0015)	$BMDL_5$ of 0.00017 µg/mL based on suppression of tetanus vaccine response in 7-year-old children (Grandjean 2012, 2017; Budtz-Jorgensen 2018). Converted to $BMDL_{5\ HED}$ of 0.0000149 µg/kg bw/day by PBPK modelling.	UF = 10: intraspecies variability (10).

[1] RIVM = Rijksinstituut voor Volksgezondheid en Milieu (National Institute for Public Health and the Environment, Netherlands)
[2] RPF = Relative potency factor
[3] U.S. EPA = United States Environmental Protection Agency

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day)	POD / Sensitive endpoint	UF
ATSDR 2021[4]	Intermediate MRL: 0.003 µg/kg bw/day	0.003 (3)	LOAEL of 8290 µg/kg bw/day based on skeletal alterations in adult offspring mice (Koskela et al 2016). Converted to $LOAEL_{HED}$ of 0.821 µg/kg bw/day.	UF = 300: use of a LOAEL (10), extrapolation from animal to human with dosimetric adjustment (3), human variability (10).
ATSDR 2021	Chronic MRL	-	Inadequate chronic study. The Butenhoff et al. (2012c) study identified the salivary gland as the most sensitive target, but these alterations were only observed in males and may have been due to an antemortem viral infection. Intermediate-duration oral studies have suggested that the immune system is a sensitive target of toxicity in mice; however, potential alterations in immune function have not been investigated in chronic-duration studies.	-

[4] ATSDR = Agency for Toxic Substances and Disease Registry (US)

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day)	POD / Sensitive endpoint	UF
FSANZ 2019[5]	TDI: 0.16 µg/kg bw/day	0.16 (160)	NOAEL of 10000 µg/kg bw/day (197 µg/mL serum) for fetal toxicity in a developmental and reproductive study in mice (Lau et al 2006). Converted to a HED of 0.4.9 µg/kg bw/day by PBPK modelling.	UF = 30: interspecies differences in toxicodynamics (3), intraspecies variability (10).
EFSA 2018[6]	Provisional TWI: 0.006 µg/kg bw/week	0.00086 (0.86)	$BMDL_5$ corresponding to chronic daily intake of 0.00008 µg/kg bw/day based on increased serum cholesterol in adults (Steenland et al 2009; Eriksen et al 2013).	No AFs were applied because the BMD modelling was based on large epidemiological studies from the general population, including potentially sensitive subgroups. A TWI was established to account for the long half-life of the contaminant.
Health Canada 2018a	TDI: 0.021 µg/kg bw/day	0.021 (21)	$BMDL_{10}$ of 50 µg/kg bw/day for hepatocellular hypertrophy in rats (Perkins et al 2004). Converted to a POD_{HEQ} of 0.521 µg/kg bw/day by PBPK modelling.	UF = 25: interspecies variability (2.5), intraspecies variability (10).

[5] FSANZ = Food Standards Australia New Zealand
[6] EFSA = European Food Safety Authority

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day)	POD / Sensitive endpoint	UF
Zeilmaker et al. 2016 (in Dutch). Summary in RIVM 2021	TDI [now replaced by the EFSA 2020 TWI]: 0.0125 µg/kg bw/day	0.0125 (12.5)	NOAEL of 7.1 µg/mL in serum based on liver toxicity in rats (Perkins et al 2004). Converted to $NOAEL_{HED}$ of 1000000 µg/kg bw/day.	UF = 80: interspecies variability (1), intraspecies variability (10), subchronic to chronic extrapolation (8)
Danish EPA 2015	TDI: 0.1 µg/kg bw/day	0.1 (100)	$BMDL_{10}$ of 456 µg/kg bw/day for liver effects in rats (Palazzolo 1993) Conversion to $BMDL_{10\ HED}$ of 3 µg/kg bw/day.	UF = 30: interspecies variation variability (3), intraspecies variability (10),
Swedish EPA 2012	DNEL: 0.0020 µg/mL serum	0.13 (130)	LOAEL of 10 µg/kg bw/day (0.15 µg/mL serum) based on effects on mammary gland development and growth in mice (White et al 2007, 2009, 2011).	UF = 75: extrapolation from LOAEL to NOAEL (3), interspecies variability (2.5), intraspecies variability (10).
UK COT 2009[7]	TDI: 1.5 µg/kg bw/day	1.5 (1500)	$BMDL_{10}$ of 300 µg/kg bw/day based on liver effects in mice.	UF = 200: inter- and intraspecies variability (100), uncertainties relating to the internal dose kinetics (2).

[7] COT = Committee on Toxicity

Table 2. HBGVs for PFOS.

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day))	POD / Sensitive endpoint	UF
U.S. EPA 2021b U.S. EPA 2022b	Chronic RfD (draft): 0.0000079 µg/kg bw/day	0.0000079 (0.0079)	$BMDL_{5RD-HED}$[8] of 0.0000791 µg/kg bw/day for decreased serum anti-diphtheria antibody concentration in children in epidemiological studies (Grandjean 2012, 2017; Budtz-Jorgensen and Grandjean 2018).	UF = 10: intraspecies variability (10).
ATSDR 2021	Intermediate MRL: 0.002 µg/kg bw/day	0.002 (2)	NOAEL of 0.000743 µg/kg bw/day based on delayed eye opening and decreased pup body weight in rats (Luebker et al 2005a). Converted to $NOAEL_{HED}$ of 0.515 µg/kg bw/day.	UF = 300: extrapolation from animal to human with dosimetric adjustment (3), human variability (10); MF[9] for concern that immunotoxicity may be a more sensitive endpoint than developmental toxicity (10).
ATSDR 2021	Chronic MRL	-	Inadequate chronic study. Immune function was not examined following chronic exposure in animal studies; the only chronic- study (Butenhoff et al. 2012b; Thomford 2002b), did not find histological alterations in immune tissues (lymph nodes, spleen, and thymus) in rats at doses as high as 1040	-

[8] RD = Relative deviation
[9] MF = Modifying factor

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day))	POD / Sensitive endpoint	UF
			µg/kg/day. Impaired immune function was the most sensitive endpoint in intermediate-duration mouse studies.	
Health Canada 2018b	TDI: 0.06 µg/kg bw/day	0.06 (60)	NOAEL of 21 µg/kg bw/day based on hepatocellular hypertrophy in rats (Butenhoff et al 2012b). Converted to POD_{HEQ} of 0.1.5 µg/kg bw/day by PBPK modelling.	UF = 25: interspecies variability (2.5), intraspecies variability (10).
EFSA 2018	Provisional TWI: 0.013 µg/kg bw/week	0.0019 (1.9)	$BMDL_5$ corresponding to chronic daily intake of 0.0017-0.0020 µg/kg bw/day (median, 0.0018 µg/kg bw/day) based on increased serum cholesterol in adults (Steenland et al 2009; Nelson et al 2010; Eriksen et al 2013).	No AFs applied because the BMD modelling was based on large epidemiological studies from the general population, including potentially sensitive subgroups. A TWI was established to account for the long half-life of the contaminant.
Danish EPA 2015	TDI: 0.03 µg/kg bw/day	0.03 (30)	$BMDL_{10}$ of 33 µg/kg bw/day based on hepatotoxicity in rats (Thomford 2002; Butenhoff et al 2012).	UF = 1230: interspecies pharmacokinetics (41), intraspecies pharmacodynamics (3), intraspecies variability (10).
Swedish EPA 2012	DNEL: 0.0.00012 µg/mL serum	0.001 (1)	NOAEL of 0.166 µg/kg bw/day (0.0178 µg/mL serum) based on immunotoxicity in mice (Peden-Adams et al 2008).	UF = 150: adjustment for exposure duration (6), interspecies variability (2.5), intraspecies variability (10).

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day))	POD / Sensitive endpoint	UF
UK COT 2009	Provisional TDI: 0.3 µg/kg bw/day	0.3 (300)	NOAEL of 30 µg/kg bw/day based on decreased serum T3 levels in in cynomolgus monkeys (Seacat et al 2002).	UF = 100: interspecies variability (10) and intraspecies variability (10).

Table 3. HBGVs for PFBA.

Authority	HBGV	Daily equivalent HBGV value (µg/kg bw/day)	POD / Sensitive endpoint	UF
ANSES 2017[10]	Itv: 24 µg/kg bw/day	24 (24000)	NOAEL of 6000 µg/kg bw/day based on liver effects (increase in absolute and relative liver weight, hepatocellular hypertrophy) in rats (Butenhoff et al 2012). Converted to $NOAEL_{HED}$ of 1764 µg/kg bw/day.	UF = 75: interspecies variability (2.5), intraspecies variability (10), extrapolation from subchronic to chronic exposure (3).

[10] ANSES = Agence Nationale de Sécurité Sanitaire de l'Alimentation, de l'Environnement et du Travail (French National Agency for Food, Environmental and Occupational Safety)

Table 4. HBGVs for PFBS.

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day)	POD / Sensitive endpoint	UF
U.S. EPA 2021c	Subchronic RfD: 1 µg/kg bw/day	1 (1000)	$BMDL_{0.5SD}$[11] $_{HED}$ of 95 µg/kg bw/day based on serum total T4 in newborn (postnatal day 1) mice (Feng et al 2017).	UF = 100: interspecies variability (3), intraspecies variability (10), database deficiencies (3).
U.S. EPA 2021c	Chronic RfD: 0.3 µg/kg bw/day	0.3 (300)	$BMDL_{0.5SD\ HED}$ of 95 µg/kg bw/day based on decreased serum total T4 in newborn (postnatal day 1) mice (Feng et al 2017).	UF = 300: interspecies variability (3), intraspecies differences (10), database deficiencies (10).
ANSES 2017	TRV: 80 µg/kg bw/day	80 (80000)	$BMDL_{10}$ of 24000 µg/kg bw/day for renal effects in rats (Lieder et al 2009b). Converted to $BMDL_{10\ HED}$ of 6060 µg/kg bw/day.	UF = 75: interspecies variability (2.5), intraspecies variability (10), extrapolation from subchronic to chronic exposure (3).

[11] SD = Standard deviation

Table 5. HBGVs for PFHxA.

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day)	POD / Sensitive endpoint	UF
ANSES 2017	TRV: 320 µg/kg bw/day	320 (320000)	NOAEL of 30000 µg/kg bw/day for renal effects in rats (Klaunig et al 2015). Converted to $NOAEL_{HED}$ of 7910 µg/kg bw/day.	UF = 25: interspecies variability (2.5), intraspecies variability (10).

Table 6. HBGVs for PFHxS.

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day)	POD / Sensitive endpoint	UF
ATSDR 2021	Intermediate MRL: 0.02 µg/kg bw/day	0.02 (20)	NOAEL of 1000 µg/kg bw/day based on thyroid follicular epithelial hypertrophy/hyperplasia in rats (Butenhoff et al. 2009a). Converted to $NOAEL_{HED}$ of 4.7 µg/kg bw/day.	UF = 300: extrapolation from animal to human with dosimetric adjustment (3), human variability (10); MF for database limitations (10).

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day)	POD / Sensitive endpoint	UF
ATSDR 2021	Chronic MRL	-	No chronic-duration oral studies in laboratory animals were identified for PFHxS and ATSDR does not extrapolate across exposure duration.	-
Swedish EPA 2012	DNEL: 0.00098 µg/mL serum	0.67 (670)	LOAEL of 300 µg/kg bw/day (44 µg/mL serum) based on haematological effects in rats (Hoberman and York 2003).	UF = 450: extrapolation for exposure duration (6), LOAEL to NOAEL (3), interspecies variability (2.5), intraspecies variability (10).
ANSES 2017	iTV: 4 µg/kg bw/day	4 (4000)	NOAEL of 1000 µg/kg bw/day based on liver effects (increase in absolute and relative liver weight, hepatocellular hypertrophy) in rats (Butenhoff et al 2009). Converted to $NOAEL_{HED}$ of 289 µg/kg bw/day.	UF = 75: interspecies variability (2.5), intraspecies variability (10), extrapolation from subchronic to chronic exposure (3).

Table 7. HBGVs for PFNA.

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day)	POD / Sensitive endpoint	UF
ATSDR 2021	Intermediate MRL: 0.003 µg/kg bw/day	0.003 (3)	NOAEL of 1000 µg/kg bw/day based on decreased body weight and developmental delays in mice (Das et al 2015). Converted to $NOAEL_{HED}$ of 1 µg/kg bw/day.	UF = 300: extrapolation from animal to human with dosimetric adjustment (3), human variability (10); MF for database limitations (10).
ATSDR 2021	Chronic MRL	-	No chronic-duration oral studies in laboratory animals were identified for PFNA and ATSDR does not extrapolate across exposure duration.	-

Table 8. HBGVs for PFOSA.

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day)	POD / Sensitive endpoint	UF
Danish EPA 2015	TDI: 0.03 µg/kg bw/day	0.03 (30)	As for PFOS	Insufficient data were available to derive a specific TDI for PFOSA. However, as the chemical structure of PFOSA is very comparable to PFOS (the amide derivate of PFOS) and as PFOSA is used as a precursor for PFOS formation it was considered justifiable to apply the TDI for PFOS to PFOSA.

Table 9. HBGVs for GenX chemicals.

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day)	POD / Sensitive endpoint	UF
U.S. EPA 2021d	Chronic RfD (final):	0.003 (3)	$BMDL_{10\ HED}$ of 10 µg/kg bw/day based on critical liver effects (constellation of liver lesions as defined by the National	UF = 3000: intraspecies variability (10), interspecies variability (3), extrapolation from subchronic to

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day)	POD / Sensitive endpoint	UF
	0.003 µg/kg bw/day		Toxicology Program Pathology Working Group) in parental female mice exposed to HFPO dimer acid ammonium salt by gavage for 53–64 days (DuPont-18405-1037, 2010).	chronic dosing duration (10), database deficiencies (10).
RIVM 2017	Provisional TDI: 0.021 µg/kg bw/day	0.021 (21)	NOAEL of 100 µg/kg bw/day based on increased albumin/globulin ratio in serum in rats (Beekman et al 2016)	UF = 4752: interspecies (toxicokinetic) variability (4), interspecies (toxicodynamic) variability (1.8), intraspecies variability (10), extra factor for possible bioaccumulation (66).

Table 10. HBGVs for PFOS, PFOA, PFNA, and PFHxS (summed).

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day)	POD / Sensitive endpoint	UF
BfR 2021[12]	TWI: 0.0044 µg/kg bw/week	0.00063 (0.63)	Implementation of the EFSA 2020 TWI for summed exposure to PFOS, PFOA, PFNA, and PFHxS. $BMDL_{10}$ of 0.0175 µg/mL for the sum of PFOA, PFNA, PFHxS and PFOS in serum in 1-year-old children based on reduced antibody response to vaccination. Converted to 0.00063 µg/kg bw/day by PBPK modelling.	EFSA 2020 TWI recommended in future assessments No AFs were applied. A TWI was established to account for the importance of long-term accumulation.
EFSA 2020	Group TWI: 0.0044 µg/kg bw/week	0.00063 (0.63)	$BMDL_{10}$ of 0.0175 µg/mL for the sum of PFOA, PFNA, PFHxS and PFOS in serum in 1-year-old children based on reduced antibody response to vaccination (Abraham et al 2020). Converted to 0.00063 µg/kg bw/day by PBPK modelling.	No AFs were applied. A TWI was established to account for the importance of long-term accumulation.

12 BfR = German Federal Institute for Risk Assessment

Table 11. HBGVs for PFOS + PFHxS (summed)

Authority	HBGV	Daily equivalent HBGV value µg/kg bw/day (ng/kg bw/day)	POD / Sensitive endpoint	UF
FSANZ 2019	TDI: 0.02 µg/kg bw/day	0.02 (20)	PFOS: NOAEL of 100 µg/kg bw/day (7.14 µg/mL serum) based on decreased parental and offspring body weight gain in a multigeneration reproductive toxicity study in rats (Luebker et al 2005b). Converted to a HED of 0.6 µg/kg bw/day by PBPK modelling. PFHxS: Insufficient data to establish a TDI	PFOS: UF = 30: interspecies variability (3); intraspecies variation (10). PFHxS: TDI for PFOS considered likely to be protective, thus PFOS and PFHxS summed for the purposes of exposure assessment and risk characterisation.

Questions for the Committee

9. Members are invited to consider this paper and in particular the following questions:

i. Does the Committee have an opinion on the available HBGVs that could be provided as part of the planned interim position paper on PFAS?

ii. Does the Committee wish to suggest any endpoints as priorities for review by the planned subgroup on PFAS?

IEH Consulting under contract supporting the UKHSA COT Secretariat
December 2022

References

ANSES, 2017. OPINION of the French Agency for Food, Environmental and Occupational Health & Safety on the "development of chronic reference values by the oral route for four perfluorinated compounds: perfluorohexanoic acid (PFHxA), perfluorohexane sulfonic acid (PFHxS), perfluorobutanoic acid (PFBA), and perfluorobutane sulfonic acid (PFBS). https://www.anses.fr/fr/system/files/SUBSTANCES2015SA0129EN.pdf

ATSDR, 2021. Toxicological profile for perfluoroalkyls. https://www.atsdr.cdc.gov/toxprofiles/tp200.pdf

BfR, 2021. PFAS in food: BfR confirms critical exposure to industrial chemicals. https://www.bfr.bund.de/cm/349/pfas-in-food-bfr-confirms-critical-exposure-to-industrial-chemicals.pdf

COT, 2009. COT statement on the tolerable daily intake for perfluorooctanoic acid. https://webarchive.nationalarchives.gov.uk/ukgwa/20200803135016/https:/cot.food.gov.uk/cotstatements/cotstatementsyrs/cotstatements2009/cot200902

COT, 2009. COT statement on the tolerable daily intake for perfluorooctane sulfonate. https://webarchive.nationalarchives.gov.uk/ukgwa/20200803134749/https:/cot.food.gov.uk/cotstatements/cotstatementsyrs/cotstatements2006/cotstatementpfos200609

Danish EPA, 2015. Perfluoroalkylated substances: PFOA, PFOS and PFOSA Evaluation of health hazards and proposal of a health based quality for drinking water, criterion soil and ground. https://www2.mst.dk/Udgiv/publications/2015/04/978-87-93283-01-5.pdf

EFSA, 2018. Risk to human health related to the presence of perfluorooctane sulfonic acid and perfluorooctanoic acid in food. https://doi.org/10.2903/j.efsa.2018.5194

EFSA, 2020. Risk to human health related to the presence of perfluoroalkyl substances in food. https://doi.org/10.2903/j.efsa.2020.6223

FSANZ, 2019. Health-based guidance values for PFAS for use in site investigations in Australia. https://www1.health.gov.au/internet/main/publishing.nsf/Content/ohp-pfas-hbgv.htm#final

Health Canada, 2018a. Guidelines for Canadian Drinking Water Quality. Guideline Technical Document. Perfluorooctanoic acid (PFOA). https://www.canada.ca/content/dam/hc-sc/documents/services/publications/healthy-living/guidelines-canadian-drinking-water-quality-technical-document-perfluorooctanoic-acid/document/PFOA_2018-1130-eng.pdf

Health Canada, 2018b. Guidelines for Canadian Drinking Water Quality. Guideline Technical Document. Perfluorooctane sulfonate (PFOS). https://www.canada.ca/content/dam/canada/health-canada/migration/healthy-

canadians/publications/healthy-living-vie-saine/guidelines-canadian-drinking-water-quality-guideline-technical-document-perfluorooctane-sulfonate/PFOS%202018-1130%20ENG.pdf

RIVM, 2017. Derivation of a lifetime drinking-water guideline for 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propanoic acid (FRD-903). https://www.rivm.nl/sites/default/files/2018-11/148-2016%20M%26V%20bijlage%20afleiding%20richtwaarde%20FRD903%20in%20drinkwater_Definitief_revisie%20jan%202017.pdf

RIVM, 2021. Revised risk assessment of GenX and PFOA in food part 1: toxicity of GenX and PFOA and intake through contaminated dairy products, eggs and fish. https://www.rivm.nl/sites/default/files/2022-04/FO_Revised%20GenX%20and%20PFOA%20in%20food%20Part1_20210901_Def%20anon.pdf

Swedish EPA, 2012. Environmental and health risk assessment of perfluoroalkylated and polyfluoroalkylated substances (PFASs) in Sweden. https://www.diva-portal.org/smash/get/diva2:770762/FULLTEXT01.pdf

U.S. EPA, 2021a. Proposed Approaches to the Derivation of a Draft Maximum Contaminant Level Goal for Perfluorooctane Sulfonic Acid (PFOS) (CASRN 1763-23-1) in Drinking Water. External peer review draft. https://sab.epa.gov/ords/sab/f?p=100:0:6516155121689:APPLICATION_PROCESS=AGENCY_REVIEW:::AR_ID:2469

U.S. EPA, 2021b. Proposed Approaches to the Derivation of a Draft Maximum Contaminant Level Goal for Perfluorooctane Sulfonic Acid (PFOS) (CASRN 1763-23-1) in Drinking Water. External peer review draft. https://sab.epa.gov/ords/sab/f?p=100:0:9934318823698:APPLICATION_PROCESS=AGENCY_REVIEW:::AR_ID:2467

U.S. EPA, 2021c. Human Health Toxicity Values for Perfluorobutane Sulfonic Acid (CASRN 375-73-5) and Related Compound Potassium Perfluorobutane Sulfonate (CASRN 29420-49-3). https://ofmpub.epa.gov/eims/eimscomm.getfile?p_download_id=542393

U.S. EPA, 2021d. Human Health Toxicity Values for Hexafluoropropylene Oxide (HFPO) Dimer Acid and Its Ammonium Salt (CASRN 13252-13-6 and CASRN 62037-80-3) (Also Known as “GenX Chemicals). https://www.epa.gov/system/files/documents/2021-10/genx-chemicals-toxicity-assessment_tech-edited_oct-21-508.pdf

U.S. EPA, 2022a. Drinking Water Health Advisory: Perfluorooctanoic Acid (PFOA) CASRN 335-67-1. https://www.epa.gov/system/files/documents/2022-06/interim-pfoa-2022.pdf

U.S. EPA, 2022b. Drinking Water Health Advisory: Perfluorooctane Sulfonic Acid (PFOS) CASRN 1763-23-1. https://www.epa.gov/system/files/documents/2022-06/interim-pfos-2022.pdf

Abbreviations

ANSES	Agence Nationale de Sécurité Sanitaire de l'Alimentation, de l'Environnement et du Travail (French National Agency for Food, Environmental and Occupational Safety)
ATSDR	Agency for Toxic Substances and Disease Registry (US)
$BMDL_x$	95^{th} Lower confidence interval of the benchmark dose corresponding to X response
BfR	Das Bundesinstitut fur Risikobewertung (German Federal Institute for Risk Assessment)
COT	Committee on Toxicity
DNEL	Derived no-effect level
EFSA	European Food Safety Authority
EPA	Environmental Protection Agency
EU	European Union
FSANZ	Food Standards Australia New Zealand
HBGV	Health-based guidance value
HED	Human equivalent dose
HPFO	Hexafluoropropylene oxide
GenX	Group of per- and polyfluoroalkyl substances
iTV	Chronic indicative toxicity value
LOAEL	Lowest observed adverse effect level
MF	Modifying factor
MRL	Minimal risk level
NOAEL	No-observed adverse effect level
PFAS	Per- and polyfluoroalkyl substances
PFBA	Perfluorobutanoic acid
PFBS	Perfluorobutanesulfonic acid
PFHxA	Perfluorohexanoic acid
PFHxS	Perfluorohexanesulfonic acid
PFOA	Perfluorooctanoic acid
PFOS	Perfluorooctane sulfonate
PFOSA	Perfluorooctanesulfonamide
PFNA	Perfluorononanoic acid

PBPK	Physiological based pharmacokinetic
POD	Point of departure
POD_{HEQ}	Human equivalent point-of-departure
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
RfD	Reference dose
RIVM	Rijksinstituut voor Volksgezondheid en Milieu (National Institute for Public Health and the Environment, Netherlands)
RPF	Relative potency factor
T3	Triiodothyronine
T4	Thyroxine
TDI	Tolerable daily intake
TRV	Chronic toxicity reference value
TWI	Tolerable weekly intake
UF	Uncertainty factor
U.S. EPA	United States Environmental Protection Agency